



2009 REPORT
ON INITIATIVES AND INCENTIVES
IN THE FIELD OF RARE DISEASES
OF THE EUROPEAN UNION COMMITTEE OF
EXPERTS ON RARE DISEASES

Joint Action to Support the Scientific Secretariat of the Rare Diseases Task Force/European Union Committee of Experts on Rare Diseases (N° 2008 22 91)

European Project for Rare Diseases National Plans Development - EUROPLAN (N° 2007 119)



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TABLE OF CONTENTS

INTRODUCTION

1. Introduction	4
2. Methodology and sources	5
3. Report structure	8

SECTION A: EUROPEAN COMMISSION AND OTHER EUROPEAN ACTIVITIES 10

Introduction	11
Aa. EUROPEAN COMMISSION	11
Aa.1 Directorate General Enterprise & Industry & EMA	11
Aa.1.1 Retrospective of DG Enterprise & EMA actions	11
Aa.1.2 Actions and Developments in 2009	15
Aa.2 Directorate General Public Health and Consumers	18
Aa.2.1 Retrospective of DG Public Health actions	18
Aa.2.1.1 Retrospective of Rare Disease Task Force actions	19
Aa.2.1.2 Projects funded by DG Public Health	20
Aa.2.2 Developments in 2009	22
Aa.2a Direct initiatives in 2009	22
Aa.2b Indirect actions in 2009	27
Aa.2.3 Developments foreseen in 2010	27
Aa.3a Direct initiatives	27
Aa.3 Directorate General Research	28
Aa.3.1 Fifth and Sixth Framework Programmes for research, technological development and demonstration activities	28
Aa.3.2 Seventh Framework Programme for research, technological development and demonstration activities	29
Ab. OTHER EUROPEAN ACTIVITIES	29
Ab.1 Other European rare diseases initiatives before 2009	29
Ab.2 Other European rare diseases initiatives and meetings in 2009	30

SECTION B: ACTIVITIES IN EU MEMBER STATES AND OTHER EUROPEAN COUNTRIES 34

B.1 EU Member States	35
B.2 Other European Countries	127

SECTION C: ANNEXES 138

ANNEX 1: Selected bibliography	138
ANNEX 2: List of contributions by country	147
ANNEX 3: List of European research projects	153
ANNEX 4: Sample EUROPLAN questionnaire	160

INTRODUCTION

1. INTRODUCTION

This document was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), formerly the Scientific Secretariat of the European Commission's Rare Diseases Task Force (RDTF), in collaboration with the European Project for Rare Diseases National Plans Development (EUROPLAN) through two contracts within the EU Programme of Community Action in the field of health: a Joint Action to support the Scientific Secretariat of the former-RDTF/EUCERD (N° 2008 22 91), which covers a three year period (starting in January 2009) and the three year European Project for Rare Diseases National Plans Development (EUROPLAN) (N° 2007 119), aimed at promoting the implementation of national plans/strategies for rare diseases.

1.1 THE SCIENTIFIC SECRETARIAT OF THE RARE DISEASE TASK FORCE/EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

One of the principal objectives of the Scientific Secretariat of the former RDTF/EUCERD is to organise the surveillance of initiatives and incentives in the field of rare diseases put into place at member state (MS) and EU levels (WP4).

This work is based on the systematic surveillance of international literature and on a systematic query of key stakeholders in the 27 Member States (MS) of the European Union. These are the members of the RDTF, MS country coordinators of Orphanet, and the 110 members of the Orphanet scientific advisory board. Queries are sent electronically by the RDTF scientific office. The data is published as news in *OrphaNews Europe*, the newsletter of the RDTF, which currently has over 11,700¹ registered readers. It was also planned to analyse this data and to produce yearly reports providing an overview of progress made towards finding a better approach to meeting the needs of the RD patient community, in order to use this information to propose recommendations for future action at the MS and EU levels.

It was planned that these reports would be produced via a three-step approach:

- 1) draft report produced by the scientific secretariat;
- 2) workshop of 20+ experts to discuss the proposed analysis, to suggest improvements and methods of dissemination, and to agree on recommendations;
- 3) dissemination of the revised document to a much wider audience composed of stakeholders to be consulted on a regular basis for the data collection to obtain their comments and criticisms, and consultation of the wider community for a duration of 2 months by putting the report on the RDTF website for public discussion.

It was planned that the yearly reports will be published electronically every year and will be made available on the Directorate General for Public Health and Consumers and RDTF websites.

1.2 THE EUROPEAN PROJECT FOR RARE DISEASES NATIONAL PLANS DEVELOPMENT (EUROPLAN)

The main goal of the EUROPLAN project is to develop recommendations on how to implement a plan/strategy for rare diseases at EU MS level. Focusing on current policies, actions and experiences in each MS in the field of rare diseases, EUROPLAN also aims to share information, models and data on effective strategies to address rare diseases. In order to achieve these goals, EUROPLAN addressed a questionnaire (see model questionnaire in Annex IV) in 2009 to key stakeholders in the field of rare diseases. A one-shot report on the state of play in the field of rare diseases was to be compiled using this data as one of the information tools to be delivered to national health authorities.

¹ Number of registered readers in October 2009.

1.3 COLLABORATION BETWEEN THE TWO PROJECTS

Although the two projects have markedly different objectives, methodologies and information sources, there is considerable overlap in the scope and content of their reports addressed to the description of the current situation. In December 2009 the coordinators of the two projects decided (with the agreement of the Directorate General for Public Health), in view of the synergy between these two reports, to produce *una tantum* a joint report on initiatives and incentives in the field of rare diseases combining the results of the EUROPLAN questionnaires and the data collected by the former RDTF/EUCERD Scientific Secretariat (already presented as a draft at the first workshop of the RDTF working group on Initiatives and Incentives on 9th November 2009) in order to produce a coherent joint document with more robust and consistent information. In order to produce this joint report, the publication of this document was rescheduled.

2. METHODOLOGY AND SOURCES

2.1 INFORMATION COLLECTION AND DATA SOURCES

The main sources of data for this report were 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, in addition to data provided by the EUROPLAN associated and collaborating partners in response to the EUROPLAN questionnaire, past reports published by the European Commission (including past reports of the working groups of the Rare Diseases Task Force) and other specialised reports on topics concerning the field of rare diseases and orphan drugs. The information sources and the collection of data are described in detail here below.

2.1.1 European Commission 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 DG Public Health², DG Research's CORDIS website³ and the pharmaceuticals pages of the DG Enterprise and Industry website⁴ as well as the site of the EMA COMP⁵ (Committee of Orphan Medicinal Products).

2.1.2 OrphaNews Europe

Data from the OrphaNews Europe⁶ newsletter for the period 2007-2009 was reviewed and analysed in order to identify initiatives, incentives and developments in the field of rare diseases. The data chosen for analysis and inclusion in the report is mainly information concerning actions of the Commission in the field of rare diseases, the development of rare disease focused projects funded by the Commission 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 France⁷ (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.

2.1.3 Rare Diseases Task Force Publications

Various reports of the RDTF have been used as sources of data to collect information on the state of affairs at both EU and Member State levels pre-2009, notably the reports of the RDTF WG on Standards of Care (concerning European Centres of Reference) produced between 2005-2008, including the *RDTF Final Report – Overview of Current Centres of Reference on rare diseases in the EU - September 2005*⁸ and the *RDTF Meeting Report: Centres of Reference for Rare Diseases in Europe – State-of-the-art in 2006 and Recommendations of*

² http://ec.europa.eu/health/ph_threats/non_com/rare_diseases_en.htm

³ http://cordis.europa.eu/home_fr.html

⁴ http://ec.europa.eu/enterprise/pharmaceuticals/pharmleg/pharmleg_en.htm

⁵ <http://www.emea.europa.eu/htms/general/contacts/COMP/COMP.html>

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

⁷ <http://www.orpha.net/actor/cgi-bin/OAhome.php>

⁸ <http://www.orpha.net/testor/doc/rdtf/wg/ECRFinalReport.pdf>

the Rare Diseases Task Force – September 2006⁹, as well as the RDTF Final Report – Assessing the European Added-Value of European Reference Networks – March 2008¹⁰.

2.1.4 Minutes of Rare Diseases Task Force Meetings

The minutes of the meetings of the RDTF held in 2009 (30 April, and 23 October respectively) 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 the second Rare Disease Day.

2.1.5 Reports on Orphan Drugs

The information provided for each Member State concerning the state of affairs in the field of Orphan Drugs is taken, when referenced, from 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*¹¹ published in 2006 by DG Enterprise and produced using data collected by the EMA and Orphanet. This information is quoted in the State of Affairs before 2009 section for each country and has been updated when information is available. 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*)¹². 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 drug availability and reimbursement for the Member State sections on France, Germany, Italy, Spain, Sweden, the Netherlands and the United Kingdom.

2.1.6 Eurordis Website and Websites of Patient Organisation Alliances

The site of the European Organisation for Rare Diseases¹³, and the book *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe* (produced using the results of the EurordisCare¹⁴ surveys), were used to provide information on Eurordis activities and projects and to collect data concerning umbrella patient organisations in each of the European Member States and country-level rare disease events. The websites of national patient alliances were also consulted for information. In addition to this the Rare Disease Day 2009 site¹⁵, maintained by Eurordis, also provided information on events at Member State level¹⁶ for the second Rare Disease Day.

2.1.7 Orphanet

Orphanet's data base was exploited to retrieve data on centres of expertise at Member State level. Orphanet also provides links¹⁷ to other web-based information services and help-lines which were used to collect information at country-level.

2.1.8 OrphaNetWork News

OrphaNetWork News is the internal newsletter of Orphanet, which communicates information to partners on Orphanet activities in each partner country. The data for this newsletter is collected through a systematic query of Orphanet Country Coordinators and Information Scientists in order to collect information concerning Orphanet country teams' involvement in rare disease meetings and conferences, as well as participation in Rare Disease Day events and partnerships. This surveillance at national level was exploited to provide information for the events section for each member state.

⁹http://www.orpha.net/testor/doc/RDTF_anna/WG/StandardsofCare/reports/RDTFContributiontoEC06FINALV ERSION.pdf

¹⁰<http://www.orpha.net/actor/EuropaNews/2008/doc/CE.pdf>

¹¹http://ec.europa.eu/health/files/orphanmp/doc/inventory_2006_08_en.pdf

¹²*Politiques relatives aux maladies orphelines et aux médicaments orphelins*
http://www.kce.fgov.be/index_fr.aspx?SGREF=3460&CREF=13646

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

¹⁴http://www.eurordis.org/article.php3?id_article=1960

¹⁵<http://www.rarediseaseday.org/>

¹⁶<http://www.rarediseaseday.org/country/finder>

¹⁷http://www.orpha.net/consor/cgi-bin/Directory_Contact.php?lng=EN

2.1.9 Orphanet Country Coordinators and Stakeholders

Orphanet Country Coordinators and information scientists are in charge of organising data collection in their country, and are also experts in the field of rare diseases, playing important roles in policy making in the field of rare diseases in their country.

Orphanet Country Coordinators and information scientists were contacted once a draft version of the section concerning their country was drawn up using the data collected from the aforementioned sources. They were asked to validate and complete the data collected on the state of affairs before 2009, and concerning the initiatives and incentives in 2009 in their country using the following categories to structure the data they could provide:

- New decisions regarding health care in the field of rare diseases (i.e. national plans);
- New initiatives to support patient organisations;
- New information services on rare diseases and orphan drugs;
- Events, conferences and meetings concerning rare diseases or orphan drugs, including Rare Disease Day 2009;
- New initiatives in the field of education and training;
- New production of best practice guidelines both clinical and for laboratory testing;
- New proposals for funding research into rare diseases and orphan drugs;
- New incentives for the pharmaceutical industry in the field of orphan drugs;
- New initiatives to facilitate access to orphan drugs and reimbursement;
- Any recent negative developments concerning initiatives and incentives for rare diseases and orphan drugs.

Orphanet Country Coordinators were also contacted in order to consult stakeholders in their country on the second draft of the report (February 2010) established using the comments gathered from participants at the RDTF expert workshop on Initiatives and Incentives (09/11/09) and results of the EUROPLAN questionnaire (see below).

2.1.10 RDTF Workshop on Initiatives and Incentives – Paris, 9 November 2009

A workshop was held at the end of 2009 to reunite experts on rare diseases to review the first draft of the RDTF Report on Initiatives and Incentives. Topics discussed included the available sources of information for this document, the completeness of the data and future steps for the validation and publication of the report. The overlap between the EUROPLAN and RDTF projects was highlighted at the meeting and possibilities for collaboration were considered. Comments from this workshop were integrated into the second draft of the report.

2.1.11 EUROPLAN questionnaire to collect information on activities dedicated to rare diseases in EU Countries

The structure of the questionnaire (a sample of this questionnaire is included in Annex IV) follows the structure of the Commission Communication on an action in the field of rare diseases¹⁸, and 19 main questions were formulated in order to collect key data on a number of actions in their country regarding:

- National plans/strategies/measures for rare diseases and related organisation;
- Funding of actions regarding rare diseases;
- Definition, inventorying and provision of information and support of rare diseases;
- Research on rare diseases;
- Rare diseases patient empowerment;
- Programmes to facilitate the provision of medicines to rare disease patients;
- Specialised social services.

The questionnaire was sent to EUROPLAN partners, who include representatives of national health authorities, expert researchers and clinicians, national alliances of rare disease patient organisations from all MS, and to a number of other experts from national health authorities not represented in EUROPLAN. The addressees of the

¹⁸ Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on “Rare Diseases: Europe's challenges” (COM(2008) 679 final)

questionnaire were asked to provide detailed information, especially information from sources in their languages, which is more difficultly accessible. Since the detail of the answers to these questionnaires was varied depending on the information available and the actions specific to the Country, a session of telephone interviews was also carried out to improve the information available, where appropriate. The collection of the information was concluded in October 2009.

Please consult Annexes 1 and 2 for a complete list of sources and contributions

2.2 REPORT PREPARATION, REVISION AND VALIDATION

From this data and documentation, this report was structured to provide a retrospective of actions at EU level and the state of affairs in the field in each EU Member State (i.e. pre-2009), as well as an inventory of initiatives and incentives undertaken in 2009 at EU and MS level. To accommodate the new objective of a joint report on initiatives and incentives in the field of rare diseases between the RDTF and EUROPLAN in early 2010, a new time frame was established and a common methodology was defined. The Scientific Secretariat of the former RDTF was charged with integrating the EUROPLAN data into the draft RDTF report.

After integration of this data, the revised report was circulated amongst stakeholders at national level (via the Orphanet Country Coordinators) for their validation and comments in February 2010. Once these comments were received from stakeholders and direct contact was made with stakeholders to clarify any ambiguities, these modifications were integrated and a final draft was prepared for validation by health authorities in Member States in April 2010.

This document was then validated by the nominated representatives of Member States at the EUCERD, representatives of the European Commission Directorate Generals for Health, Research, and Enterprise and Industry, the EMA and partners of the EUROPLAN project: this validation was carried out in April-May 2010 by the Scientific Secretariat of the former RDTF/EUCERD and EUROPLAN.

The present document was presented to the EUCERD during their first meeting (9-10 December 2010) for approval.

3. REPORT STRUCTURE

The report is structured into two main parts: the first main section concerns initiatives and incentives at EU level, and the second main section concerns Initiatives and Incentives at EU Member State level, with a secondary section concerning four other non-EU European countries where information was available. Annex I is a bibliography outlining the sources used to produce this 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. Annex II is a list of contacts who have contributed to the report, organised by country with mention of validating authority in each country. Annex III is a list of research projects concerning rare diseases funded by the DG Research 5th, 6th and 7th Framework Programmes. Annex IV is a sample of the EUROPLAN questionnaire.

The main section concerning the initiatives and incentives at EU level is split into four sections: the first three sections deal with each European Commission Directorate General having a major influence on rare disease and orphan drug policy in turn: DG Enterprise and Industry (including the work of the EMA), DG Public Health, and DG Research. The last section gives details of other transversal rare disease initiatives in 2009 and meetings held at a European level in 2009, as well as information on .

The sections dealing with the three Directorates General of the European Commission are split into two main sub-sections: firstly, a retrospective of actions pre-2009, and secondly an account of initiatives, incentives and developments in 2009. The section concerning the actions of DG Public Health in 2009 is divided into two separate areas: direct initiatives and indirect initiatives.

The main section concerning the initiatives and incentives in each of the 27 Member States (plus Croatia and Turkey as candidates for EU membership, and Norway and Switzerland as Orphanet country teams were able to provide information on rare disease initiatives and incentives for these countries) is organised in alphabetical order by country. The information on each country is clearly divided into two sections: the first describing the

state of affairs in the field of rare diseases before 2009, and the second outlining the developments made in the field of rare diseases at Member State level so far in 2009 (this includes advances made in the development of national plans and strategies for rare diseases).

The first section describing the state of affairs in each Member State before 2009 covers the following categories in relation to rare diseases¹⁹:

- Definition of a rare disease;
- National plan for rare diseases and related actions;
- Centres of expertise²⁰;
- Registries;
- Neonatal screening policy;
- National alliances of patient organisations and patient representation;
- Sources of information on rare diseases and national help lines;
- National rare disease events²¹;
- Hosted rare disease events²²;
- Research activities and E-Rare partnership;
- Participation in European projects;
- Orphan drug committee and incentive;
- Orphan drug availability;
- Specialised social services.

The second section on initiatives and incentives and developments in 2009 in each Member State covers the topics as outlined above, for which information was provided based on the topics given to Orphanet Country Coordinators (see section 2.1.9 above). This information is organised under the same headings as the section concerning initiatives and incentives in place before 2009 in order to facilitate comparison.

Only topics where information was identified in each country was considered in order to have a fair approach. The categories for which information is provided depends wholly on the information available for 2009 following data collection from the described sources and contact with Orphanet country coordinators and stakeholders. If no detail has been given for a topic, the mention 'no specific activity reported' has been added.

The report is followed by its Annexes as aforementioned and described.

¹⁹ Supplementary information, when spontaneously provided, on best practice guidelines, genetic testing, education and training has been included.

²⁰ Official centre of expertise means officially designated via a (ministerial) procedure.

²¹ As announced in OrphaNews Europe.

²² As announced in OrphaNews Europe.

SECTION A

EUROPEAN COMMISSION AND OTHER EUROPEAN ACTIVITIES

INTRODUCTION²³

Rare diseases, including those of genetic origin, are life-threatening or chronically debilitating diseases which are of such low prevalence (less than 5 people affected per 10'000 people in the European Union, as defined by the European Orphan Drug regulation) that special combined efforts are needed to address them so as to prevent significant morbidity, perinatal or early mortality, or a considerable reduction in an individual's quality of life or socio-economic potential. It is estimated that between 5'000 and 8'000 distinct rare diseases exist today, affecting between 6% and 8% of the population in total thus affecting between 27 and 36 million people in the European Union. Most of the people represented by these statistics suffer from less frequently-occurring diseases affecting one in 100 000 people or less. The definition of a rare disease as having a prevalence of 5 in 10000 first appeared in EU legislation in Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products²⁴. The Community action programme on rare diseases including genetic diseases for the period 1 January 1999 to 31 December 2003 then applied this definition to the field of public health.

European cooperation aims to bring together the scarce resources for rare diseases fragmented across EU Member States. European action aims to help patients and professionals collaborate across Member States so as to share and coordinate expertise and information. This will be achieved through (for example) networks linking centres of expertise in different countries, and by making use of new information and communication technologies ("E-Health"). The European Commission (EC) aims to develop successful existing actions, such as the previous health programme on rare diseases, the Research and Technological Development Framework Programmes, and the specific regulatory framework already in place to provide additional incentives for the development of 'orphan' drugs for these conditions.

Aa. EUROPEAN COMMISSION

The European Commission has a coordinated approach to the field of rare diseases and orphan drugs in the areas of research, public health, regulatory aspects of pharmaceuticals and access to treatment. Three Directorates General of the European Commission are implicated in initiatives and/or incentives at European Union level in the field of rare diseases and orphan drugs: the Directorate General Enterprise and Industry, the Directorate General Health and Consumers, and the Directorate General Research.

A retrospective of the actions of these three Directorates General in the field is provided below, along with a report of initiatives and incentives in the field in 2009.

Aa.1 EUROPEAN COMMISSION DIRECTORATE GENERAL (DG) ENTERPRISE AND INDUSTRY & EMA²⁵

Aa.1.1 Retrospective of DG Enterprise and European Medicines Agency (EMA) actions

The European Commission is responsible for proposing pharmaceutical legislation. The European Parliament and the Council as the Community legislators then adopt and maintain legislation in this field.

²³ http://ec.europa.eu/health/ph_threats/non_com/rare_diseases_en.htm

²⁴ http://ec.europa.eu/health/files/eudralex/vol-1/reg_2000_141/reg_2000_141_en.pdf

²⁵ This section is based on and includes information from <http://www.ema.europa.eu/> and www.emea.europa.eu. Before 2010 the EMA was known as the EMEA.

Aa.1.1.1 Orphan Medicinal Product Regulation²⁶

The orphan medicinal product regulation (Regulation (EC) No 141/2000) was adopted in December 1999 and came into force in the European Union in 2000. Nine years after its implementation, the Committee for Orphan Medicinal Products (COMP²⁷) celebrated its 100th meeting in April 2009.

The Orphan Drug Regulation addresses the need to offer incentives for the development and marketing of drugs to treat, prevent, or diagnose rare conditions; without such incentives, it is unlikely that products would be developed for rare diseases as the cost of developing and marketing products for these disorders would not be recovered by sales. The Regulation delineates the designation criteria, outlines the procedure for designation, and provides for incentives for products receiving an orphan designation. The incentives contained in the legislation aim to assist sponsors receiving orphan drug designations in the development of medicinal products with the ultimate goal of providing medicinal products for rare diseases to patients.

Orphan designation can be based on a number of factors: the prevalence of the condition; the return generated by the product would be insufficient to justify investment; the severity of the condition; and the existence of alternative products. The first two criteria are mutually exclusive, whilst the third and fourth criteria always have to always be addressed. To receive designation, a product must target a life-threatening or chronically debilitating condition that affects no more than five in 10,000 persons (which currently corresponds to about 250,000 persons in the EU). Many rare conditions have a much lower prevalence.

Alternatively to the rarity of the condition, sponsors can also apply if they are able to justify that without incentives the development costs of the product will not be recovered by the return obtained once the product is on the market. Any application for orphan drug designation must also describe all authorised methods of treatment (or diagnosis or prevention) existing for the orphan indication being applied for; in cases where authorised products already exist for the condition, the sponsor is asked to justify what the significant benefit would be for patients who would receive the proposed orphan product. What would be the clinically relevant advantage for patients if the proposed orphan product is marketed, or how would the drug contribute to their care²⁸? Normally this criterion is assessed at a very early stage in the drug development process, therefore at the time of designation the arguments are usually based on assumptions that will have to be confirmed at the time of marketing authorisation, when efficacy and safety data are available.

Aa.1.1.2 EMA Committee for Orphan Medicinal Products (COMP)²⁹

Since 2000, there is a Committee for Orphan Medicinal Products (COMP) at the European Medicines Agency (EMA). The COMP is comprised of health professionals representing each of the Member States, three patient representatives, and three other representatives nominated by the EC after recommendation from the EMA. The Committee meets once a month and it is responsible for reviewing applications from persons or companies seeking 'orphan medicinal product designation' for products they intend to develop for the diagnosis, prevention or treatment of life-threatening or very serious conditions that affect not more than 5 in 10,000 persons in the European Union. The Commission adopts decisions on designation based on an opinion from the COMP. The COMP is also responsible for advising the European Commission on the establishment and development of a policy on orphan medicinal products in the EU, and assists the Commission in drawing up detailed guidelines and liaising internationally on matters relating to orphan medicinal products. The COMP is presently chaired by Professor Kerstin Westermarck (Sweden) and co-chaired by Ms Birthe Byskov Holm (Patient Representative, Denmark). The COMP was a pioneer in including patient representatives as full members and the experience has illustrated the great added-value of this collaboration, which contributes to the quality of the opinions adopted for orphan designation.

The achievements of the committee can be summarised by the 634 positive opinions on orphan designation adopted from the 910 applications submitted for designation up to the COMP's 100th meeting in April 2009³⁰. The success rate for applications is almost 70%. The number of applications that currently receive

²⁶ This section reproduces information from

http://ec.europa.eu/health/rare_diseases/orphan_drugs/strategy/index_en.htm

²⁷ http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000123.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028e32

²⁸ This is the definition of significant benefit, as defined in the implementing regulation (EC) No 847/2000.

²⁹ This section reproduces information from

<http://www.ema.europa.eu/htms/general/contacts/COMP/COMP.html>

³⁰ These figures reflect the achievements after 100 COMP meetings (the 100th meeting took place in April 2009), as reported in OrphaNews Europe <http://www.orpha.net/actor/EuropaNews/2009/090325.html>

orphan designation in 60 days, therefore without needing further clarification, is approximately 70%. With regard to the therapeutic areas attracting most designations, oncology has been the most represented with more than 40% of positive opinions on designation, followed by products for the musculoskeletal and nervous system (12%) and cardiovascular and respiratory systems (11%). Importantly, of the total number of positive opinions adopted, 64% are for conditions with prevalence lower than three in 10,000 persons. The Committee has received many applications for innovative products and has designated, amongst others, fusion proteins, monoclonal antibodies, cell and gene therapy products, and oligonucleotides to be developed for the treatment of rare diseases.

The development of orphan medicinal products is supported by incentives for development and placement on the market as provided for in the Orphan Regulation. Protocol Assistance is provided by the Scientific Advice Working Party in collaboration with the COMP. Protocol assistance offers advice on the development of orphan drugs with regards to regulatory, quality, safety and efficacy issues.

Aa.1.1.3 Regulation of Clinical Trials³¹

Clinical trials are investigations in humans intended to discover or verify the effects of one or more investigational medicinal products ("IMPs").

Requirements for the conduct of clinical trials in the EU are provided for in the "Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use" (known more commonly as the "Clinical Trials Directive"³²). In its Communication of 10 December 2008 to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on "Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector", the Commission announced that an assessment would be made of the application of the Clinical Trials Directive. This assessment would consider, in particular, various options for improving the functioning of the Clinical Trials Directive with a view to making legislative proposals, if appropriate, while taking the global dimension of clinical trials into account.

The Clinical Trials Directive was reinforced by the "Commission Directive 2005/28/EC³³ of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products": this Directive is better known as the "Good Clinical Practice Directive".

Clinical trials submitted in any marketing authorisation application in the EU are required to be conducted in accordance with the Clinical Trials Directive. If the clinical trials are conducted outside the EU, but submitted in an application for marketing authorisation in the EU, they have to follow the principles which are equivalent to the provisions of the Clinical Trials Directive (cf. Annex I, point 8 of the "Directive 2001/83/EC³⁴ of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use", known as the Community Code for medicinal products³⁵).

A European database – EudraCT³⁶ – contains all ongoing or completed interventional clinical trials of medicinal products falling within the scope of Directive 2001/20/EC, i.e. with at least one investigator site in the EU (including the European Economic Area) and commencing after implementation of the Directive 2001/20/EC by the Member States. This database gives the competent authorities of the Member States, EMA and the Commission the necessary information to communicate on clinical trials and to maintain oversight of clinical trials and IMP development. This provides for enhanced protection of clinical trial subjects and patients receiving IMPs.

Paediatric clinical trials that form part of a Paediatric Investigation Plan (PIP)³⁷, but that are conducted in third countries, will also be included in the near future (paediatric clinical trials with sites in the EU/EEA are already available).

³¹ This section reproduces information from http://ec.europa.eu/enterprise/sectors/pharmaceuticals/human-use/clinical-trials/index_en.htm

³² http://www.wctn.org.uk/downloads/EU_Directive/Directive.pdf

³³ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:091:0013:0019:en:PDF>

³⁴ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm#dir200183

³⁵ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol1_en.htm#dir200183

³⁶ <https://eudract.emea.europa.eu/>

³⁷ http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000302.jsp&menu=menus/special_topics/special_topics.jsp&mid=WC0b01ac058002d4ea&jsenabled=true

Aa.1.1.4 Regulation on Advanced Therapies³⁸

Amongst emerging new technologies, therapies and medicines are regenerative medicine, more personalised treatments, as well as the development of nanomedicines. The Commission monitors scientific progress and new technological developments with a view to reviewing the regulatory framework so as to make safe, novel treatments available to patients as early as possible.

Advanced therapy medicinal products are new medical products based on genes (gene therapy), cells (cell therapy) and tissues (tissue engineering). These advanced therapies herald revolutionary treatments of a number of diseases or injuries, such as skin in burn victims, Alzheimer, cancer or muscular dystrophy. They have a huge potential for patients and industry.

The lack of an EU-wide regulatory framework in the past led to divergent national approaches which hindered patients' access to products, hampered the growth of this emerging industry, and ultimately affected the EU competitiveness in a key biotechnology area.

On 13 October 2007, the European Parliament and Council adopted the Regulation on Advanced Therapies (Regulation (EC) 1394/2007³⁹) designed to ensure the free movement of advanced therapy products within Europe, to facilitate access to the EU market and to foster the competitiveness of European companies in the field, while guaranteeing the highest level of health protection for patients.

The main elements of the Regulation are:

- A centralised marketing authorisation procedure, to benefit from the pooling of expertise at European level and direct access to the EU market.
- A new and multidisciplinary expert Committee (Committee for Advanced Therapies), within the European Medicines Agency (EMA), to assess advanced therapy products and follow scientific developments in the field.
- Technical requirements adapted to the particular characteristics of these products.
- Special incentives for small and medium-sized enterprises.

The regulation also marks the recognition that a number of advanced therapy products actually combine biological materials, such as tissues or cells, and chemical structures such as metal implants or polymer scaffolds. These combination products lie at the border of the traditional pharmaceutical area and other fields (e.g. medical devices). They therefore cannot be regulated as 'conventional' drugs and need adapted requirements. In addition, it should be borne in mind that a significant share of economic operators involved in this field are not large pharmaceutical companies, but rather small and medium-sized enterprises or hospitals.

Aa.1.1.5 Regulation on Medicinal Products for Pediatric Use⁴⁰

New legislation governing the development and authorisation of medicines for paediatric use (Regulation (EC) N° 1901/2006)⁴¹ entered into force in the European Union on 26 January 2007. This regulation sets up a system of requirements, rewards and incentives together with horizontal measures to ensure that medicines are researched, developed and authorised to meet the therapeutic needs of children. The key objectives of the Regulation are: to ensure high-quality research into the development of medicines for children; to ensure, over time, that the majority of medicines used by children are specifically authorised for such use; and to ensure the availability of high-quality information about medicines used by children.

The key measures included in the EU Regulation are:

- the establishment of an expert paediatric committee within the EMA⁴²;
- a requirement at the time of marketing authorisation applications for new medicines and line-extensions for existing patent-protected medicines for data on the use of the medicine in children resulting from an agreed paediatric investigation plan;

³⁸ This section reproduces information from <http://ec.europa.eu/enterprise/sectors/pharmaceuticals/human-use/advanced-therapies/>

³⁹ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:324:0121:0137:en:PDF>

⁴⁰ This section reproduces information from http://ec.europa.eu/enterprise/sectors/pharmaceuticals/human-use/paediatric-medicines/index_en.htm and <http://www.ema.europa.eu/htms/general/contacts/PDCO/PDCO.html>

⁴¹ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:378:0001:0019:en:PDF>

⁴² <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:378:0001:0019:en:PDF>

- a system of waivers from the requirement for medicines unlikely to benefit children and a system of deferrals of the timing of the requirement to ensure medicines are tested in children only when it is safe to do so and to prevent the requirements delaying the authorisation of medicines for adults;
- a reward for compliance with the requirement in the form of a six-month extension to the supplementary protection certificate - SPC (in effect, a six-month patent extension on the active moiety);
- for orphan medicines, a reward for compliance with the requirement in the form of an additional two-years of market exclusivity added to the existing ten-years awarded under the EU's Orphan Regulation;
- a new type of marketing authorisation, the PUMA, which allows ten years of data protection for innovation (new studies) on off-patent products;
- measures to increase the robustness of pharmacovigilance and to maximise the impact of existing studies on medicines for children;
- an EU inventory of the therapeutic needs of children to focus the research, development and authorisation of medicines;
- an EU network of investigators and trial centres to conduct the research and development required;
- a system of free scientific advice for the industry, provided by the EMA;
- a public database of paediatric studies;
- a provision on EU funding into research leading to the development and authorisation of off-patent medicines for children.

The main responsibility of the Paediatric Committee (PDCO) at the EMA is to assess the content of paediatric investigation plans and adopt opinions on them in accordance with Regulation (EC) 1901/2006 as amended. This includes the assessment of applications for a full or partial waiver and assessment of applications for deferrals. The PDCO is not responsible for marketing-authorisation applications for medicinal products for paediatric use. This remains fully within the remit of the Committee for Medicinal Products for Human Use (CHMP). However, the CHMP or any other competent authority may request the PDCO to prepare an opinion on the quality, safety and efficacy of a medicinal product for use in the paediatric population if these data have been generated in accordance with an agreed paediatric investigation plan.

Aa.1.2 Actions and Developments in 2009

Aa.1.2.1 EMA 2008 annual report: sustained activity for orphan drugs

The European Medicines Agency Annual Report for 2008 describes the year as one of “consolidation and steady progress” while qualifying the assessment processes for medicines, including orphan medicinal products, as “intensive”. In 2008 the EMA received 119 orphan designation applications, of which 86 positive opinions were issued by the Committee for Orphan Medicine Products (COMP). Of these, oncology products once again were in the majority. In 2008, almost two-thirds of orphan designations concerned products for paediatric populations. In terms of marketing authorisation, there were 13 orphan drug applications amongst the total 103 requests, up slightly from 2007 but down from 2006. Of the 66 new products receiving marketing authorisation in 2008, the EMA report singles out a dozen – half of which are for rare disorders – as being especially noteworthy in terms of public-health interest. The report also documents the ongoing protocol assistance for orphan medicinal product development, continued support for small and medium-sized enterprises (SMEs), and the establishment of the EMA’s sixth scientific committee – the Committee for Advanced Therapies (CAT) – which is expected to be highly relevant to rare disease treatment development. Finally, the report outlines the considerable activities undertaken to strengthen and expand European and international cooperation and to further engage consumers, patients, and health professionals. The actions to improve communication and transparency are also detailed. A full report⁴³ and a summary report⁴⁴ are available.

⁴³ http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2009/12/WC500016589.pdf

⁴⁴ http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2009/12/WC500016564.pdf

Aa.1.2.2 EMA 2009 Work Programme - sustained support and new mechanisms fostering orphan drug development

The European Medicines Agency (EMA) released its Work Programme for 2009⁴⁵ at the end of February 2009. Adopted in late December 2008, the 2009 Work Programme outlines its strategic and budgetary agenda for the year. Section 2.1 is dedicated to Orphan Medicinal Products. Amongst new issues figuring in this year's work programme is the anticipated increase in the volume of applications stemming from three sources: the Paediatric Regulation; the Advanced Therapies Regulation; and the implementation of a common application with the FDA. Another issue revolves around the "growing complexity of review of designation criteria prior to marketing authorisation" featuring an increasing number of challenges to orphan market exclusivity by companies offering competitor products. The Work Programme estimates some 130 products will receive designation this year, revealing a sustained, slightly increasing volume (119 were designated in 2008). Amongst the objectives and initiatives for the year are the maintenance of core activities; a review of the EMA/FDA common application; the initiation of EMA/FDA annual reporting activities for orphan products; further development of contacts with non-EU regulatory agencies regarding international collaboration; and the implementation of EC guideline on Article 8(2) of Regulation (EC) No 141/2000 concerning the orphan product market exclusivity period. A pilot project planned for 2009 will "assess the evidence base for orphan drugs" in collaboration with the Belgian Healthcare Knowledge Centre. In terms of Scientific Advice and Protocol Assistance, the EMA anticipates growth in the number of applications, "with a steady progression of questions on alternative clinical-trial designs; comparability; biomarkers; advanced therapies; and conditional marketing authorisation. There will be an increased number of scientific-advice requests in combined areas in both adult and paediatric development". The volume of applications from SMEs is also expected to increase.

Aa.1.2.3 Public consultation of orphan designation document

The COMP drafted a document for public consultation at the beginning of 2009, entitled Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation (EMEA/COMP/15893/2009)⁴⁶. This document has been drafted with view of a possible revision of the 'Guideline on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation' (EMEA/COMP/66972/2004), released in September 2004.

Aa.1.2.4 Reduced fees for orphan drug applications

Designated orphan medicinal products are now eligible for reductions for all fees payable under Community rules pursuant to amended Regulation (EEC) 2309/93. Covered in the reductions, applicable to orphan products designated in accordance with Regulation (EC) 141/2000, are the fees for pre-authorisation activities (protocol assistance such as scientific advice), as well as for products using the centralised procedure: the application for marketing authorisation, inspections, and post-authorisation activities. Taking effect on 1 February 2009, the fee revisions reflect a policy of enhanced support for micro- small- and medium-sized enterprises (SMEs). An EMA press release states: *"In the revised policy for 2009, the fee reduction for new applications for marketing authorisation to SMEs is increased to 100%. The fee reduction for post authorisation activities including annual fees to SMEs in the first year after granting a marketing authorisation is also increased to 100%. The 100% fee reduction for protocol assistance and 100% fee reduction for pre-authorisation inspections are maintained for all applicants. The 50% fee reduction for new applications for marketing authorisation submitted by applicants that are not SMEs is also maintained"*⁴⁷.

Aa.1.2.5 EMA - FDA joint effort to promote good clinical practices

As part of the ongoing confidentiality agreement between the European Commission, the European Medicines Agency, and the US Food and Drug Administration, a new initiative was launched for an 18 month pilot phase on 1 September 2009. The Good Clinical Practice Initiative - a reflection of both the increasing globalisation of clinical studies and limited inspection resources - defines its objectives as *"the sharing of information on inspection planning, policy and outcomes and the conduct of collaborative inspections"*. The small patient populations typically available for rare disease medicinal product trials dispose such trials to international participation. By harmonising inspection procedures, the new initiative is expected to play a key role in

⁴⁵ http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2010/01/WC500046686.pdf

⁴⁶ <http://www.emea.europa.eu/pdfs/human/comp/1589309en.pdf>

<http://www.orphandrugexperts.com/downloads/COMP%20paper%20on%20medical%20plausability.pdf>

⁴⁷ http://www.ema.europa.eu/docs/en_GB/document_library/Public_statement/2009/09/WC500003876.pdf

ensuring that trials are conducted under safe, ethical, and uniform conditions. One of the principle objectives for the pilot phase of the initiative includes the exchange of Good Clinical Practice-related information “contained in applications for scientific advice, orphan medicines designation, paediatric investigational plans, marketing authorization or post-authorization activities of significant public health interest”. In a press release, the FDA and EMA announced that they “are looking to partner with applicants/sponsors who are willing to volunteer during the pilot phase of the initiative to engage in dialogue and planning of joint inspections involving applications that are anticipated to be submitted fairly simultaneously to both regulatory agencies within the next 12 months”.

Aa.1.2.6 New EMA scientific committee for advanced therapy products

The EMA announced at the start of 2009 the formation of the Committee for Advanced Therapies (CAT)⁴⁸ – the EMA’s sixth scientific committee. Created following new European Union legislation concerning the regulation of advanced-therapy medicinal products, the CAT met for the first time on 15 January 2009. Three types of advanced therapy products defined in the EU legislation: gene therapy products, somatic cell therapy products and tissue engineered products. The CAT will “prepare a draft opinion on each advanced-therapy medicinal product submitted to the EMA for evaluation as part of a marketing-authorisation application, prior to the adoption of a final opinion by the Committee for Medicinal Products for Human Use (CHMP)” which will be submitted to the European Commission for decision.

Aa.1.2.7 Assessment of the EC Clinical Trials Directive

The Clinical Trials Directive, implemented in 2004, was developed in order to harmonise European regulatory systems pertaining to the clinical research environment, improve the protection of study participants, optimise safety information, and ensure quality and data credibility across Europe. However, the directive came under fire from some scientists who accused the measure of hindering academic research, resulting in fewer new trials initiated with fewer patients enrolled. An increased workload for ethics committees was cited amongst the causes for slowing trial initiation⁴⁹.

A one-year project financed by the Seventh Framework Programme to measure and analyse the impact of the directive on clinical research in respect to different stakeholders, the Impact on Clinical Research of European Legislation (ICREL) project involved a longitudinal, retrospective, observational and comparative survey conducted with different stakeholders from each European country – competent authorities, ethics committees, and sponsors (public and private) - in order to assess how the Clinical Trials Directive has impacted the number, size, nature, costs, resources, workload and performance relating to clinical trials. The results of this project have been compiled into a report that was published online in mid-June 2009. The ICREL data suggests that large pharmaceutical companies seem less affected by the new legislation than small- and medium-sized enterprises (SME) and non-commercial sponsors. An increase in workload was identified amongst all the stakeholders. There was also an increase in fees to competent authorities and to ethics committees. The cost of insurance dramatically increased for commercial sponsors, though not for non-commercial sponsors. Furthermore, an increase in clinical trial costs as a result of the Clinical Trials Directive was of particular concern to SMEs, non-commercial sponsors and the sponsors of orphan drug trials. The survey detected a significant increase from 2003 to 2007 in the number of biotechnology product and orphan drug trials, considered to reflect more the new orphan drug regulation as well as scientific and technological progress rather than the implementation of the Clinical Trials Directive. The report⁵⁰ concludes with a discussion of the findings and a series of conclusions and recommendations.

Aa.1.2.8 Advances in the process of increasing transparency in clinical trials for children

New measures were moved forward in February 2009 to expand the transparency of information on clinical trials for medicinal products involving paediatric populations. The *Guidance on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency (EMA), in accordance with Article 41 of Regulation (EC) No 1901/2006*⁵¹, published in the 4 February 2009 *Official Journal of the European Union*, is designed to “increase the availability of information on the use of medicinal products in the paediatric population and to

⁴⁸ http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000126.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac05800292a5

⁴⁹ <http://www.orpha.net/actor/EuropaNews/2006/060409.html#EUPol>

⁵⁰ http://www.efgcp.be/downloads/icrel_docs/Final_report_ICREL.pdf

⁵¹ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:378:0001:0019:en:PDF>

avoid unnecessary repetition of studies". The guidance delineates the information to be registered with EudraCT⁵², the clinical trials database of the European Union and concerns both trial protocol and trial results. The data to be furnished are destined for both the general public and for professionals in the fields of medicine, research, and the pharmaceutical industry. The guidelines also set out the timeframe for providing information and the means through which information is to be made available. The European Medicines Agency has the task of revising EudraCT to render the specified information public. A draft of the guidance underwent a period of public consultation in 2008. With an estimated 80% of all rare disorders affecting children, this measure to increase transparency is expected to augment the safety and efficacy of treatment development for this population.

Aa.1.2.9 Increase in the number of applications for orphan designations in 2009

The COMP at the EMA announced at the end of year that 150 applications for orphan medicinal product designation had been received in 2009, a 25% increase on 2008.

Aa.1.2.10 Reconfiguration of European Commission portfolios

It was announced at the end of 2009 that the portfolio of the DG for Public Health and Consumers will be expanded to take responsibility for pharmaceuticals, including the EMA. This change is in line with the political organisation of Member States, where policy for medicinal products is generally the responsibility of the country's health department.

Aa.2 EUROPEAN COMMISSION DIRECTORATE GENERAL (DG) PUBLIC HEALTH AND CONSUMERS

Aa.2.1 Retrospective of DG Public Health actions in the field of rare diseases

The Community action programme on rare diseases, including genetic diseases, was adopted by the European Commission for the period 1 January 1999 to 31 December 2007. The aim of the programme was to contribute, in co-ordination with other Community measures, to ensuring a high level of health protection in relation to rare diseases. As a first EU effort in this area, specific attention was given to improving knowledge and facilitating access to information about these diseases.

Rare diseases are now one of the priorities in the second programme of Community action in the field of health (2008-13)⁵³. According to the DG Public Health Work Plans for the implementation of the Public Health Programme, the two main lines of action are the exchange of information via existing European information networks on rare diseases, and the development of strategies and mechanisms for information exchange and co-ordination at EU level to encourage continuity of work and trans-national co-operation.

Furthermore, regarding rare diseases projects, DG Public Health prioritises networks, which centralise information on as many rare diseases as possible - not just a specific group or a single disease - to improve information, monitoring and surveillance.

On 11 November 2008, the European Commission adopted the Communication on Rare Diseases: Europe's challenge⁵⁴ setting out an overall Community strategy to support Member States in diagnosing, treating and caring for the 36 million EU citizens with rare diseases. The Communication on European Action in the Field of Rare Diseases, entitled Rare Diseases: Europe's Challenges, was drafted by the European Commission in close collaboration with the Rare Diseases Task Force between June and October 2007. This Communication focuses on three main areas: 1) improving recognition and visibility of rare diseases, 2) supporting policies on rare diseases in MS for a coherent overall strategy, and 3) developing cooperation,

⁵² http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/2009_02_04_guideline.pdf
http://ec.europa.eu/health/files/clinicaltrials/technical_guidance_en.pdf

⁵³ http://ec.europa.eu/health/ph_programme/pgm2008_2013_en.htm

⁵⁴ http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf

coordination and regulation for rare diseases at EU level. The document opened for public consultation⁵⁵ in mid-November 2007: interested parties were invited to comment on and respond to 14 key questions about rare diseases and explore relevant issues. Almost 600 contributions were received from 15 MS during the three-month consultation period, outdistancing the previous contender for most responses by over 400 comments. (The average number of responses to a consultation is 60). This reaction was taken as a sign of proof of the pertinence of the Communication on Rare Diseases and the desire across Europe to see its provisions implemented in the near future. The comments received were consulted and the document was adapted accordingly. Following this, the Communication was subject to an impact assessment that studied the political and financial consequences, amongst other considerations, between March and June 2008. It then went for an inter-service consultation from July 2008 through October 2008 involving DG Enterprise, DG Research, DG Information and Society, DG Budget, DG Employment, DG Relex, DG Market and the legal service of the European Commission. Finally, on 11 November 2008, the Communication on rare diseases was adopted via oral procedure, by the college of Commissioners, along with a proposal for a European Council Recommendation on a European action in the field of rare diseases.

The Council adopted on 8 June 2009 the proposal for a Council Recommendation on an action in the field of rare diseases. The Recommendation engages the responsibility of Member States and concentrates on supporting and strengthening the adoption before the end of 2013 of national plans and strategies for responding to rare diseases, on improving recognition and visibility of rare diseases, on encouraging more research into rare diseases and forging links between centres of expertise and professionals in different countries through the creation of European reference networks in order to share knowledge and expertise and, where necessary, to identify where patients should go when such expertise cannot be made available to them. The role of patients' organisations is also highlighted as particularly important.

Aa.2.1.1 EC Rare Diseases Task Force (RDTF) - Retrospective of actions

In January 2004, the European Commission Public Health Directorate created the Task Force on Rare Diseases (RDTF), established via Commission Decision 2004/192/EC of 25 February 2004 on the programme of Community action in the field of public health (2003 to 2008). The RDTF was charged with:

- advising and assisting the European Commission Public Health Directorate in promoting the optimal prevention, diagnosis and treatment of rare diseases in Europe, in recognition of the unique added value to be gained for rare diseases through European co-ordination;
- providing a forum for discussion and exchange of views and experience on all issues related to rare diseases.

Its members included current and former project leaders of European research projects related to rare diseases, member state experts and representatives from relevant international organisations (EMA, WHO, OECD).

In the first 4 years of its mandate, the RDTF created three working groups reflecting topics it considered to be priorities in the field of rare diseases.⁵⁶

The WG on Standards of Care created in June 2005 worked on the concept of Centres of Expertise (CE) and European Reference Networks (ERN) in the field of Rare Diseases. Its work feeds into a more general reflection on CE and ERN undertaken by the EC's High Level Group on Health Services and Medical Care. The group also considered discussions on genetic testing, genetic screening, and orphan drugs: reports were produced on European Centres of Reference (2005, 2006), Assessing treatable rare diseases and the proportion of patients eligible for treatment (2007), Assessing the European Added-Value of ERN (2008).

The WG on Coding and Classification, in collaboration with the WHO on the ICD (International Classification of Diseases), contributed to the revision of the existing ICD-10 in view of the adoption in 2015 of the new ICD-11 considering all other existing methods of classification to ensure transparency, with meetings held in 2006, 2007 and 2008.

The WG on Public Health Indicators (PHI) considered a selection of rare diseases with high priority for epidemiological surveillance. The WG determined the definition of rare diseases which can be identified in mortality certificates and will work on a feasibility study for using mortality data as public health indicators. The

⁵⁵ http://ec.europa.eu/health/ph_threats/non_com/docs/raredis_comm_draft.pdf

⁵⁶ <http://www.orpha.net/testor/cgi-bin/OTmain.php?PHPSESSID=43c50b5eec72a9b89f68faad7a33b30d&UserCell=workingGroup>

first meeting was in January 2006 with a report on the subject in March 2008. A report was also produced following a 2008 workshop on Patient Registries and Databases.

OrphaNews Europe is the bi-monthly electronic newsletter of the Rare Diseases Task Force. Every two weeks it publishes news and comments of interest to the rare diseases community: patients, healthcare professionals, researchers, industry professionals and health policy makers.

Aa.2.1.2 Projects funded by DG Public Health

Aa.2.1.2.1 EU projects creating networks of action in the field of rare diseases

Various projects were supported in the framework of the Programme for Community Action on Rare Diseases⁵⁷ for 1 January 1999 to 31 December 2003 and the EU Public Health Programme 2003-2008⁵⁸ in order to improve the exchange of information via existing European information networks on rare diseases, to promote better classification, to develop strategies and mechanisms for exchanging information between people affected by a rare disease, volunteers and professionals, to define relevant health indicators and develop comparable epidemiological data at EU level, and to support an exchange of best practise and develop measures for patient groups and also aid the development of European Reference Networks of Centres of Expertise and the identification of rare diseases.

Amongst the projects currently selected for funding by DG Public Health are⁵⁹: EU Eurocat project, the EU ENERCA project, the EU SCN project, the EU Rare Forms of Dementia project, the EU MUSCLENET project, the EU CAUSE project, the European Information Network on Paediatric Rheumatic Diseases project, the EU EDDNAL project, The EU project Establishing European Neurofibromatosis Lay Group Network, EU Information Network for Immunodeficiencies Project, EU TEAM project - Transfer of expertise on rare metabolic diseases in adults, European Myasthenia Gravis Network, European Autism Information System, Orphanet, Surveillance of rare cancers in Europe (RARECARE), European Register on Cushing's Syndrome (ERCUSYN), European Haemophilia Safety Surveillance System, European Project for Rare Diseases National Plans Development (EUROPLAN), PRES Network for Autoinflammatory Diseases in childhood (EuroFever), and European network for central hypoventilation syndromes: Optimising health care to patients (EU-CHS).

Aa.2.1.2.2 Orphanet

Orphanet⁶⁰ is the reference portal for information on rare diseases and orphan drugs in Europe. Orphanet was established in 1997 by the French Ministry of Health (*Direction Générale de la Santé*) and the INSERM (*Institut National de la Santé et de la Recherche Médicale*). Both agencies are still funding the core project. The European Commission funds the encyclopaedia and the collection of data in European countries (since 2000 with DG Public Health grants and since 2004 with DG Research funding). Orphanet is accessed by 20,000 users each day from over 200 countries. Orphanet provides direct online access to all stakeholders to: an inventory of rare diseases and an encyclopaedia in 6 languages; a search by sign and symptom function to facilitate diagnosis; expert clinics in Europe including reference centres and European networks; medical laboratories and available tests; patient organisations; ongoing research including clinical trials and registries; an inventory of orphan drugs; OrphaNews France and Europe (newsletters about scientific and political progress in the field of rare diseases); and the thematic studies and reports offered by the *Orphanet Report Series*. Orphanet data is collected in each European Member State and is expert validated.

Aa.2.1.2.3 European Reference Networks for Rare Diseases (ERN)

DG Public Health established the High Level Group on Health Services and Medical Care⁶¹ as a means of taking forward the recommendations made in the reflection process on patient mobility. One of the working groups of this High Level Group is focusing on reference networks (centres of reference) for rare diseases.

Some principles have been developed regarding European Reference Networks (ERNs) for rare diseases, including their role in tackling rare diseases and other conditions requiring specialised care, patient volumes and some criteria that such centres should fulfil. ERNs should also serve as research and knowledge

⁵⁷ http://eur-lex.europa.eu/pri/en/oj/dat/1999/l_155/l_15519990622en00010005.pdf

⁵⁸ <http://www.orpha.net/testor/cgi-bin/OTmain.php?PHPSESSID=43c50b5eec72a9b89f68faad7a33b30d&UserCell=workingGroup>

⁵⁹ http://ec.europa.eu/health/rare_diseases/projects/index_en.htm

⁶⁰ www.orpha.net

⁶¹ http://ec.europa.eu/health/ph_overview/co_operation/mobility/high_level_hsmc_en.htm

centres, updating and contributing to the latest scientific findings, treating patients from other Member States and ensuring the availability of subsequent treatment facilities where necessary. The definition of European reference networks should also reflect the need for services and expertise to be appropriately distributed across the enlarged European Union.

The suggested conditions for designation as a European reference centre are:

- sufficient activity and capacity to provide relevant services at a sustained level of quality
- capacity to provide expert advice, diagnosis or confirmation of diagnosis, to produce and adhere to good practice guidelines and to implement outcome measures and quality control
- multi-disciplinary approach;
- high level of expertise and experience, as documented through publications, grants or honorific positions, teaching and training activities, etc.
- strong contribution to research
- involvement in epidemiological surveillance, such as registries
- close links and collaboration with other expert national and international centres, and capacity to network
- close links and collaboration with patient associations, where they exist
- appropriate arrangements for patient referrals from other EU countries
- appropriate capacities for diagnosing, following-up and managing patients, with evidence of good outcomes, where applicable

Current EU-funded networks of reference for rare diseases are: Dyscerne (European network of centres of expertise for dysmorphology), ECORN-CF (European centres of reference network for cystic fibrosis), Paediatric Hodgkin Lymphoma Network (Europe-wide organisation of quality controlled treatment), NEUROPED (European network of reference for rare paediatric neurological diseases), EUROHISTIONET (study group on histiocytosis), TAG (Together Against Genodermatoses – improving healthcare and social support for patients and families affected by severe genodermatoses), PAAIR (Patients' Association and Alpha-1 International Registry Network), EPNET (European network of centres of reference for porphyria)/EPI (European Porphyria Initiative), RBDD (Rare Bleeding Disorders Database network) and ENERCA (European network for rare and congenital anaemia). A list of participating countries is in Annex 3 of this document.

Aa.2.1.2.4 EU Projects supporting cooperation between rare diseases organisations

Projects were supported in the framework of the Programme of Community Action on Rare Diseases⁶³ for 1 January 1999 to 31 December 2003 and the EU Public Health Programme 2003-2008⁶⁴ in order to strengthen collaboration at European level among patient organisations, develop partnerships among all alliances and develop European recommendations and national action plans⁶⁵.

Another significant priority EU action is to increase the visibility and operational capacity of organisations and networks active in the field of rare diseases. In this context, the EU has supported several projects managed by Eurordis, the European Organisation for Rare Diseases. Eurordis is a patient-driven alliance of patient organisations and individuals active in the field of rare diseases⁶⁶.

The Rare Disease Patient Solidarity project (RAPSODY⁶⁷) ran from 2006 to 2008 and was aimed at improving access to, and quality of, fundamental services for patients, families and patient organisations, as well as health professionals. The project included the creation of the Network of Rare Disease Help Lines, with the aim to increase the service provided by help lines by creating a common approach and sharing expertise, to provide support and training to these help lines, to improve the visibility of these services at national and European levels, to increase funding opportunities for the individual help lines and the network, and to ensure that the membership policy promotes excellence. Other aims of the project were to promote networks of respite care centre and therapeutic recreation programmes.

⁶³ http://eur-lex.europa.eu/pri/en/oj/dat/1999/l_155/l_15519990622en00010005.pdf

⁶⁴ http://eur-lex.europa.eu/pri/en/oj/dat/2002/l_271/l_27120021009en00010011.pdf

⁶⁵ Projects financed to support this action include RAPSODY, PARACELUS, EU PARD, POLKA and OPERA.

⁶⁶ <http://www.eurordis.org/>

⁶⁷ www.rapsodyonline.eu

The POLKA⁶⁸ project was launched in September 2008 and aims to develop strategies and mechanisms for exchange of information amongst people affected by rare diseases as well as organise support for European Networks of Reference for rare diseases in an effort to establish guidelines for best practice on treatment, and to share knowledge on rare diseases, together with evaluation of performance. The POLKA project also supports the organisation of the 2010 European Conference on Rare Diseases to be held in Krakow, Poland (13-15 May 2010).

Aa.2.2 Developments in 2009

Aa.2.2a Direct initiatives in 2009

Aa.2.2a.1 European Commission health work plan for 2009 continues supporting rare disease projects and networks

The European Commission on 23 February adopted a Work Plan for 2009 implementing the second programme of Community action in the field of health (2008-2013). Amongst the rare disease initiatives earmarked for funding are two calls for tenders that contribute to the implementation of the Commission Communication on Rare Diseases: Europe's challenges: 1) evaluation of population newborn screening practices in Member States; and 2) repertorying rare disease information, diagnosis and treatment using existing European initiatives (in particular Orphanet). To support rare disease pilot reference networks and networks of information, there is a call for proposals for new projects as well as a call for operating grants that enable existing networks to continue.

Aa.2.2a.2 Council Recommendation on rare diseases

On 8 June 2009, the Council approved a Council Recommendation on an action in the field of rare diseases⁷⁰. In early 2009, the European Parliament and the European Social and Economic Committee issued opinions on the Proposal for a Council Recommendation, overwhelmingly supporting the contents of the crucial document. The amendments issued during this process were incorporated into the final text adopted on 8 June 2009 by the European Council of Ministers - a body that serves to define the general political guidelines of the European Union and is the main decision-making agent. Every Council meeting is attended by one minister from each EU country. For the meeting on the rare disease Recommendation, it was typically the ministers of health who attended.

Some countries already have national rare disease plans in place. France was the first country to implement a national plan specifically for rare diseases; Bulgaria, Portugal, Greece and Spain have since followed suit. Other MS are in the midst of defining strategies for rare disease research, diagnostics, treatments, and care. And still other countries are gathering momentum and expertise to launch the process.

The seven key themes of the Council recommendations are:

- *I. Plans and strategies in the field of rare diseases* – calls on the MS to elaborate and adopt a plan or strategy by the end of 2013.
- *II. Adequate definition, codification and inventorying of rare diseases* – evokes the common definition of a rare disease as a condition affecting no more than 5 per 10 000 persons; aims to ensure that rare diseases are adequately coded and traceable in all health information systems based on the ICD and in respect of national procedures; and encourages MS to contribute actively to the inventory of rare diseases based on the Orphanet network.
- *III. Research on rare diseases* – calls for the identification and fostering of rare disease research at all levels.

⁶⁸ http://img.rarediseaseday.org/polka/polka_brochure_final.pdf

⁷⁰ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF>

- *IV. Centres of expertise and European reference networks for rare diseases* – asks the MS to identify and facilitate networks of expertise based on a multidisciplinary approach to care, and foster the diffusion and mobility of expertise and knowledge.
- *V. Gathering the expertise on rare diseases at European level* - MS should share best practices, develop medical training relevant to the diagnosis and management of rare diseases, coordinate European guidelines, and, to minimise the delay in access to orphan drugs, MS should share clinical/therapeutic added-value assessment reports at the Community level.
- *VI. Empowerment of patient organisations* - the MS should consult patient representatives on policy development; facilitate patient access to updated information on rare diseases; promote patient organisation activities.
- *VII. Sustainability* – long-term sustainability in the field of information, research and healthcare of infrastructures must be ensured.

Aa.2.2a.3 Commission Decision C(2009)9181 establishing a European Union Committee of Experts on Rare Diseases

The European Commission decision of 30 November 2009, published in the *Official Journal of the European Union*, formally established a European Union Committee of Experts on Rare Diseases. This new structure, evoked in Point 7 of the Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe's Challenges, adopted on 11 November 2008, recommends that the European Commission be assisted by a European Union Advisory Committee on Rare Diseases: *"The preparation and implementation of Community activities in the field of rare diseases require close cooperation with the specialised bodies in Member States and with the interested parties. Therefore, a framework is required for the purpose of regular consultations with those bodies, with the managers of projects supported by the European Commission in the fields of research and public health action and with other relevant stakeholders acting in the field."*

Thus, *"the Committee acting in the public interest shall assist the Commission in formulating and implementing the Community's activities in the field of rare diseases, and shall foster exchanges of relevant experience, policies and practices between the Member States and the various parties involved"*.

Specifically, the European Union Committee of Experts on Rare Diseases is charged with the following responsibilities:

- assisting the Commission in the monitoring, evaluating and disseminating the results of measures taken at Community and national level in the field of rare diseases;
- contributing to the implementation of Community actions in the field, in particular by analysing the results and suggesting improvements to the measures taken;
- contributing to the preparation of Commission reports on the implementation of the Commission Communication and the Council Recommendation;
- deliver opinions, recommendations or submit reports to the Commission either at the latter's request or on its own initiative;
- assisting the Commission in international cooperation on matters relating to rare diseases;
- assisting the Commission in drawing up guidelines, recommendations and any other action defined in the Commission Communication and in the Council Recommendation;
- providing an annual report of its activities to the Commission.

The new Committee will consist of 51 members, including one representative from the ministries or government agencies responsible for rare diseases to be designated by the government of each Member State; four patient organisation representatives; four pharmaceutical industry representatives; nine representatives of ongoing and/or past Community projects in the field of rare diseases financed by the programmes of Community action in the field of health, including three members of the pilot European Reference Networks on rare diseases; six representatives of ongoing and/or past rare diseases projects financed by the Community Framework Programmes for Research and Technological Development; and one representative of the European Centre for Disease Prevention and Control. The Committee will elect a chairperson and three vice-chairpersons, with a one-year term of office, from different categories of members of the Committee. The new Committee may establish temporary Working Groups consisting of external experts for specific missions.

A call for expressions of interest was published for the patient organisation, industry, rare diseases research projects under Framework Programmes for Research and Technological Development, and rare

diseases projects under Health Programmes representatives of the new Committee. The deadline for submitting an expression of interest for any of these representative roles was 21 December 2009.

The European Union Committee of Experts on Rare Diseases replaces the European Commission's Rare Diseases Task Force (RDTF) established via Commission Decision 2004/192/EC of 25 February 2004 on the programme of Community action in the field of public health (2003 to 2008).

Aa.2.2a.4 EC Rare Diseases Task Force: Developments in 2009

Aa.2.2a.4.1 Joint Action to support the Rare Diseases Task Force's Scientific Secretariat

A Joint Action to support the RDTF's Scientific Secretariat started in January 2009 for a three year period, to help promote action on the prevention of rare diseases and to provide analysis and technical assistance in support of the development or implementation of a policy in the area of rare diseases and orphan drugs (OD). This joint action also aims to contribute to the revision of the International Classification of Diseases in the field of Rare Diseases.

The aims of the project include:

- the provision of scientific support for the activities of the RDTF by identifying existing documentable indicators that are relevant to rare diseases and collecting data on a yearly basis;
- the dissemination political and scientific information to all stakeholders through ad-hoc reports and an electronic newsletter (OrphaNews Europe), including information on national and EU incentives;
- liaising between EU agencies and services and major stakeholders to enhance collaboration and maximise input and outcomes;
- the provision assistance to the RDTF on other scientific issues that may be identified in the course of the project.

The traceability of rare diseases in health information systems will also be improved thanks to this project by:

- assigning International Classification of Diseases codes (ICD10) to all rare diseases;
- proposing changes to improve the classification in view to the future adoption of the ICD11; using the technical platform developed by the WHO and with the assistance of an international expert group that will be established;
- cross-referencing with other classification systems such as MedDRA and SNOMED-CT.

The information produced as a result of this joint action is to be posted on the Orphanet website, in a format adapted to the needs of the information system community to maximise its use.

Annual workshops are organised within the scope of the project around three working groups: indicators for rare diseases (10 November 2009), initiatives and incentives for rare diseases (9 November 2009) and the coding and classification of rare diseases (27 January 2010). The previous RDTF working groups have been discontinued.

Aa.2.2a.4.2 Rare Diseases Task Force Meetings

Two meetings of the EC Rare Diseases Task Force took place, in April and October 2009 respectively. Amongst the topics discussed at the 30 April 2009 meeting were the Council Recommendation, the possible roadmap for implementing the Council Recommendation and Communication, the Commission Decision to set up a European Union Committee of Experts on Rare Diseases, the outcomes of the second Rare Disease Day, and a review of the progress made by the EUROPLAN project and the projects of the Joint Action on the support of the RDTF's Scientific Secretariat.

Amongst the topics discussed at the 23 October 2009 meeting were the state of play of the Commission Decision setting up a EU Committee of Experts on Rare Diseases to replace the RDTF; the implementation of the Second Health Programme and the Work Plan 2010; the situation of ERN on rare diseases including a decision to analyse the scope of the existing ERN pilot projects; the classification and coding of rare diseases including the revision of the WHO International Classification of Rare Diseases; the state of play of the EUROPLAN project; and the preparation of the European Conference on Rare Diseases in Krakow, May 2010.

Aa.2.2a.5 National Strategies and Plans for Rare Diseases in Europe – Recent Developments

The Council Recommendation on an action in the field of rare diseases⁷¹ concentrates on supporting and strengthening the adoption before the end of 2013 of national plans and strategies aimed at addressing rare diseases. The Council recommends that Member States should establish and implement plans or strategies for rare diseases at the appropriate level or explore appropriate measures for rare diseases in other public health strategies, in order to aim to ensure that patients with rare diseases have access to high quality care, including diagnostics, treatments, habilitation for those living with the disease and, if possible, effective orphan drugs, and in particular:

- elaborate and adopt a plan or strategy as soon as possible, preferably by the end of 2013 at the latest, aimed at guiding and structuring relevant actions in the field of rare diseases within the framework of their health and social systems;
- take action to integrate current and future initiatives at local, regional and national levels into their plans or strategies for a comprehensive approach;
- define a limited number of priority actions within their plans or strategies, with objectives and follow-up mechanisms;
- take note of the development of guidelines and recommendations for the elaboration of national action for rare diseases by relevant authorities at national level in the framework of the ongoing European Project for Rare Diseases National Plans Development (EUROPLAN) selected for funding over the period 2008-2011 in the first programme of Community action in the field of public health.

EUROPLAN involves at present representatives of the national health authorities of 21 EU MS, with the aim of promoting health care planning for rare diseases at national level. The Council Recommendation defines the goal of the project as the *“development of guidelines and recommendations for the elaboration of national action for rare diseases by relevant authorities at national level”*.

The recommendations will provide information on the different steps to develop a strategic plan and, more importantly, it will highlight priority areas and actions of intervention in the field of rare diseases.

The project aims to collect and disseminate information on EU MS national initiatives on rare diseases, on expectations on national plans for rare diseases and on best practices contributing to share experiences, data and effective strategies to address rare diseases

The National Centre for Rare Diseases (Istituto Superiore di Sanità, Italy) is the leading organisation; 30 countries and Eurordis (the European Organisation for Rare Diseases) participate in the project. This ensures a broad representation of different EU MS contexts and experiences and patients' points of view. In addition, the project ensures an inclusive and wide engagement of stakeholders: ministries, regional and local authorities, health care planners, programme managers, health care professionals, researchers and patients.

The expected outputs of EUROPLAN are:

- To stimulate a discussion and reach a consensus on the importance of national plans for structuring all relevant actions in the field of rare diseases;
- To list priority areas and actions of intervention to address rare diseases;
- To promote the development of national plans for rare diseases within EU MS and provide an instrument to support countries in designing national plans for rare diseases according to the EU Communication on Rare Diseases⁷².

The elaboration of a “Council Recommendation on a European action in the field of rare diseases” will ensure that common policy guidelines are shared everywhere in Europe. The recommendations developed by EUROPLAN promoting national plans and best practices for rare diseases within EU MS will link national efforts with a common strategy at European level. This “double-level” approach will ensure that progress is globally coherent and follows common orientations throughout Europe.

A workshop was held on 17th September 2009 to discuss the draft guidelines and recommendations for the development of national plans elaborated by the EUROPLAN project and future steps for developing methodological guidance on how to develop comprehensive and integrated strategies for guiding and

⁷¹ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF>

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

structuring all relevant actions in the field of rare diseases. A revised version of this draft report will soon be published. The draft recommendations for national plans and strategies will be sent in spring 2010 to the EU Committee of Experts on Rare Diseases and the health authorities of each of the 27 Member States for comments before these recommendations are finalised.

National conferences and workshops on the subject of national plans and strategies, supported by this project, will begin in 2010 and will have a political dimension. The conferences will share a similar structure in order to better analyse results, and a final report will be published after each event.

Aa.2.2a.6 Calls for Proposals and Projects funded in 2009

The European Commission has published the Work Plan for 2009 for the implementation of the second programme of Community action in the field of health. The publication of the Work Plan was followed by the calls for proposals. The Executive Agency for Health and Consumers (EAHC)⁷³ published calls for proposals for projects, operating grants, conferences and joint actions.

The financial contributions may, where appropriate, include joint financing by the Community and one or more Member States or by the Community and the competent authorities of other participating countries. The Calls presented new funding opportunities for the European organisations active in the area of public health. The total budget available for the execution of the 2009 Work Plan is €48.2 million. The selected proposals address important problems in the European public health field are in line with the Commission's priorities expressed in the Work Plan. The successful proposals concentrate on aspects of public health that cannot be achieved on a national level. They should ensure a significant impact across the EU.

The deadline for submission of proposals was 20 May 2009. Three proposals were retained in the field of Rare Diseases: a one year contract for the development of Orphanet; CARE-NMD – Dissemination and Implementation of the Standards of Care for Duchenne muscular Dystrophy in Europe (including Eastern countries); Social economic burden and health-related quality of life in patients with rare diseases in Europe (BURQOL–RD). Two conferences on rare diseases were funded in 2009: the 2nd Pan-European Conference on Haemoglobinopathies (Thalassaemia International Federation); and the European Autism Action 2012: Working Conference on a European Strategic Plan for Autism, Dublin 2009 (Irish Autism Action). An Operating Grant was awarded to Eurordis.

Aa.2.2a.6.1 Call for Tender: Evaluation of population newborn screening practices for rare disorders in Member States of the European Union (EUNENS)

In July 2009 a call for tender was launched for an evaluation of the current situation of newborn screening practices for rare diseases in the MS of the EU. A need to identify what are the current practices in the Member States has been identified: for what reasons the diseases to be screened are selected, how the decisions to expand the list of diseases are taken, what are the technologies used and what organisation is in place to ensure comprehensive screening of all newborns and to evaluate the performance of the programmes.

The expected outcomes of the evaluation are:

- An extensive report on the practices of NBS for rare disorders implemented in all the Member States including number of centres, estimation of the number of infants screened and the number of disorders included in the NBS as well as reasons for the selection of these disorders.
- Identification of types of medical management and follow-up implemented in the Member States.
- Establishment of a network of experts analysing the information and formulating a final opinion containing recommendations on best practices and recommending a core panel of NBS conditions that could be included in all MS practices;
- Developing a decision-making matrix that could be used by Member States programs to systematically expand (or contract) screening mandates.

This call was awarded to the Istituto Superiore di Sanità in Italy.

⁷³ <http://ec.europa.eu/eahc/index.html>

Aa.2.2b Indirect actions in 2009

Aa.2.2b.1 Draft Cross-border Healthcare Directive

The European Parliament adopted a draft directive on 23 April 2009 that facilitates cross-border healthcare in the European Union. The proposal, approved by a majority of 297 votes (120 votes against and 152 abstentions), aims to eliminate obstacles hindering patients from seeking treatment in another Member State. The proposed directive will also clarify patient rights to reimbursement for treatment obtained abroad. The proposed directive will have no impact on the rights of each Member State to determine which health benefits they will provide. Thus, if a particular treatment is not reimbursed in a patient's home country, it will not be reimbursed if accessed in another Member State. Member States would be able to require prior authorisation for "hospital care" – a term that Parliamentarians prefer Member States to define, rather than the Commission – and reimbursement would match the amount that patients would receive in their home country. However, the Parliament amended the text for patients affected by rare diseases. Amendment 66 states that *"patients affected by rare diseases should have the right to access healthcare in another Member State and to get reimbursement even if the treatment in question is not among the benefits provided for by the legislation of the Member State of affiliation"*. Furthermore Amendment 88 stipulates that *"Patients with rare diseases shall not be subject to prior authorisation"*. Another amendment favourable to rare diseases is Amendment 102: *Member States shall facilitate the development of the European reference networks of healthcare providers, in particular in the area of rare diseases* Amendment 106 refers to the list of specific criteria and conditions that the European reference networks must fulfil, adding a list of rarer disease areas to be covered.

Aa.2.2b.2 European Commission's Alzheimer Communication

The European Commission adopted in late July 2009 a Communication⁷⁴ on a European initiative for Alzheimer disease and other dementias along with a proposal for a Council Recommendation⁷⁵ on measures to combat neurodegenerative diseases through joint programming of research activities. The Communication encompasses rare forms of dementia – which include frontotemporal dementia, Pick disease (lobar atrophy), Binswanger disease, and Lewy-Body dementia. The Communication makes reference to data from a project conducted by European Union patient platform Alzheimer Europe with the support of the European Commission that identified significant rare forms of dementia. The Communication encourages national and collaborative efforts in four key areas: prevention, the coordination of research across Europe, disseminating best practice for treatment and care, and the development of a common approach to ethical matters concerning the rights, autonomy, and dignity of people with dementia.

Aa.2.2b.3 Reconfiguration of European Commission portfolios

It was announced at the end of 2009 that DG Public Health and Consumers will be expanded to take responsibility for pharmaceuticals, including the EMA. This change is in line with the political organisation of Member States, where policy for medicinal products is the responsibility of the country's health department.

Aa.2.3 Developments foreseen in 2010

Aa.2.3a Direct initiatives

A.2.3a.1 European Commission health work plan for 2010

The European Commission on 18 December 2009 adopted the Work Plan for 2010 implementing the second programme of Community action in the field of health (2008-2013) which will continue the support to rare disease projects and networks. Amongst the rare disease initiatives earmarked for funding are two proposals for Joint Actions that contribute to the implementation of some relevant aspects of the Commission Communication on Rare Diseases: Europe's challenges: 1) a technical action to support the development of the

⁷⁴ http://ec.europa.eu/health/ph_information/dissemination/documents/com2009_380_en.pdf

⁷⁵ http://ec.europa.eu/health/ph_information/dissemination/documents/rec2009_379_en.pdf

Orphanet database on rare diseases and orphan drugs which is run by a large consortium of European partners and which is the most important rare diseases database in the world: in order to implement the establishment of a dynamic EU inventory of rare diseases it will be necessary to further develop the database, and 2) a technical action to support the European Surveillance on Congenital Anomalies (EUROCAT) network which is run by a large consortium of European partners in order to create a sustainable prevalence data system for 95 congenital anomaly subgroups which are to be updated annually. In order to improve procedures to access orphan medicinal products a call for tender concerning the creation of a mechanism for the exchange of knowledge between Member States and European authorities on the scientific assessment of the clinical added value for orphan medicines will be also launched.

Aa.3 DIRECTORATE GENERAL (DG) RESEARCH

Aa.3.1 Fifth and Sixth Framework Programmes for research, technological development and demonstration activities

Research on rare diseases has been supported for more than twenty years through past Framework Programmes for research, technological development and demonstration activities.

During the Fifth Framework Programme (FP5: 1998-2002) the thematic programme “Improving the quality of life and management of living resources” included, amongst other topics, fundamental and clinical research in the field of rare diseases. Support was provided for multinational research into rare diseases, applying advances in modern technology to diagnosis, treatment, prevention and surveillance through epidemiology. 47 projects were funded for about €64 million in total.

Under the subsequent Sixth Framework Programme (FP6: 2002–2006), one of the seven thematic areas supported projects with a focus on “Life sciences, genomics and biotechnology for health”. This thematic area stimulated and sustained multidisciplinary research to exploit the full potential of genome information to underpin applications to human health. In the field of applications, the emphasis was on research aimed at bringing basic knowledge through to the application stage (translational approach), to allow real, consistent and coordinated medical progress at European level and to improve the quality of life. This thematic area was twofold, one of the aspects being the fight against major diseases, including rare diseases. FP6 saw a significant increase in the funding for rare disease projects: around €230 million for a total of 59 projects, also including an ERA-Net project (E-Rare). Overall this allowed for the mobilisation of researchers to tackle the fragmentation of research and the production of new knowledge, but also a better coordination of research at EU level, and the fostering of the dialogue with all stakeholders, including patients.

Examples of FP6 projects⁷⁶ include EuroWilson, TREAT-NMD, OrphanPlatform and E-Rare. The FP6 ERA-Net for research programmes on rare diseases (E-Rare, financed for 4 years from 2006-2010)⁷⁷ is a network of ten partners responsible for the development and management of national/regional research programmes on rare diseases. This project helps develop synergies among the national and/or regional research programmes of the participating countries, to establish a common research policy on rare diseases and to coordinate their national/regional research programmes, notably through the setting up of joint strategic activities and transnational calls for proposals. A first transnational call for proposals was launched by E-Rare in 2007⁷⁸: six E-Rare partners (France, Germany, Italy, Israel, Spain and Turkey) participated in the call and 13 projects were selected for funding.

⁷⁶ <http://cordis.europa.eu/lifescihealth/major/rare-diseases-projects-1.htm>

⁷⁷ <http://www.e-rare.eu/>

⁷⁸ <http://www.e-rare.eu/Announcements/1st-Joint-Call.html>

Aa.3.2 7th Framework Programme for research, technological development and demonstration activities

The Seventh Framework Programme of the European Union for research, technological development and demonstration activities (FP7, 2007-2013⁷⁹) is composed of four main specific programmes – “Cooperation”, “Ideas”, “People” and “Capacities” – including cross-cutting issues such as support for SMEs, international cooperation, the contribution of research to EU policy, and the inclusion of societal considerations. Rare disease research features under the heading of the Health theme, one of ten themes proposed under the specific programme on “Cooperation”. This specific programme is designed to gain or strengthen leadership in key scientific and technological areas by supporting trans-national cooperation between universities, industry, research centres, public authorities and stakeholders across the European Union and the rest of the world.

Specifically, the focus for rare disease research collaborative in FP7 is on pan-European studies of natural history, pathophysiology, and the development of preventive, diagnostic and therapeutic interventions. This sector includes rare Mendelian phenotypes of common diseases. Supported projects should help identify and mobilise the critical mass of expertise in order (i) to shed light on the course and/or mechanisms of rare diseases, or (ii) to test diagnostic, preventive and/or therapeutic approaches, to alleviate the negative impact of the disease on the quality of life of the patients and their families, as appropriate depending on the level of knowledge concerning the specific (group of) disease(s) under study.

The European Commission has already published several calls for proposals in various thematic areas of FP7. The “Cooperation” 2010 work programme of the Health Theme called for an ERA-Net on rare diseases and collaborative research projects for the clinical development of substances with a clear potential as orphan drugs⁸⁰.

Up to early 2010, a total of 20 projects, with a global budget of €75 million, have been selected for funding under the rare diseases area (section 2.4.4) of the Health Theme. A full list of projects concerning rare diseases supported by the Framework Programmes is available in Annex 3 of this document.

Ab. OTHER EUROPEAN ACTIVITIES

Ab.1 OTHER EUROPEAN RARE DISEASES INITIATIVES BEFORE 2009

Ab.1.1 Pharmaceutical Forum

The Pharmaceutical Forum⁸¹ was set up in 2005 as a three year process by Vice-President Verheugen and former Commissioner Kyprianou, in order to find relevant solutions to public health considerations regarding pharmaceuticals, while ensuring the competitiveness of the industry and the sustainability of the national health-care systems. This high-level ministerial platform for discussion between Member States, EU institutions, industry, healthcare professionals, patients and insurance funds focused its work on three main topics: information to patients on diseases and treatment options; pricing and reimbursement policy and relative effectiveness. The last Ministerial meeting, on 2 October 2008, concluded the three year exercise with the adoption of the final report gathering Final Conclusions and Recommendations. It also included all technical documents and projects developed by the three working groups to support implementing actions addressed to the European Commission, Member States and interested stakeholders.

⁷⁹ http://cordis.europa.eu/fp7/home_en.html

⁸⁰ ftp://ftp.cordis.europa.eu/pub/fp7/docs/wp/cooperation/health/a_wp_201001_en.pdf

⁸¹ http://ec.europa.eu/pharmaforum/index_en.htm

In that framework, the members of the working group on pricing and reimbursement decided to focus on how to improve access to orphan medicines. Indeed, Orphan medicines amplify the common tensions in the field of pricing and reimbursement: assessing and rewarding innovation is difficult, budget optimisation is challenged and access for patients is limited in several countries. In spite of many policy initiatives increasing the number of newly developed orphan medicines, many of these are not available for all EU citizens.

Based on the paper "Improving access to orphan medicines for all affected EU citizens"⁸² developed by its members, The High Level Pharmaceutical Forum recommended the following⁸³: Member State authorities, stakeholders and the Commission should strengthen their efforts to ensure access to orphan medicines in all EU Member States. They are therefore called upon to take up the appropriate ideas developed in the Working Group Pricing regarding i) early dialogue on research and development, ii) exchange of knowledge on the scientific assessment of the clinical added value, iii) specific pricing and reimbursement mechanisms and iv) increased awareness on orphan diseases.

Ab.2 OTHER EUROPEAN RARE DISEASES INITIATIVES AND MEETINGS IN 2009

Ab.2.1 Czech presidency of the European Union

Under the term of the Czech EU Presidency that ran from January to June 2009, several conferences and workshops were held in relation to rare diseases, including an international conference⁸⁴ in Prague to address the treatment of rare diseases in relation to EU legislation. This event was devoted to a discussion of the objectives of the EU in the area of diagnosis and treatment of rare diseases and to the respective tasks ascribed to the individual EU member states in the EU Council Recommendation on European Action adopted under the Czech presidency at the meeting of EU27 Ministers of Health in Luxembourg on 9 June 2009.

Prague Declaration

An outcome of the ministerial conference entitled *eHealth for Individuals, Society, and Economy* that took place in Prague from 18–20 February 2009 was the adoption of the Prague Declaration⁸⁵ on eHealth and a call for action on building an eHealth area for European citizens. The principal objective of the Prague Declaration "is to sum up the current state of the Europe-wide effort to use information and communication technologies (ICT) in healthcare for the benefit of patients as well as economic efficiency of the health sector. It also aims to determine further steps to be taken at the level of Member States as well as European institutions. At the same time, a common European eHealth area should be built, where individual national systems will be able to communicate with one another. Integrating eHealth solutions into national health strategies of the Member States will also be of great importance". The Prague Declaration was prepared in cooperation with the EU Member States. The ministerial conference targeted the various impacts of the eHealth solutions and processes. Amongst the presentations, ICT tools for rare diseases demonstrated how rare diseases provide a perfect example of the relevance of ICT tools in improving access to services and providing information at the European level. This presentation demonstrated the value of the various eHealth applications Orphanet has on offer for patients, health professionals, researchers, policy makers, and industry, across Europe and beyond. Other EU-funded rare disease electronic informational projects were cited including ECORN-CF, a shared knowledge database answering patient and professional queries on cystic fibrosis, and DYSCERNE, which provides an electronic forum for experts to submit cases of difficult-to-classify developmental anomalies.

Ab.2.2 Swedish presidency of the European Union

On 1 July 2009, Sweden took over the Presidency of the European Union (EU), completing the 18-month troika started under France and continued by the Czech Republic. The country holding the EU Presidency acts as the driving force behind the EU's legislative and political activities and works to broker compromises between the

⁸² http://ec.europa.eu/pharmaforum/docs/pricing_orphans_en.pdf

⁸³ Conclusions and Recommendations of the High Level Pharmaceutical Forum 2005-2008, Recommendation 7.3 on Access to medicines for EU citizens http://ec.europa.eu/pharmaforum/docs/final_conclusions_en.pdf

⁸⁴ <http://vzacna-onemocneni.cz/>

⁸⁵ <http://www.ehealth2009.cz/Pages/108-Prague-Declaration.html>

EU Member States. The most important task for the three-Presidency team was to establish a common 18-month programme for all three presidencies. Following on the momentum initiated by France and sustained by the Czech Republic, during which the historical adoption of the Council Recommendation on an Action in the Field of Rare Diseases was achieved in June 2009, Sweden, less than one month into its turn at the helm of the EU Council Presidency, organised a conference of experts to push the envelope further. The conference “Assessing Drug Effectiveness – Common Opportunities and Challenges for Europe” (28-29 July 2009) gathered stakeholders from throughout Europe to discuss how to develop cooperation across Europe for the collection and sharing of data on drug effectiveness and safety following marketing authorisation. Speakers included Thomas Lönnngren, Executive Director of the EMA, along with representatives from government, industry, research, and patient organisations. A workshop specific to orphan drugs – an area for which cooperation is considered critical as most individual countries have too few patients and resources to sustain a comprehensive follow-up scheme – brought together a panel of experts. The conference moved forward the process of post-marketing assessment harmonisation via the decision to develop a pilot model “for structured follow-up for initial testing on an orphan drug” for which several candidate products were proposed by the workshop panellists. A meeting took place in autumn bringing together stakeholders interested in participating in the pilot project.

Ab.2.3 Rare Diseases Day 2009

The 2nd Rare Disease Day (RDD), initiated and coordinated by Eurordis focussed on patient centred care (“Patient Care, a Public Affair!”). This year 19 national alliances helped organise the day at local level and 600 patient groups participated in Europe: in total 30 countries were involved in RDD. The target audiences of the day were policy makers (health authorities, national parliamentarians, European parliamentarians and candidates) as well as the general public, media, health professionals, academics and researchers.

A website was created especially for the event, with information on the activities of each participating country. Other web-based platforms such as Facebook and YouTube were used to promote RDD. In total, 21.000 visits were made to www.rarediseaseday.com this year. Media coverage of the day was strong with over 1500 media articles in total. The 2nd Rare Disease Day also spread beyond Europe with the participation of the US (organised by NORD – the National Organisation for Rare Disorders), Canada, Argentina, Colombia, Australia, Taiwan and China.

The event received the patronage of EU Commissioner for Health Androulla Vassiliou, who attended the Rare Disease Day book launch of “*The Voice of 12.000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe*”⁸⁶ at the European Commission in Brussels. This book provides an analysis of data collected through the EurordisCare2 and EurordisCare3 surveys. These surveys investigated patients’ experiences and expectations regarding access to diagnosis and to health services, for a few but significantly relevant rare diseases across Europe. A dinner debate, hosted by MEP Antonios Trakatellis (Rapporteur of the Parliament’s Opinion on the Council Recommendation on Rare Diseases), was also held at the European Parliament and was attended by policy-makers at the European Commission, patient advocates, parliamentarians and the representatives of the biopharmaceutical industry. Rare Disease Day 2009 also saw lobbying action at national level (Spain, UK, US, China), and also provided the momentum in the push for national plans and strategies (Belgium, Spain, Portugal, Bulgaria, Ireland, Czech Republic), as well as creating momentum in the push for Centres of Expertise (i.e. visit of Centre for Rare Disorders by MEP in Denmark), and in the construction of emerging national alliances (Switzerland, Australia). Rare Disease Day also provided a focus for fund raising – this year’s *Telefon* in Catalonia was dedicated to rare diseases.

Rare Disease Day also played an important role in raising awareness amongst the general public (this was helped through VIP and celebrity patronage this year) to inform, educate and involve the public in the issues surrounding rare diseases.

Ab.2.4 E-Rare 2nd Joint Transnational Call

The partners of E-Rare, ERA-Network for research programmes on rare diseases, launched the second joint transnational call (JTC) at the end of 2008/beginning of 2009. The ten countries that joined the 2nd Transnational Call are France, Germany, Israel, Spain, Turkey, the Netherlands, Portugal, Italy, Austria and Greece: 4 additional funding organisations from 4 Member States joined the 2nd JTC. The financial input of each partner research funding agency/ministry has allowed for the funding for 16 transnational research consortia

⁸⁶ http://www.eurordis.org/article.php3?id_article=1960

with 75 participating research teams from 10 countries for a total research budget of €9.6 million. A list of funded projects is available⁸⁷.

Ab.2.5 Proposal to harmonise qualifications for clinical genetics as medical specialty adopted by European Union of Medical Specialists

The European Union of Medical Specialists (UEMS), a non-profit organisation founded in 1958 to determine high quality standards harmonising specialist training for European physicians, represents some 1.5 million European medical specialists in 38 specialist sections throughout 35 national member associations. In April 2009, the UEMS Council adopted the text entitled *Description of Clinical Genetics as a Medical Specialty in EU: Aims and objectives for specialist training*⁸⁸. The document, which defines educational goals for a specialisation in genetic medicine, has already been endorsed by the European Society of Human Genetics, the UEMS Multidisciplinary Joint Committee for Clinical Genetics, and the UEMS Specialist Sections & European Boards. This is good news for rare disease patients in countries where clinical genetics is not yet recognised: Belgium, Greece and Spain.

Ab.2.6 International Conference on Rare Diseases

The 5th ICORD meeting was held at the Istituto Superiore di Sanità in Rome, Italy, 23-25 February 2009. Topics discussed included rare diseases as a public health issue, EU actions in the field of rare diseases, the second Rare Diseases Day, support of networks and patient organisations in rare diseases, facilitating cooperative efforts of the regulatory processes, WHO International Classification of Diseases and rare diseases emphasis, policy initiatives for rare diseases research and orphan products, EUROPLAN and national plans for rare diseases research and orphan products development, linking academic discoveries and industry product development strategies, linking patients to research programs and treatment centres, the value of patient registries and experiences in recruiting patients for clinical trials.

Ab.2.7 Six Central European countries form alliance to share rare disease resources

Both government representatives and rare diseases experts from six Central European countries (Austria, Czech Republic, Germany, Hungary, Italy, and Slovenia) met in August 2009 at an informal meeting that took place at the initiative of the Austrian Ministry of Health and the European Health Gastein to discuss possibilities for a comprehensive improvement of cross-border cooperation in the treatment of rare diseases, and possibilities for practical implementation of this initiative. This was followed by a formal meeting at the 12th European Health Forum Gastein in September 2009. Since 2008 this annual health forum has a segment dedicated specifically to rare diseases.

Participating countries agreed to cross-border cooperation in research and care, to help develop a coordinated profile of requirements stipulating the criteria that must be adhered to by future centres of expertise and to identify and establish centres of expertise for certain diseases or disease groups. Existing specialised hospitals and institutes are to be involved in order to utilise their knowledge as efficiently as possible. Establishing these networks of centres of expertise is meant to specifically facilitate a more intense transfer of know-how; patients are to be provided with simple and rapid options for taking advantage of the services in centres of expertise abroad, and the development of a patient database is to create a better basis for studies and research projects. In addition to this, a coordination office in each country is to be established to coordinate the national networks, to coordinate transnational cooperation and to provide information to physicians and patients.

Cooperation is open for additional partners. The results from the meeting of experts are to be presented to the health authorities of the participating countries. The initiative aims to open the first centre of expertise in 2010.

Ab.2.8 EPPOSI Meetings

EPPOSI (European Platform for Patients' Organisations, Science and Industry) is an EU patient-led partnership between patients' organisations, science and industry, founded in 1994 for the exchange of information and discussion of policies in EU human healthcare. EPPOSI's primary mission is to establish a strong European alliance of patients' organisations, academic science and industry jointly working on healthcare policies towards treatment and prevention of serious diseases.

⁸⁷ <http://www.e-rare.eu/images/stories/e-rarejtc2009fundedprojects.pdf>

⁸⁸ <http://admin.uems.net/uploadedfiles/1305.pdf>

EPPOSI focuses on building dialogue, consensus positions and policy recommendation for the benefit of EU patients and consumers. These consensus positions have provided building blocks for: the establishment of the European Orphan Medicinal Products Regulation; the advancement of biomedical research and the value of innovation; the timely access to innovative medicines; several rare-disease therapy developments and partnerships; East-West European collaboration amongst patient groups; and biobanking.

EPPOSI held two workshops in 2009 in the field of Rare Diseases and Orphan Drugs. The EPPOSI Workshop on Registries for Rare Disorders (18-19 March 2009) was attended by 60 delegates from 15 countries, representing patients, researchers, clinicians, industry, policy makers, regulators and registry operators. The workshop identified areas where establishment of best practice guidelines, advice and templates could save time and money. The workshop concluded that a working group needs to be established to look into providing tools such as customisable, downloadable software. The workshop also highlighted that more attention should be paid when setting up registries in order to exchange data, and to establish common data standards.⁸⁹ The 10th EPPOSI Workshop on Partnering for Rare Diseases Therapy Development took place on 26-27 October, 2009. One of the main issues discussed by stakeholders was the threat to policy continuity and funding for rare diseases posed by the economic downturn. Recommendations from the workshop included: additional policy measures and incentives to promote R&D in the field of Rare Diseases and Orphan Drugs; awareness raising initiatives and training for medical professionals in order to improve chances for early diagnosis; European collaboration (creation of an EMA working group) for the assessment of clinical added value of orphan medicines; conditional reimbursement of orphan medicines upon approval at EU level (based on revised report on the clinical added value); and that priority needs to be given to setting up Centres of Expertise and European Reference Networks for diseases for which orphan drugs are approved, to speed up access and promote diagnostic and care standards.

⁸⁹ Report on EPPOSI Workshop on Patients' Registries for Rare Disorders – Need for Data Collection to Increase Knowledge on Rare Disorders and Optimize Disease Management and Care – 18-19 March 2009

SECTION B

ACTIVITIES IN EU MEMBER STATES AND OTHER EUROPEAN COUNTRIES

B.1 EU MEMBER STATES

B.2 OTHER EUROPEAN COUNTRIES

B.1 EU MEMBER STATES

B.1.1 AUSTRIA

B.1.1.1 State of affairs before 2009

Definition of a rare disease

In the past, there has been no official definition of rare diseases in Austria; on an informal basis, stakeholders in Austria accepted the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

A national plan on rare diseases is in the early stages of development at the Austrian Ministry of Health (BMG): the Austrian Orphanet team has been instructed by the BMG to assemble a subcommittee for rare diseases covering the main stakeholders in the field. By the end of 2008, the subcommittee, comprising 17 members from 13 different organisations or institutions (including 3 from the BMG), has been established and commissioned to draft a plan of action.

On the occasion of the First European Rare Disease Day on 29 February 2008, the Austrian Orphanet team and 35 patient support groups initiated a petition for rare diseases named "National Action Plan for Rare Diseases in Austria". The petition defined nine requirements for improving the situation for all persons concerned with rare diseases. The five main topics were:

- the definition of a specific rare disease status for all patients with a defined rare disease;
- a separated financial plan for diagnostics, treatment and prevention of rare diseases with a governmental guarantee;
- establishment of officially labelled centres of reference and centres of competence for rare diseases or groups of rare diseases and – subsequently – establishment of a strong network between these centres aiming to provide a clearly visible and easy to access expert service for as many rare diseases as possible;
- a specific funding source for research on rare diseases;
- the implementation of a national rare diseases task force to support and advice decision makers in the ministry of health.

Between 15 February and 16 March 2008, 4346 support declarations were collected (either via the Orphanet-Austria website, or corresponding sign-up sheets). On 29 February, the petition and the first 2,000 signatures were handed over to the Austrian Minister of Health, Dr. Andrea Kdolsky: she promised to support the objectives of the petition wherever possible.

Centres of expertise

Currently, there is one well recognised centre of expertise for rare diseases in Austria, the "Spezialambulanz Genodermatosen" for Epidermolysis bullosa in Salzburg. It is expected that some further centres of expertise will be identified as soon as (a) the criteria for European centres of expertise from the EC Task Force on Rare Diseases have been adopted in Austria and (b) the national plan of action for rare diseases has been implemented successfully.

Registries

Currently, no nationwide, general and comprehensive registry for rare diseases patients exists in Austria. Approximately 13 registries for individual rare diseases or groups of rare diseases are run by specialised clinics or networks of experts from different clinics. Some registries are supported by corresponding patient support groups. Some of the European Registries Austria participates in are EUROCARE CF, AIR, EMSA-SG, EUROCAT and ENRAH.

Neonatal screening policy

Neonatal screening is carried out for all newborns for the following diseases and conditions: adrenogenital syndrome, carnitine-acylcarnitine translocase deficiency, carnitine palmitoyltransferase I deficiency, carnitine

palmitoyltransferase II deficiency, carnitine transporter defect, citrullinemia / argininosuccinate lyase deficiency, congenital hypothyroidism, cystic fibrosis, galactosaemia, glutaric acidemia type I, glutaric acidemia type II / multiple acyl-CoA dehydrogenase deficiency, homocystinuria and hypermethionemia, isobutyryl CoA dehydrogenase deficiency, isovaleric academia, β -Ketothiolase deficiency, long-chain 3-hydroxy acyl-CoA dehydrogenase deficiency / trifunctional protein deficiency, maple syrup urine disease, medium-chain acyl-CoA dehydrogenase deficiency, methylmalonic aciduria / propionic academia, multiple carboxylase (holocarboxylase) deficiency, phenylketonuria and hyperphenylalaninemia, short-chain acyl-CoA dehydrogenase deficiency, tyrosinemia type I (II), very long-chain acyl-CoA dehydrogenase deficiency, 2-Methyl 3-hydroxy butyryl-CoA dehydrogenase deficiency, 3-Hydroxy-3-methylglutaryl-CoA lyase deficiency, 3-Methylcrotonyl-CoA carboxylase deficiency, and 3-Methylglutaconic aciduria type I.

National alliances of patient organisations and patient representation

There is currently no specific national alliance of patient organisations for rare diseases in Austria. However, there are several independent regional umbrella organisations for patient organisations in general, all based in Vienna:

- *Arbeitsgemeinschaft (ARGE) Selbsthilfe*
- *Selbsthilfe-Unterstützungsstelle für gesundheitsbezogene Selbsthilfegruppen (SUS)*
- *Martha-Frühwirt-Zentrum*

The *ARGE Selbsthilfe* constitutes a “supra-umbrella” to a set of regional umbrella organisations, established and administrated at county level (*ARGE Selbsthilfe* Carinthia, Upper Austria, Lower Austria, Salzburg, Styria, Tyrol, Vorarlberg, and Vienna); the *ARGE Selbsthilfe* can provide limited funding (up to €900 for a period of 6 months, repeated applications are 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 *SUS* (as part of the *Fonds Soziales Wien*) provides all kinds of administrative support, but does so without funding; similarly, the *Martha-Frühwirt-Zentrum* offers administrative support and rooms or offices for the activities of patient organisations, but again without direct funding.

Sources of information on rare diseases and national help lines

Since 2002 there is a dedicated Orphanet team in Austria, currently hosted by the Institute of Neurology at the Medical University of Vienna. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. There is no official information centre in Austria for information on rare diseases apart from Orphanet.

National rare disease events

On 29 February 2008, the first European Rare Disease Day, members of 11 patient support groups assembled at the general hospital Vienna together with the Orphanet Austria team to hand over the petition for a national plan of action for rare diseases to the Austrian Health Minister (see above) and to inform patients, physicians and visitors about the rare diseases they represent. On the same day, another information event took place in Salzburg, organised by an Austrian patient support group for Klinefelter’s syndrome.

In August 2008 representatives of around 20 patient organisations participated at a meeting in Vienna, organised by the Austrian Orphanet team, to formally elect the two official representatives (and their replacements) for the subcommittee for rare diseases (see above).

Research activities and E-Rare partnership

Currently, there exists no specific and explicit funding policy for rare diseases in Austria. In theory, funding is available through grant applications at different funding bodies (for instance, the *Fonds zur Förderung der wissenschaftlichen Forschung (FWF)*, the *Nationalbank*, or minor resources such as the *Fonds des Bürgermeisters der Bundeshauptstadt Wien*); however, funding follows a bottom-up approach, meaning that applications from all medical disciplines and, in some instances, totally unrelated medical, as well as non-medical, research fields compete each other in a peer-review selection process, eventually resulting in a selection bias towards projects addressing more common diseases.

An alternative source of funding is provided by occasional project calls launched by the Austrian Ministry of Science. In the past 4 years, one of these calls was dedicated to rare diseases. Moreover, some fundraising patient organisations finance rare disease research projects.

In line with this, Austria was not an official partner in the E-Rare consortium before 2009 and did not participate in the first E-Rare Joint Transnational Call in 2007.

Participation in European projects

Austria participates in the following European Reference Networks for rare diseases: EUROHISTIONET, NEUROPED (main partner), Paediatric Hodgkin Lymphoma Network and PAAIR. Austria participates in the following European research projects for rare diseases: BNE, CLINIGENE, EMSA-SG, EMINA, ENRAH, ENCE-PLAN, EURIPFNET, EUROTRAPS, EURO-LAMINOPATHIES, EUROPEAN LEUKEMIA NET, EURO-IRON1, GENESKIN, LYMPHANGIOGENOMICS, MYELINET, NEUTRONET, NEUROPRION, PERXISOMES, PNSEURONET, PROTHETS, PULMOTENSION, PWS, RHORCOD, RD PLATFORM, SIOPEN-R-NET and SARS/FLU-VACCINE. Austria contributes to the following European registries: AIR, EUROCARE CF, EMSA-SG, EUROCAT and ENRAH. Austria contributes to the EUROPLAN project. Austria is part of the SOPEN-R-NET research network.

Orphan drug committee and incentives

According to information collected for the publication of the first *“Inventory of Community and Member States’ incentive measures to aid the research, marketing, development and availability of orphan medicinal products”* the Austrian Drugs Act (2001) provides for *“the waiving of fees (e.g. for marketing authorisation or variations) for orphan drugs authorised through the national procedure (applicable until 20 November 2005, date from which the centralised route of marketing authorisation of designated orphan medicinal product became mandatory)¹”*.

Orphan drug availability

As soon as marketing authorisation is provided, orphan drugs are available quite quickly in Austria. Prescription, however, can be hampered by administrative burdens, since reimbursement for orphan drugs (like any other drug) is provided by regional health insurance companies, and therefore any decision concerning the payment is organised at the county, and not the national, level. As a result, specialists might have to repeatedly address many contacts in different insurance bodies and deliver certificates and other paperwork before treatment of a patient with an orphan drug is approved. Approval or rejection may depend on the place of residence of the patient and that decisions may differ from one county to another.

Specialised social services

No specific activity reported.

B.1.1.2 New initiatives and incentives in 2009

Definition of a rare disease

Working on the draft for the national plan of action, the subcommittee for Rare Diseases decided unanimously that this plan will officially adopt the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

A subcommittee for Rare Diseases, in charge of drafting a national action plan for rare diseases, have already met four times in 2009. During the second meeting, the committee decided to adopt the following working strategy:

- (a) When elaborating the draft, the work will be divided into several work packages comprising:
 - a general text document (the “framework” of the action plan) containing:
 - i) the introduction (with a section on general aspects of rare diseases, the official definition, a section on ethical and equality aspects, and one on principal objectives of the plan),
 - ii) the definition of the nine to ten strategic priorities (titles and description of the background and problems; other paragraphs that delineate specific objectives, measures, costs, schedule for the implementation, and specific monitoring will be outlined in detail later),

¹ *Inventory of Community and Member States’ incentive measures to aid the research, marketing, development and availability of orphan medicinal products. Revision 2005 (p7).*

- iii) a final section defining the general mode of monitoring.
- nine to ten strategic priorities tackling/addressing the following topics:
 - i) recognition of the specificity of rare diseases (codification in the health care system, documentation of an official rare disease status, etc);
 - ii) improving awareness and knowledge about rare diseases (addressees: general public, health care personnel, professionals);
 - iii) improving health care pathways and quality (in particular adopting criteria for, and subsequently establishment of, centres of expertise and centres of competence);
 - iv) support of a comprehensive information system for rare diseases (i.e. Orphanet);
 - v) improving early diagnosis; promoting development and clinical implementation of screening tests;
 - vi) improving equal access to established therapies; promoting development and clinical implementation of new therapies;
 - vii) establishing selective funding for research on rare diseases;
 - viii) establishing a permanent advisory board for rare diseases;
 - ix) improving the epidemiological knowledge on rare diseases (establishment of a national or a trans-national/cross-border registry);
 - x) establishing a national coordination centre/office for rare diseases (linked to priority “iii”).
- (b) As soon each draft for a work package is finished, it will be reviewed by experts from the highest advisory board of the Austrian Ministry of Health and, after approval, referred to the political decision process. This strategy was developed to ensure that:
 - the final document fulfils the standards of a comprehensive plan of action,
 - individual priorities can be implemented as soon as possible without any delay caused by the elaboration of other work packages.
- (c) The draft of the framework of the action plan was planned for November 2009 and the political discussion process was planned before the end of 2009.

Centres of expertise

See the actions foreseen by the National Plan for Rare Diseases (“Improving health care pathways and quality”).

Registries

See the actions foreseen by the National Plan for Rare Diseases (“National/Cross-border registry”). The Austrian Ministry of Health currently explicitly refuses to financially support selected individual patient registries.

Sources of information on rare diseases and national help lines

See the actions foreseen by the National Plan for Rare Diseases (“Coordination centre/office”).

National alliances of patient organisations and patient representation

Thematically restricted support for patient organisations might be part of the future National Plan for Rare Diseases, integrated into the priority “Improving awareness and knowledge about rare diseases”. However, the Austrian Ministry of Health recently declared that the possibility of a prospective basic funding for patient organisations strongly depends on the definition of common, transparent criteria, which have to be fulfilled, as a prerequisite, in order to financially support these associations.

Information services on rare diseases and orphan drugs

See the actions foreseen by the National Plan for Rare Diseases (“Coordination centre/office”).

National rare disease events

Orphanet Austria organised the First March for Rare Diseases in Austria, held in Vienna on 28 February 2009, which was attended by many stakeholders including the regional director general (section for consumer health and preventive measures) of the Austrian Ministry of Health. On the same day, a further information event was organised by the aforementioned Austrian patient support group for Klinefelter’s syndrome in Salzburg.

Hosted rare disease events

The 7th World Congress on Melanoma was held on 12-16 May 2009 in Vienna. The annual conference of the European Society of Human Genetics was held in Vienna from the 23 to 26 May. On 2 October 2009, an international workshop on rare diseases was hosted by the Austrian Ministry of Health during the annual meeting of the European Health Forum Gastein, focusing in particular on the needs and advantages of cross-border collaboration in the field of rare diseases².

Research activities and E-Rare partnership

One strategic priority in the Austrian national plan will be the implementation of a defined, separate funding budget in the main existing research bodies, which will be specifically dedicated for research on rare diseases, as aforementioned in the National Plans segment (“Establishing a selective funding for research on rare diseases”). Austria joined the second E-Rare Joint Transnational Call in 2009, and around €580,000 of funding was granted for Austrian teams participating in 3 projects.

Orphan drug availability

See the actions foreseen by the National Plan for Rare Diseases (“Recognition of the specificity of rare diseases” and “Improving equal access to established therapies”).

B.1.2 BELGIUM **B.1.2.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in Belgium accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

The main institutional actor in Belgian rare disease and orphan drug policy is the National Institute for Health and Disability Insurance (NIHDI).

A request was made by the Fund for Rare Diseases and Orphan Drugs to the Belgian Minister of Health and Social Affairs, on 12 December 2008 for political and financial support to the Fund so as to advance the development of a Belgian Plan for Rare Diseases. An additional request was made for financial support for the umbrella patient association “Rare Diseases Organisation Belgium” (RaDiOrg).

A national plan for cancers, including rare cancers³ already exists in Belgium, which also takes into account the situation of rare cancers. In Belgium rare cancers are therefore sometimes excluded from new actions for rare diseases. A plan for chronic diseases (which includes some rare diseases) also exists in Belgium.

Expenditures for rare diseases are covered by the general health system budget and there is no budget specifically allocated to rare diseases: a study to reveal ‘hidden costs’ is planned. A Special Solidarity Fund is also in place which can be used for patients whose costs are not covered by the health care system (for example some orphan drug costs).

Lists of diseases are used in the conventions, such as those of the National Institute for Health and Disability Insurance (NIHD) (the body in charge of reimbursements) for the clinical centres that diagnose and treat patients with certain rare diseases.

Centres of expertise

In Belgium there are several centres specialised in one rare disease or a group of rare diseases. Some of these centres are recognised by the NIHDI and work under a convention. These centres include: the centres for human genetics, cystic fibrosis centres, and the centres for metabolic diseases and neuromuscular diseases.

² Cf. Section A] European Commission and Europe Wide Activities, part D] Rare Diseases meetings in Europe in 2009.

³ The definition of rare cancers is complicated and still under discussion in Belgium. One of the proposed definitions uses an incidence of less than 600 cases per year (for a total of 60.000 cases, thus 1%).

Registries

There are some national registries for specific rare diseases, or groups of diseases, such as cystic fibrosis and rare cancers. Belgium contributes to European registries including EUROCAT, AIR, ECFS, RBDD, ESID, ENRAH, EUNEFRON and EURECHINOREG

Neonatal screening policy

Neonatal screening in Belgium is organised by the *Vlaams Agentschap Zorg en Gezondheid* (Flanders) and *La Direction générale de la santé du Ministère de la Communauté française* (French community). The program in Flanders encompasses screening for following 11 metabolic diseases: phenylketonuria/hyperphenylalaninemia, congenital hypothyroidism, congenital adrenal hyperplasia, biotinidase deficiency, medium-chain acyl-CoA dehydrogenase deficiency (MCAD), multiple acyl-CoA dehydrogenase deficiency (MADD), glutaric acidemia type I, isovaleric acidemia, maple syrup urine disease (leucinosi), propionic acidemia and methylmalonic acidemia. In the French community neonatal screening is provided for 7 metabolic diseases: phenylketonuria, congenital hypothyroidism, maple syrup urine disease (leucinosi), galactosaemia, tyrosinemia, histidinemia and homocystinuria.

National alliances of patient organisations and patient representation

Rare Diseases Organisation Belgium (RaDiOrg) is a non-profit organisation established in January 2008. RaDiOrg regroups around 80 patient organisations for rare diseases in Belgium and is affiliated with Eurordis. RaDiOrg organises the Rare Disease Day and receives funding for this event.

In general, the financial situation and activities of patient organisations in Belgium differs greatly, including differences between the regions (Flanders and the Walloon region). The Walloon region supports the LUSS patient organisation platform.

Patients are well represented in meetings concerning the rare disease situation in Belgium: RaDiOrg and two other patient organisation platforms (VPP and LUSS) are recognised representatives of patients in the Fund.

Sources of information on rare diseases and national help lines

Since 2001 there is a dedicated Orphanet team in Belgium, currently hosted by the Centre of Human Genetics at the Catholic University of Leuven. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no official information centre or website on rare diseases other than Orphanet and no rare diseases helpline in Belgium, although the feasibility of running a rare diseases helpline is under discussion.

RaDiOrg maintains an informative website (www.radiorg.be) which publishes information on rare diseases and patient groups in Belgium. The websites www.weesziekten.be and www.maladiesrares.be provide additional information on the actions of the Fund for Rare Diseases and Orphan Drugs, in both French and Dutch.

The Fund for Rare Diseases has contacted representatives of different university hospitals to initiate a common strategy to collect information on the number of rare disease patients and treatments. Scientific board meetings for the Belgian Orphanet site started in 2008 to validate the data already gathered on the existing rare disease services and research activities in Belgium.

National rare disease events

A symposium was organised by the Fund for Rare Diseases and Orphan Drugs under the patronage of her Royal Highness Princess Astrid in November 2006. RaDiOrg organised a national meeting around the topic of Rare Diseases to mark Rare Disease Day in 2008.

Hosted rare disease events

The secretariat of EPPOSI, the European Platform for Patients' Organisations, Science and Industry is based in Brussels and the city hosts regular EPPOSI workshops on themes based on health care policies and treatment in the field of rare diseases.

Research activities and E-Rare partnership

There are no specific research programmes for rare diseases in Belgium. The FNRS (National Fund for Scientific Research) is a full, contracting member, of the E-Rare consortium, participating in the whole decision and implementation process of E-Rare although Belgium has not participated in E-Rare's first two Joint Transnational Calls. The FNRS also provides funding for applied research on rare diseases and has also created a contact group to foster public information. Rare disease research also benefits from initiatives such as programmes to stimulate translational R&D. Some fundraising patient organisations also finance rare disease research.

Participation in European projects

Belgium participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, EPNET, EPI, ENERCA, EUOHISTIONET, NEUROPED, PAAIR, RBDD and TAG. Belgium participates in the following European research projects for rare diseases: ANTIMAL, CONTICANET, CHEARTED, ESDN, ENRAH, EURAMY, EUREGEN, EUROCARE-CF, EUROSCA, EVI-GENORET, FASTEST-TB, EUNEFRON, EUROAGENTEST, EUROGLYCANET, GENESKIN, GEN2PHEN, HUE-MAN, KALADRUG-R, LEISHMED, IMMUNOPRION, MITOTARGET, MYASTAID, NANOTRYP, NEOTIM, NEUROPRION, PEROXISOMES, PULMOTENSION, PWS, RATSTREAM, RD PLATFORM, SIOPEN-R-NET, STEM-HD, TB-DRUG OLIGOCOLOR and WHIPPLE'S DISEASE. Belgium contributes to the following European registries: EUROCAT, AIR, ECFS, RBDD, ESID, ENRAH, EUNEFRON and EURECHINOREG. Belgium contributes to the EUROPLAN project.

Orphan drug committee and incentives

The Belgian steering group on orphan diseases and orphan drugs had their first informal meeting in March 2006: this group was composed of representatives from patient organisations, industry, genetic centres, therapeutic centres, hospital pharmacies, the HTA agency, insurance groups, the federal health institution and a member of parliament. The steering group organised a national symposium^{4,5} on orphan drugs in November 2006. The steering group has gone on to develop a strategy to increase awareness in Belgium concerning the problems rare diseases present and the reimbursement of orphan drugs. In December 2007, the steering committee was officially integrated into the "Fund for Rare Diseases and Orphan Drugs" in the King Baudouin Foundation of Belgium. At the end of 2008, ad hoc working parties were created by this committee to address the issues related to orphan drugs and rare diseases and to develop strategic solutions.

In addition to this, since 2006, at the initiative of the NIHIDI, the revenues of orphan drugs are no longer subject to so called 'pharmaceutical taxes' (i.e. taxes, earmarked for social security, on sales of reimbursable drugs).

Orphan drug availability⁷

Since 2001, Orphan drugs obtain Marketing Authorisation (MA) through the centralised procedure at the EMA. According to information collected for the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*, "in Belgium, one of the most important measures has been the adoption of the Royal Decree of 8 July 2004 on the reimbursement of orphan medicinal products. This Decree, which entered into force on 20 July 2004, created a 'Committee of Doctors for Orphan Medicinal Products' within the Healthcare service of the INAMI (Institut national d'assurance maladie invalidité – National Invalidity Insurance Institute), the body responsible for issuing opinions on orphan medicinal products when an opinion is required, including with regard to evaluating individual rights to reimbursement. It also evaluates the existing reimbursement conditions for these products and draws up an annual activity report"⁸.

Drug reimbursement decisions are taken by the Minister of Social Affairs, after advice from the Drug Reimbursement Committee (DRC). Orphan drugs follow the same procedure as Class I pharmaceutical products, i.e. products for which the company claims a therapeutic added value. However, unlike for Class I pharmaceutical products, no pharmaco-economic evaluation has to be submitted for orphan drugs. A decision on the reimbursement is taken within 180 days following the submission of the reimbursement request.

⁴ <http://www.weesziekten.be/symposiumfr.htm>

⁵ <http://www.maladiesrares.be/symposiumfr.htm>

⁷ This section has been written with information from the section on Belgium in the *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp35-45).

⁸ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. Revision 2005* (p8).

At the end of December 2008, 31 orphan drugs were eligible for reimbursement in Belgium (including two products that do not have EMA orphan drug status, but that are reimbursed for an orphan indication) for a total of 35 orphan indications⁹. Orphan drugs are fully reimbursed; although for some of them reimbursement depends on prescription by specialists belonging to one of the recognised centres that provide treatment.

In normal circumstances, the specialist (affiliated to a recognised centre or a hospital for a certain disease) first obtains the approval of a Medical Advisor of the patient's sickness fund to prescribe the medicine. The Medical Advisor is able, but is not obliged to, request the advice of a "College of Medical Doctors for Orphan Drugs" (CMDOD). In practice, all sickness funds have agreed to refer all requests to the CMDOD if one exists. Separate Colleges exist for separate products and the DRC decides whether or not a College is established. At the end of April 2009, there were 18 colleges for 31 orphan drugs. Individual reimbursement decisions are made on a case by case basis by the CMDOD and are valid for a 12 month period¹⁰.

The Law of 1 May 2006 provides for Compassionate Use programs (in case of a medicinal product without a MA in Belgium), or Medical Need programs (in case of a medicinal product with a MA in Belgium but for another indication)¹¹. A last possibility for non-reimbursed pharmaceutical products is reimbursement by the Special Solidarity Fund (SSF). Conditions for Compassionate Use or reimbursement through the SSF are defined by law. In 2007, orphan drugs accounted for about 35% of the SSF's total budget.

Specialised social services

Facilities for respite care and therapeutic recreational programmes are under investigation but do not currently exist in a structured fashion for rare diseases. Governmental measures for the integration of handicapped persons already exist in Belgium by means of social and financial support.

B.1.2.2 New initiatives and incentives in 2009

National plan for rare diseases

A hearing on Rare Diseases and Orphan Drugs was held at the Belgian Parliament on 13 January 2009 which gave official recognition and a budget for the Rare Diseases and Orphan Drugs Fund. In February 2009, the Fund for Rare Diseases and Orphan Drugs presented draft work plans on several topics envisaged to become priorities of the Belgian national plan.

Five workgroups were put in place to consider:

1. data collection regarding rare diseases (Orphanet/registries),
2. financial aspects (broad approach),
3. information services/ awareness building,
4. coordination of rare disease patient care (expert centres)
5. the 2009 EPPOSI symposium on rare diseases to be held in Belgium.

During the summer of 2009 a new working group dedicated to "Access to orphan drugs" started its activities. The Fund for rare diseases and orphan drugs also hired two scientific journalists and a consultancy firm to aid in the development of the national plan.¹²

Sources of information on rare diseases and national help lines

The FAMHP (Federal Agency for Medicines and Health Products) developed an interactive website in collaboration with Pharma.be and the Belgian ethical committees. The website is aimed at ethical committees, industry and the FAMHP in order to provide on line registration, approval and follow-up of clinical trial dossiers in Belgium. The website is in a test phase. The FAMHP also intends to develop a Belgian website/portal for the general public in the future. The site would be similar to the European IFPMA-portal and will be in line with the transparency position with relation to clinical trials¹³.

⁹ KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (p39).

¹⁰ KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp43-44).

¹¹ KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (p40).

¹² www.weesziekten.be / www.maladiesrares.be

¹³ "Joint Position on the disclosure of clinical trial information via clinical trial registries and databases", 10th of November, 2009, www.ifpma.org/clinicaltrials.

Guidelines

Two new conventions were written by the NIHDI for haemophilia and chronic renal diseases.

National rare disease events

RaDiOrg Belgium participated in the organisation of Rare Disease Day 2009 in Belgium: Princess Astrid gave her support to the initiative and acted as patron of the event. A symposium was held on 30 October 2009 by the NIHDI on '5 Years of Colleges for Orphan Drugs'.

Hosted rare disease events

EPPOSI organised two workshops in 2009 in Brussels in the field of Rare Diseases and Orphan Drugs: the EPPOSI Workshop on Registries for Rare Disorders (18-19 March 2009) and the 10th EPPOSI Workshop on Partnering for Rare Diseases Therapy Development took place 26-27 October, 2009. The EC European Patients' Forum Conference was held on the 25 March 2009 in Brussels. The EuroGentest Symposium on Accreditation and Quality was held in Leuven on 18-19 June 2009. The TREAT-NMD/NIH International Conference was held in Brussels (17-19 November 2009).

Orphan drug availability

A study "*Policies for Orphan Diseases and Orphan Drugs*¹⁴", compiled by the Belgian Health Care Knowledge Centre, was published in June 2009. This is a comprehensive English-language report that compares the Belgian orphan drug reimbursement policy with other countries, estimates the current budget impact of orphan drugs, forecasts the expected future budget impact, and offers recommendations for policy makers concerning orphan drugs. In Belgium 31 orphan drugs are currently reimbursed, two of which do not have orphan drug status, but are nonetheless reimbursed for an orphan indication¹⁵.

A symposium was held on 30 October 2009 by the NIHDI on '5 Years of Colleges for Orphan Drugs'.

B.1.3 BULGARIA

B.1.3.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Bulgaria accept the definition of a prevalence of no more than 5 in 10'000 individuals.

National plan 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). Bulgaria's National Plan for Rare Diseases is currently active and consists of nine priorities targeting all rare diseases:

- Collection of epidemiological data for rare diseases in Bulgaria by creation of a national register;
- Improvement of the prevention of genetic rare diseases by enlarging the current screening programmes;
- Improvement of the prevention and diagnostics of genetic rare diseases by introducing new genetic tests, decentralisation of the laboratory activities and easier access to medico-genetic counselling;
- Integrative approach to the prevention, diagnostics, medical treatment and social integration of patients and their families;
- Promotion of the professional qualification of medical specialists in the field of early diagnostics and prevention of rare diseases;
- Feasibility study on the necessity, possibility and criteria for the creation of a reference centre for rare diseases of functional type;
- Organisation of a national campaign to inform society about rare diseases and their prevention;
- Support and collaboration with NGOs and patient associations for rare diseases;

¹⁴ Link to the report: http://www.kce.fgov.be/index_en.aspx?SGREF=5211&CREF=13651

¹⁵ *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (p39).

- Collaboration with the other EU members.

The total budget of the plan is around 22.1 million Bulgarian leva (€11.3 million): this includes the cost of provision of clinical services for rare disease patients. Funding for rare disease policies is also provided by the Ministerial Order 34 for expensive treatments and the National Health Insurance Fund.

Centres of expertise

Currently, there is no official designation procedure for centres of expertise for rare diseases in Bulgaria. The national plan will carry out a feasibility study on the necessity, possibility and criteria for the creation of a centre of expertise for rare diseases. However, there are several academic centres that are specialised as centres of research, treatment and management for rare diseases, i.e. cystic fibrosis, mucopolysaccharidosis, Gaucher disease and neuromuscular diseases. Treatment with orphan drugs is reimbursed in these centres, which also manage the provision of very expensive orphan drugs.

Neonatal screening policies

Currently, mass neonatal screening for congenital hyperthyroidism and phenylketonuria are performed in Bulgaria. One of the national plan's priorities is to enlarge the current screening programs.

Registries

Two national registries concerning rare diseases have been identified: the National Registry of Patients with Thalassaemia major and the National Cancer Registry. Bulgaria also contributes to the EURO CARE CF and TREAT-NMD European registries.

National alliances of patient organisations and patient representation

The National Alliance of People with Rare Diseases (NAPRD) in Bulgaria is an umbrella organisation of 24 rare disease patient groups. It aims to create a link between the people with rare diseases and the representatives of the social and healthcare system. The Alliance works for the right to timely and equal medical care. The organisation also lobbies for the creation of adequate laws in the field of the protection of the rights of the people with rare diseases.

Public funding is available for national patient organisations in Bulgaria, such as the NAPRD. Patient representatives are members of the management board of the National Health Insurance Fund, the committee for transparency at the Ministry of Health and the national consultative committee on rare diseases.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Bulgaria, currently hosted by the Information Centre for Rare Diseases and Orphan Drugs (ICRDOD). This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. The ICRDOD is a free educational and informative service in Bulgarian and English, providing personalised replies to requests from patients, families and medical professionals. It operates a multilingual website (www.raredis.org) and a rare disease help line - (032) 57 57 97.

ICRDOD¹⁶ is a project and activity of the Bulgarian Association for Promotion of Education and Science (BAPES¹⁷) - a non-government non-profit organisation, registered under the Bulgarian law on legal persons with non-profit purposes in 2003.

National rare disease events

Every January, there is an annual meeting of the Consultants of the Information Centre for Rare Diseases and Orphan Drugs (ICRDOD). In 2010, ICRDOD will launch an annual national conference on rare diseases.

Hosted rare disease events

Bulgaria organised and hosted in 2005, 2006, 2008 and 2009, the annual "Eastern European Conference on Rare Diseases and Orphan Drugs".

Research activities and E-Rare partnership

In Bulgaria, there is no specific call for rare diseases at the national fund for research, although rare disease related projects can apply. Bulgaria is not currently a partner of E-Rare.

¹⁶ <http://www.raredis.org/>

¹⁷ <http://bapes.raredis.org/>

Participation in European projects

Bulgaria participates in the following European Reference Network for rare diseases: Dyscerne. Bulgaria participates in the following European rare disease research project: EUROGLYCANET. Bulgaria contributes to the following European registries: EUROCARE CF and TREAT-NMD. Bulgaria contributes to the EUROPLAN project.

Orphan drug committee and incentives

A specialised committee at the Ministry of Health is responsible for decisions concerning the reimbursement of orphan drugs in Bulgaria. It is expected, that from 2010, orphan drugs will be supplied by the National Health Insurance Fund.

Orphan drug availability

Orphan drugs in Bulgaria are available through two mechanisms: 1) the national positive reimbursement drug list (appendix 3 and 4 of this list gives a list of drugs for rare diseases that should be 100% reimbursed by public resources); 2) Ministerial Order 34 for expensive treatments: this Order defines a list of rare diseases, drugs and places for diagnosis and treatment. Several pharmaceutical companies donate orphan drugs on a volunteer basis in the country.

Aldurazyme, Exjade, Fabrazyme, Glivec, Litak, Myozyme, Naglazyme, Revatio, Somavert, Tasigna, and Ventavis are registered and reimbursed in Bulgaria.

Specialised social services

Respite care services and therapeutic recreational programmes are provided in certain medical centres in Bulgaria and are partially reimbursed by the National Health Insurance Fund.

B.1.3.2 New initiatives and incentives in 2009**National plan for rare diseases**

The National Plan for Rare Diseases – genetic disorders, congenital malformations and nonhereditary diseases is, as of 2009, in action and being implemented.

Centres of expertise

In May 2009, The Bulgarian Association for Promotion of Education and Science launched a new initiative, a highly specialised medical centre for rehabilitation and education of people with rare diseases "RareDis". The main idea is to upgrade the services of the Information Centre for Rare Diseases and Orphan Drugs, by launching a tertiary-level rehabilitation centre, aimed at improving the quality of life of people with rare diseases.

New information services on rare diseases and orphan drugs

Two new sections, "Registries and Statistics" and "Frequently Asked Questions (FAQ)", have been added to the www.raredis.org site, where epidemiological data about the rare diseases in Bulgaria and the EU along with lists of orphan drugs with market authorisation are available along with basic definitions and guidelines concerning rare diseases.

National rare disease events

On 23 February 2009 a press-conference was held at BTA. Representatives of the National Alliance of People with Rare Diseases, the Information Centre for Rare Diseases and Orphan Drugs, and patient organisations attended this event. On 28 February 2009 local activities were organised in 5 of the largest cities in Bulgaria (Sofia, Plovdiv, Pleven, Stara Zagora and Sliven). The day ended with a charity concert at the National Palace of Culture in Sofia. Bulgaria's First lady Mrs Zorka Parvanova was the official patron of all the events.

On 10 July 2009 a meeting "How to learn to live with a disease" with Mrs. Madlen Algefari was held in Plovdiv. The event was organised by the Association of HAE Patients, the Information Centre for Rare Diseases and Orphan Drugs and the National Alliance of People with Rare Diseases.

On the occasion of the First School Day (15 September 2009) patient associations from the National Alliance of People with Rare Diseases organised a procession with the motto "For a fair chance for our

children". The initiative aimed to draw the attention of society and the state to patients with rare diseases and to eliminate discrimination concerning their medical treatment.

Hosted rare disease events

In 2009 the Eastern European Conference on Rare Diseases and Orphan Drugs was supported and co-funded by a grant from the European Union's Public Health Programme.

B.1.4 CYPRUS

B.1.4.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Cyprus accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Cyprus, though steps are being made to establish a National Committee for Rare Diseases.

Centres of expertise

There are currently no official designated centres of expertise for rare diseases in Cyprus. However, the Cyprus Institute of Neurology and Genetics operates as a centre of research, treatment and management for various neurological and genetic conditions. The Clinical Genetics Clinic, located both at the Cyprus Institute of Neurology and Genetics and Archbishop Makarios III Hospital, is involved in the management of over 2000 patients and their families living with or at risk of a genetic condition in Cyprus. The Cyprus Thalassaemia Centre is the main centre for screening (neonatal and childhood), counselling and management of thalassaemia on the island.

Registries

Several registries have been formed by patient organisations at various genetics clinics. Cyprus participates in the EUROCARE CF European registry.

Neonatal screening policy

There are schemes for neonatal screening, which include screening of phenylketonuria, congenital hyperthyroidism and Duchenne Muscular Dystrophy.

National alliances of patient organisations and patient representation

Although there is currently no national alliance for rare disease patient organisations, such an organisation, when created, will be eligible for annual funding. There is an effort to create a national alliance of rare disease patient organisations.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Cyprus, currently hosted by the Archbishop Makarios II Medical Centre Genetic Department. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

Information on rare diseases is also published by Gene Net Cyprus¹⁸, a project that aims to create a network for genetic diseases bringing together health professionals patients and families. The project has produced trilingual leaflets on genetic conditions in Cyprus: 6 leaflets were published in English, Turkish and Greek. All these documents are available on the new website www.genenet.org.cy/ which provides links to Orphanet.

¹⁸ <http://www.genenet.org.cy/>

National rare disease events

The Cyprus Institute of Neurology and Genetics (CING) has organised or co-organised meetings and conferences on rare disease themes.

Hosted rare disease events

The most recent international events organised or co-organised by The Cyprus Institute of Neurology and Genetics (CING) were: the Third Meeting of the EuroMyasthenia Network (December 2008); the Second European Symposium on Rare Anaemias (13-14 March, 2008); the Thalassochip Workshop (20 June 2008); the First International Conference of the Cyprus Society of Human Genetics (3-4 October 2008); the Romania and Cyprus Information Society - A mini guide to advances i2010 (31 October 2008).

Research activities and E-Rare partnership

Funding opportunities for rare disease research are offered by the Cyprus Research Promotion Foundation and the Cyprus Institute of Neurology and Genetics. Cyprus is not currently a member of E-Rare and does not participate in their calls.

Participation in European projects

Cyprus participates in the following European Reference Networks for rare diseases: Dyscerne, ENERCA and TAG. Cyprus participates in the following rare disease research projects: EUROPEAN LEUKEMIA NET, LEISHMED and MYELINET. Cyprus contributes to the following European registry: EUROCARE CF. Cyprus contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

Reimbursement is available for the compassionate use of orphan drugs.

Specialised social services

No specific activity reported.

B.1.4.2 New initiatives and incentives in 2009**National plan for rare diseases and related measures**

The Minister of Health of the Republic of Cyprus, Christos Patsalides announced on 28 February 2009 that in order to coordinate the best possible existing services for treating rare diseases, and to develop research activities, the Ministry would establish a National Committee for Rare Diseases and apply a strategic plan for rare diseases. The committee will be responsible for key activities such as establishing a registry of rare diseases in Cyprus, the organisation of preventive programmes and the upgrading and expansion of centres for diagnosis, therapy and treatment. The plan will also include the development of research activities (in collaboration with the pharmaceutical industry) in efforts to offer greater support to patients and their families.

Education and training

In 2009 a series of lectures on rare diseases were held for paediatric interns and trainee nurses. Paediatric interns also received training concerning rare genetic diseases and supervision at the Clinical Genetics Clinic (CIC).

National rare disease events

For Rare Disease Day 2009 a press conference was organised by the Ministry of Health of Cyprus and the Thalassaemia International Federation, with the collaboration of rare disease associations. A Telethon was organised by CING in collaboration with the Muscular Dystrophy Association of Cyprus (15-17 June 2009): this event helps raise awareness concerning genetic and neurological diseases and €265,000 were raised to finance CING research activities in the field and support the association. Several articles in newspapers/magazines and television/radio programmes helped increase awareness of rare genetic diseases and related current efforts and initiatives.

Hosted rare disease events

The 9th Congress of the Mediterranean Society of Myology was held on 20-22 March in Nicosia.

B.1.5 CZECH REPUBLIC **B.1.5.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in the Czech Republic accept the European Orphan Drug Regulation definition of a prevalence no more than 5 in 10'000 individuals.

National plan for rare diseases and related measures

Discussions to develop a national plan for rare diseases are underway at the Ministry of Health since early 2009. The Czech National Strategy for Rare Diseases (2010-2020) will build upon existing initiatives in the country as well as establishing new components. The Czech Republic already has a number of rare disease resources and activities in place, including reference centres. Currently, there is no specific funding for rare disease measures: all expenditures are financed from the current national health insurance.

Centres of expertise

There are specialised centres for rare diseases, two of which are the national centre for the diagnosis and treatment of Gaucher disease, and for cystic fibrosis. The value of these hubs 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 drugs is reimbursed in these centres and these centres manage the provision of very expensive orphan drugs. The organisation of additional specialised centres will be a part of the Czech strategy. Another important and internationally recognised institution is the Institute for Inherited Metabolic Disorders which deals centrally with these diseases at national level.

In terms of diagnostic services, there are over 50 molecular laboratories in the country. Together, they offer diagnostic tests for more than 492 different rare diseases. Genetic counselling exists for all families at risk. Clinical genetics services are available throughout the entire country, with every major district having such services, both at private and/or state based levels. Genetic services are carried out in compliance with all international professional standards and are fully covered by the national health insurance system.

Registries

The Czech Republic contributes to some European registries such as EURO CARE CF and TREAT-NMD, as well as the SCNIR international registry.

Neonatal screening policy

Neonatal screening is routinely performed for phenylketonuria, congenital adrenal hyperplasia and congenital hypothyroidism. Pilot studies have been conducted for 9 other metabolic disorders since 2005 (hyperphenylalaninemia; maple syrup urine disease; glutaric aciduria type I; medium-chain acyl-CoA dehydrogenase deficiency; long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency; carnitine palmitoyl transferase 1 deficiency; carnitine palmitoyl transferase 2 deficiency; and carnitine acylcarnitine translocase deficiency) and for cystic fibrosis since 2006. These tests were adopted nationally by the as of 1 October 2009.

National alliances of patient organisations and patient representation

There is currently no national alliance of rare disease patient organisations in the Czech Republic. Creating an alliance for rare disease patient groups is a provision of the national strategy being developed, together with the Coalition for Health Association. However, there are over 40 patient organisations in the Czech Republic. Some groups benefit from aid from the Ministries of Health and of Labour and Social Affairs; the system will be streamlined under the Czech strategy for rare diseases.

Sources of information on rare diseases and national help lines

Since 2006 there is a dedicated Orphanet team in the Czech Republic, currently hosted by the University Hospital Motol and the Second School of Medicine of Charles University Prague. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. There is no official information centre for rare diseases in the Czech Republic other than Orphanet. A website and a help line for rare diseases are under consideration. Patient organisation web sites are one of the few national sources of information for rare diseases in the Czech language. A web based information service on neonatal screening is available (<http://novorozenecky-screening.cz>).

National rare disease events

No specific reported activity.

Research activities and E-Rare partnership

Rare diseases research is conducted under several funding bodies: the internal grant agency of the Czech Ministry of Health (www.mzcr.cz), the grant agency of the Czech Republic (www.gacr.cz), and the grant agency of the Charles University Prague (www.gauk.cz). Currently 15 different research projects in the field of rare diseases are registered with Orphanet, focusing on 30 different rare disorders. At least three projects are targeting specific genes. The Czech Republic is not currently a partner of the E-Rare research programme on rare diseases.

Participation in European projects

The Czech Republic participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, EPNET, EPI, ENERCA Paediatric Hodgkin Lymphoma Network, NEUROPED and PAAIR. The Czech Republic participates in the following European rare disease research projects: CLINIGENE, ENCE PLAN, EUMITOCOMBAT, EURO-PADNET, EUROCARE-CF, EUROPEAN LEUKEMIA NET, EUROAGENTEST, EUROGLYCANET, HUE-MAN, MYORES, NEUROSIS, PNSEURONET, RD PLATFORM, SARS/FLU VACCINE, SCRIN-SILICO and SIOPEN-R-NET. The Czech Republic contributes to the following European registries: EUROCARE CF, EUROCAT and TREAT-NMD. The Czech Republic is also a partner country of the Severe Chronic Neutropenia International Registry (SCNIR), monitoring the clinical course, treatment, and disease outcomes in patients with severe chronic neutropenia.

The Czech Republic also participates in many international-level activities including ERNDIM (a consortium for quality assessment in biochemical genetics for rare disease) and EUROPLAN, developing guidelines for national rare disease plans.

Orphan drug committee and incentives¹⁹

SUKL, the State Institute for Drug Control, is the regulatory body in the Czech Republic responsible for the regulation and surveillance of human medicinal products and medical devices, including orphan drugs. According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*, the Czech Republic has a number of mechanisms in place to encourage orphan drug development. For example "administrative fees are not charged for applications for the registration of medicinal products or for an amendment, extension or transfer of registration of a medicinal product or for authorisations for parallel import of a medicinal product, if the application concerns a medicinal product included in the register of orphan medicinal products under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.

"Under §65(2)(b) of Act No 79/1997 Coll. On medicines, amending and supplementing other acts, as amended, the State Institute for Drug Control may refrain from recovering costs where these concern operations which are in the public interest or may have especially important implications for the wider population. These operations include applications for: authorisation/registration of clinical assessments of medicinal products and notification to the submitter of additions to the records in cases concerning the evaluation of an orphan medicinal product, and consultation and opinions on such applications; application for registration of an orphan medicinal product and application for amendment, extension or transfer of

¹⁹ This section is written with information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*. Revision 2005 (pp9-10)

registration or application for authorisations for parallel import of an orphan medicinal product and consultation and opinions on applications concerning orphan medicinal products.

“Under §26d(1) of Act No 79/1997 Coll. On medicines, amending and supplementing other acts, as amended, the State Institute for Drug Control may, in the case of orphan medicinal products in justified cases meeting the conditions laid down by decree, allow the registration of a medicinal product or the placing on the market of individual batches of a medicinal product even where the data are indicated on the packaging in a language other than Czech.”²⁰

Orphan drug availability

There are 51 registered orphan medicines of which 28 are currently distributed on a centre basis and are completely reimbursed. The country has compassionate use programme for specific orphan drugs, and therapeutic programmes that allow for the use of certain non-authorised medicinal products, usually coordinated by specific centres. Ad hoc committees exist for very expensive orphan drugs, which are centre-based. Not all orphan drugs are reimbursed. In 2008 a cap to the co-payment by patients of 5000 CZK (€187) per year was established for prescription medicines.

Specialised social services

A few patient organisations also offer recreational services, such as summer camps for children or rehabilitation/therapeutic weekends for adult patients. These are usually fully reimbursed by the Ministry of Social Affairs. The *Act on social services for people with disabilities* came into force in 2007, improving the access to social services for rare disease patients: these schemes are reimbursed and are fully funded from social insurance and are coordinated by the Ministry of Social Affairs.

B.1.5.2 New initiatives and incentives in 2009

National plan for rare diseases and related measures

The Czech National Strategy is under negotiation with the Ministry of Health, having developed a working party of expertise to define each element of the plan (2010-2020). A budget is currently being determined for the plan which will be launched in 2010: a dedicated website (www.vzacnenemoci.cz) has been put in place for the plan. As is the case with many EU countries, the Czech Republic has its own distinct language, however, there is a proximity to the Slovakian language that may allow the two countries to share resources within the context of the plan.

Neonatal screening policy

From 1 October 2009 neonatal screening has been expanded to 9 other metabolic disorders (hyperphenylalaninemia; maple syrup urine disease; glutaric aciduria type I; medium-chain acyl-CoA dehydrogenase deficiency; long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency; carnitine palmitoyl transferase 1 deficiency; carnitine palmitoyl transferase 2 deficiency; and carnitine acylcarnitine translocase deficiency) and cystic fibrosis. This measure was accompanied by a new central Ministry of Health-sponsored website for Neonatal Screening. Neonatal screening is now available for 13 disorders (<http://www.novorozenecky-screening.cz/>).

Hosted rare disease events

As was the case with France, the role of EU presidency has served to boost the country's level of activity in the field of rare diseases. Under the term of the Czech EU Presidency that ran from January through June 2009, several conferences and workshops were held. An international conference²¹ took place in Prague (21 May 2009) to address the treatment of rare diseases in relation to EU legislation. This event was devoted to a discussion of the objectives of the EU in the area of diagnosis and treatment of rare diseases and to the respective tasks ascribed to the individual EU member states in the EU Council Recommendation on European Action adopted under the Czech presidency at the meeting of EU27 Ministers of Health in Luxembourg on 9 June 2009. Participants at the conference reviewed the ongoing preparations of the Czech National Strategy for

²⁰ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. Revision 2005 (pp9-10)*

²¹ <http://vzacna-onemocneni.cz/>

Rare Diseases and discussed access to orphan drugs in the country as well as the role of patient organisations in improving access to such advanced treatments.

The 6th European Regional Meeting of the International Society of Neonatal Screening was held in Prague (26-28 April 2009).

B.1.6 DENMARK

B.1.6.1 State of affairs before 2009

Definition of a rare disease

No official definition exists for rare diseases at the moment in Denmark. The National Board of Health tends to define rare diseases as affecting no more than 500 patients in the Danish population. Rare Disorders Denmark and the Danish Centre for Rare Diseases and Disabilities (*Center for små handicapgrupper*²²) define rare diseases as affecting no more than 1'000 patients in the Danish population.

National plan for rare diseases and related measures

There is currently no national plan for rare diseases in Denmark, though Rare Diseases Denmark (the national rare disease alliance) is lobbying for a plan. The Danish National Board of Health launched a special report on rare diseases in 2001 with recommendations for rare diseases in general and 14 specific rare diseases to be cared for at 2 specialised rare diseases centres. These two centres were established in Copenhagen and Aarhus, respectively, dealing mainly with paediatric patients. The report also gave a number of other recommendations which have not yet been implemented.

Current expenditure for rare diseases is within in the general health system budget of the regions and municipalities: there are no dedicated funds for rare diseases, except for the dietary treatment of phenylketonuria which is directly financed from the state budget.

Centres of expertise

There are two centres of expertise for rare diseases in the health care system in Denmark (as mentioned above) at university level plus the established catalogue of referral centres designated by the National Board of Health due to rarity, complexity, multidisciplinary and costly diagnosis of the condition (diseases or procedures)²³.

Neonatal screening policy

National neonatal screening schemes are in place for phenylketonuria, hypothyroidism and adrenal hyperplasia. Neonatal screening to detect hearing impairment was started as a pilot project and is now implemented as a national programme.

Registries

No centralised register for rare diseases currently exists in Denmark, but a number of mainly research based registries and biobanks exist although there is currently no public register of these existing registries and biobanks dealing with rare diseases. The Serum Institute has hosted registry and biobank of all newborn screening blood samples since 1980. The Kennedy Centre maintains biobanks on specific rare disorders as Menkes disease and various genetic eye diseases. All visually handicapped children are registered until the age of 18. Furthermore, several research departments have registries of rare diseases patients. Denmark contributes to some European registries such as EURO CARE CF, EMHG and EUROCAT.

²² www.csh.dk

²³ For more information: *Centres of Reference for RD in Europe: State of the art in 2006 and recommendations of the RDTF* (p.9) <http://www.eucerd.eu/upload/file/Publication/RDTFECR2006.pdf>

National alliances of patient organisations and patient representation

Rare Disorders Denmark is the national alliance of 36 rare disease patient organisations, founded in 1985. In addition there are further 20 other patient organisations for rare disorders. Patient organisations are eligible to receive limited funding from the Ministries of Health and Social Affairs and have an obligation to capacity build in order improve integration of patients in schools and at the work place.

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 the board of CSH and currently holds the chair.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Denmark, hosted by the John F. Kennedy Institute. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

A state-funded information centre on rare diseases, the Danish Centre for Rare Diseases and Disabilities (*Center for små handicapgrupper*²⁴) is in place since 1990 and has a public database containing short descriptions in Danish on rare diseases. The centre provides information, as well as guidance, especially on social issues, and provides contact with patient organisations. The CSH also runs a rare disease help line which provides information and support. The CSH also maintains a database of approximately 400 rare disease patients who are currently without patient organisation representation for their disease. The CSH also contributes to Rarelink.eu, the Nordic website compiling links relating to information on rare diseases.

National rare disease events

On 26 February 2004, Rare Disorders Denmark and The Danish Cancer Society hosted a conference on Orphan Drugs at the Danish Parliament. The conference gathered a wide range of scientists, health care professionals, patient organisations, Danish pharmaceutical and biotech companies, authorities and politicians. The conference illustrated the state of the art in rare diseases research and the need for special initiatives for this domain.²⁵

Research activities and E-Rare partnership

There are no specific programmes for rare diseases research in Denmark and Denmark is not currently an E-Rare partner.

Participation in European projects

Denmark participates in the following European Reference Networks for rare diseases: Dyscerne, EPI, NEUROPED, Paediatric Hodgkin Lymphoma Network, PAAIR and RBDD. Denmark participates in the following European research projects for rare diseases: CILMALVAC, EURHAVAC, EMSA-SG, EUROCRAN, EUROGLYCANET, EUROPEAN LEUKEMIA NET, EMVDA, EUNEFRON, HDLOMICS, HUE-MAN, HUMALMAB, LEISHMED, MMR-RELATED CANCER, MYASTAID, NEUROKCNQPATHIES, NEUROPRION, NM4TB, PULMOTENSION, SPASTICMODELS, SIOPEN-R-NET, SERO-TB, TB TREATMENT MARKER and VACCINES4TB. Amongst others, Denmark contributes to the following European registries: EUROCARE CF, EMHG and EUROCAT. Denmark contributes to the EUROPLAN project.

Orphan drug committee and incentives

The Danish Medicines Agency provides free scientific advice in the development of Orphan Drugs.²⁶ There is currently no committee dedicated to Orphan Drugs and/or rare diseases in Denmark.

Orphan drug availability

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*, there are no specific programmes to facilitate the provision of medicines to rare diseases patients in Denmark. However, on a case by case basis the

²⁴ www.csh.dk

²⁵ <http://www.sjaeldnediagnoser.dk/documents/00105.pdf>

²⁶ This section is written with information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*. Revision 2005 (pp10-11)

Danish Medicines Agency can authorise *“the sale or dispensing of medicinal products that are not marketed in Denmark for other purposes than clinical investigations (cohort or named patient supply). Patients with life-threatening diseases for which there are no well-documented treatment options can be offered experimental treatment (named patient supply only).”*²⁷

Specialised social services

Respite care services are sometimes provided by municipalities. Patient organisations organise informal therapeutic recreational activities and can sometimes receive government financial support. Services are provided and funded by the government to enable help integrate patients with rare diseases into daily life, both at school and work.

B.1.6.2 New initiatives and incentives in 2009

Centres of expertise

In June 2009 public regional hospital departments and private hospitals of the 36 medical specialities applied for designations as specialised regional centres or highly specialised national centres for different rare diseases. The designation is expected in March 2010 and the designation will last for a duration of 3 years where after a revision is due.

Neonatal screening policy

At the start of 2009, health authorities added testing for 15 additional inborn errors of metabolism to the Danish newborn screening programme. Neonatal screening is now available for maple syrup urine disease, ASL, CTD, medium chain acyl-CoA dehydrogenase deficiency, long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency, glutaric acidemia type 1, MMA, PA, MCD, tyrosinemia type 1 and biotinidase defect. Furthermore, the timing for drawing the blood samples (done by heel-prick) will be brought forward from five days to within 48-72 hours following birth, allowing for the earlier intervention and treatment. Neonatal hearing screening was also introduced as a national programme.

National alliances of patient organisations and patient representation

Rare Disorders Denmark has developed a tool, Social Profiles, to promote dialogue between rare disease patients and professionals. The profiles have been developed through a process involving rare disease patient organisations and are currently available for 15 rare diagnoses, with more to come. The profiles are published on the “Rare Citizen” website www.sjaeldenborger.dk.

Sources of information on rare diseases

A government funded 3-year project “Learn to live with a rare disease” will aim at creating a concept for patient education in the field of rare diseases. The project is led by Rare Disorders Denmark in collaboration with the CSH.

A Nordic clinical quality database with information on patients with rare diseases is hosted by the department of clinical genetics at Rigshospitalet in Copenhagen.

National rare disease events

On the occasion of Rare Disease Day 2009 (28 February 2009), Rare Disorders Denmark hosted a series of lectures and talks targeting students and employees in the health sector so as to raise awareness about rare diseases in the medical field. In addition to this Danish candidates for the European Parliament received a letter from Rare Disorders Denmark explaining why European cooperation regarding rare diseases and handicap is so essential, in addition to information on current EU initiatives.

²⁷ This section is written with information from the *Inventory of Community and Member States’ incentive measures to aid the research, marketing, development and availability of orphan medicinal products . Revision 2005* (pp 10)

B.1.7 ESTONIA

B.1.7.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Estonia accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is currently no plan for rare diseases in Estonia and there no preparations for a rare disease plan are currently underway. Rare disease costs are currently included within the general health system budget as there are no specific funds dedicated to rare diseases.

Centres of expertise

There are currently two clinical genetics centres specialising in the diagnosis and treatment of rare diseases in Estonia, Tartu University Hospital and Tallinn Children's Hospital.

Registries

There is currently no national rare diseases registry in Estonia. Estonia participates in the EURO CARE CF European registry.

Neonatal screening policy

For early detection of all developmental disorders, including rare disorders, there is a consensus agreement that all infants and children with any developmental disorders should be referred to one of tertiary children's hospital in Estonia: Children's Clinic of Tartu University Hospital or Tallinn Children's Hospital. Both hospitals have medical genetics services for early detection and prevention²⁸. Early detection or treatment of rare diseases is provided using DNA diagnostics and neonatal screening programmes are in place for phenylketonuria, congenital hypothyroidism and Duchenne and Becker muscular dystrophy since 1995.

National alliances of patient organisations and patient representation

There is currently no national alliance for rare disease patient organisations in Estonia. Support for patients' associations comes from a national budget for *Eesti Patsientide Esindusühing* (Estonian Patients' Associations). In addition there are plans to use funds from the gambling tax for project-based financing of patients' associations.

Patient organisations are represented on the council of the Estonian Health Insurance Fund and grants are available for patient organisations to attend these meetings.

Sources of information on rare diseases and national help lines

Since 2004, there is a dedicated Orphanet team in Estonia, currently hosted by the Estonian Biocentre. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. There is no official information centre for rare diseases in Estonia other than Orphanet and there is no help line for rare diseases.

Education and training

There are special advanced courses for physicians (2-3 courses per year) on rare disorders, aimed at improving the early detection and diagnosis of certain rare diseases (Prader-Willi syndrome, Angelmann syndrome, SMA, Dravet Syndrome, etc).

National rare disease events

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.

²⁸ <http://www.kliinikum.ee/geneetikakeskus/>

Hosted rare disease events

No specific activity reported.

Research activities and E-Rare partnership

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*, *Eesti Teadusfond* (Estonian Science Foundation) supports research on rare diseases at national level on the basis of appropriate applications, but there is no distinction from other projects not related to rare diseases (approximately 600-800'000 EEK available over four years)²⁹. Some projects that involve research on rare diseases are financed by Targeted Financing from the Estonian Government (congenital adrenal hyperplasia, phenylketonuria, Prader-Willi syndrome). Estonia is not currently a partner of the E-Rare Project.

Participation in European projects

Estonia participates in the following European Reference Network for rare diseases: PAAIR. Estonia contributes to the following European registries: EURO CARE CF. Estonia participates in the following European rare disease research projects: AAVEYE, EURAPS, MOLDIAG-PACA and RD PLATFORM. Estonia contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

There is no concrete list of orphan medicines for reimbursement and no specific programmes to facilitate the provision of medicines to rare disease patients. Reimbursement of the cost of medicines to patients comes from joint medical-insurance funds on the basis of *Eesti Haigekassa's* (Estonian Health Insurance Fund) medicine reimbursement budget in accordance with the diagnosis, where the criterion for establishing the selection of corresponding diagnoses is not so much the incidence of the disease as its seriousness and mortality, the possibility of an epidemic, the need for alleviating the associated pain or other humane considerations, its chronic nature together with the impairment caused to the quality of life, and the match with the financial possibilities of the medical insurance scheme. Children under the age of 4 are entitled to 100% drug reimbursement. Rare diseases are also included in the catalogue of described diagnoses for reimbursement.

Specialised social services

The Estonian Agrenska Foundation, founded by several sources including Agrenska Sweden, the University of Tartu, the Estonian Board of Disabled People, the Tartu University Hospital Foundation, and *Stenstroms Skjortfabrik Eesti* provides counselling and care for families with children with rare disorders. Like its Swedish counterpart, the Estonian Agrenska Foundation targets the family, offering a family-centred counselling system that should be able to cover all of Estonia in the coming future. The service focuses on families of children with disabilities, offering psychosocial, educational and medical information and support. The reimbursement of these services varies from full reimbursement to partial payment by patients. Every family with a disabled child is entitled to a fixed sum per year from the government for respite care services. The Maarja Village Foundation (founded by the Tartu Toome Rotary Club) runs a residential centre which accommodates up to 33 young people with mental disabilities. Therapeutic recreational programmes exist for certain rare diseases (Prader Willi for example) and are provided by patient organisations and are partially reimbursed. Services exist to promote the integration of patients with disabilities in schools and in the work place and are financed by the government.

²⁹ This section is written with information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*. Revision 2005 (pp 11)

B.1.7.2 New initiatives and incentives in 2009

Education and training

In 2009 the number of number of advanced courses on rare disorders organised by the Department of Continuing Education at the Tartu Medical University increased, due to rising interest in the subject. These were held on 12-13 November 2009 and further courses are planned in 2010.

National rare disease events

The annual meeting of the Estonian Society of Human Genetics was held on 23-24 October 2009 and featured talks concerning rare diseases (i.e. genetic causes of hereditary hearing loss in children in Estonia).

B.1.8 FINLAND

B.1.8.1 State of affairs before 2009

Definition of a rare disease

There is no official definition for rare diseases in Finland. The definition in most Nordic countries of rare disease is a disease with a prevalence of no more than 100 people per 1,000,000 inhabitants. This definition has been used for practical purposes. At present the parties involved in the field of rare diseases are gradually introducing the common EU definition: in matters concerning orphan drugs Finland already applies the Orphan Drug regulation definition of no more than 5 in 10'000 EU inhabitants.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases, though the first steps have been taken in the process. Discussion between the Finnish Ministry of Social Affairs and Health, the National Institute for Health and Welfare and the Harvinaiset Network for Rare Diseases about co-operation in this matter are under way. Current expenditures for rare diseases fall within the general health system budget with additional ad hoc funding on the basis of rare disease projects.

Centres of expertise

There are currently no official centres of expertise for rare diseases in Finland. However, the departments for different medical specialities in university hospitals act as reference centres for rare diseases, and certain university hospitals specialise in paediatric operations related to rare diseases, such as congenital heart defects, cleft lip or palate, craniofacial malformations, glaucoma, retinoblastoma and biliary atresia according to the decree of the Ministry of Social Affairs and Health (767/2006) based on a law for specialised medical treatment (1062/1989).

Registries

There are two legally specified registries concerning rare diseases: the Finnish register of congenital anomalies and the Finnish register of visual impairment. In addition, rare inherited cancers are included in the Cancer Register. Finland contributes to European registries including TREAT-NMD and EUROCAT.

Neonatal screening policy

All newborns are screened for hypothyroidism. In addition to this, paediatricians organise screening for phenylketonuria in newborns of non-Finnish origin.

National alliances of patient organisations and patient representation

There is currently no organised national alliance of rare disease patient organisations in Finland.

There is no official or unofficial body representing rare diseases patients or patient organisations in social decision making. Individual patient organisations may be consulted on their opinion about forthcoming legislation, but the bodies to be consulted on such matters have not been defined. The Ministry of Social Affairs and Health has a council of the disabled which represents all groups of the disabled including rare disease patients.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Finland, currently hosted by the Medical Genetics Department of Vaestoliitto, the Family Federation of Finland. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

Established in 1993, the Harvinaiset Network is a network of non-governmental, non-profit organisations which provides information on rare diseases and services, raises awareness of the needs of people with rare diseases and organises courses for patients and their families. Harvinaiset also maintains an internet portal with information about rare diseases in Finnish and is a part for the Rarelink project, a Nordic link collection with contact details for those looking for information on rare diseases. This network is funded by RAY, Finland's Slot Machine Association, as are other patient organisations offering web-based information.

Most providers of web-based information on rare diseases have phone or web answering services and a possibility to make on-site visits: they provide general information about diseases, contacts for treatment, advocacy, rehabilitation, psychological support and support from patient organisations or peer support groups.

National rare disease events

There is no tradition of annual rare disease events in Finland, but the Harvinaiset Network organises every other year a seminar promoting co-operation between stakeholders in Finland.

Research activities and E-Rare partnership

Research in the field of rare disease has been focused on diseases of so-called Finnish Disease Heritage; nearly 40 rare inherited diseases are over-represented in Finland in comparison to other populations. Most of the genes associated with these diseases have been mapped and cloned in Finland during the last 20 years. Also rare forms amongst more common ones, like hereditary nonpolyposis colorectal cancer (HNPCC), hereditary connective tissue diseases, and long QT syndrome, have been studied.

On the whole there are many sources that fund research programmes in Finland, including research into rare diseases. Medical research is funded by means of a special State contribution for university hospitals; the total amount in 2008 was around 337 million FIM. Part of this funding for research goes towards research on orphan medicinal products. Five universities with medical faculties also have programmes of their own. The Finnish Academy and private foundations also finance rare disease research programmes. Finland is not currently a partner of the E-Rare project.

Participation in European projects

Finland participates in the following European Reference Networks for rare diseases: Dyscerne, EPNET and EPI. Finland participates in the following European research projects for rare diseases: BNE, CLINIGENE, EUGINDAT, EUMITOCOMBAT, EURAPS, EUREGENE, EURO BONET, EURO GENTEST, EUROPEAN LEUKEMIA NET, GEN2PHEN, LYMPHANGIOGENOMICS, NEUROPRION, PEROXISOMES, PROTHETS, PULMOTENSION, TREAT-NMD and RD PLATFORM. Finland contributes to the following European registries: TREAT-NMD and EUROCAT. Finland contributes to the EUROPLAN project.

Orphan drug committee and incentives³⁰

The Finnish Medicines Agency (*Fimea*, which before the 1st November 2009 was known as the National Agency for Medicines *Lääkelaitos*) gives free administrative and scientific advice to bodies developing orphan medicinal products. Furthermore, the special status of orphan medicinal products has been taken into account in inspection and authorisation procedures. *Fimea* also maintains a registry of clinical trials.

The National Technology Agency *Tekes* (*Teknologian kehittämiskeskus*) launched the Drug 2000 programme at the beginning of 2001, an initiative which ended in 2006: the objective of this programme was to boost drug development, to create new (and expand existing) research networks, to enhance the competitiveness of service units and enterprises in the field of research and to stimulate new international business in the medical field. The programme was also financed by the Finnish Academy and Sitra, with a total annual funding of 100-150 million FIM.

³⁰ This section was written with information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. Revision 2005* (pp11-12)

The evaluation criteria are the same for all medicinal products; no exceptions for orphan drugs are stated in the Health Insurance Act. However, the health economic evaluation is not always required from the marketing authorisation holder of orphan drug if justified by the applicant.

Orphan drug availability

According to the 2005 *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products* in the section concerning Finland, "all medicines with a wholesale price approved by the Pharmaceuticals Pricing Board are automatically entitled to reimbursement under the basic refund category. The basic reimbursement is currently 42% of the purchasing price. In certain diseases or conditions, lower (72%) or higher (100%) special reimbursement is available.

"A reasonable wholesale price refers to the maximum price at which the product may be sold to pharmacies and hospitals. The holder of marketing authorisation must be able to justify the reasonableness of the proposed wholesale price for a medicinal product that is to serve as a basis for the reimbursement payments. The application must include a detailed, comprehensive assessment of the cost of the drug therapy and the benefits expected to be gained thereby. Moreover, the application must include an evaluation of the product in relation to alternative drug treatments and other therapies. The application must also include the validity period of the pharmaceutical patent or a supplementary protection certificate, an estimate of the sales volume and number of users of the product over the next three years as well as the approved price and ground for reimbursement of the product in other EEA countries.

"Applications concerning medicinal products containing a new active substance must contain a health economic evaluation. When considering the reasonableness of the proposed wholesale price, the Pharmaceuticals Pricing Board takes into account the cost of the drug therapy and the benefits to be gained from its use as regards both the patient and the overall health care and social costs. The Pricing Board will also consider the cost of the treatment alternatives, the prices of comparable medicinal products and the price of the medicine in question in other EEA countries. Manufacturing, research and development costs are also taken into consideration when making a decision on application, if they are considered relevant by the applicant, as are the funds allocated for reimbursement payments.³¹"

Specialised social services

Respite care services are available and local authorities are responsible for their provision, but some are equally provided by private institutions: patients and families often have to provide co-payment. Therapeutic recreational programmes are available under different forms and patients have to partially pay for these services though some funding can be provided by RAY. Services for transport, modifications for housing arrangements, day-care, interpreter (sign language etc), personal assistants etc are available for those with handicaps by local authorities, provided for by the law 380/1987 in 1987 (updated 1267/2008 and 981/2008).

B.1.8.2 New initiatives and incentives in 2009

National plan for rare diseases and related actions

Finland participates in a project (running from 2009 to 2010) to publish a report concerning cooperation possibilities between Nordic countries in the field of rare diseases. The project is supported by the Nordic Council of Ministers, and is entitled "*Kartläggning av möjliga nordiska samarbetsområden anknutna till små och sällsynta diagnosgrupper*" ("Report on possibilities for co-operation between the rare disease groups in Nordic Countries"). The goal of the project is to create recommendations for Nordic cooperation in all fields: medical, social, psychological and pedagogical.

Neonatal screening policy

The Ministry of Social Affairs and Health decided in 2009 to expand newborn screening for: Congenital adrenal hyperplasia (CAH), MCAD deficiency, LCHAD deficiency, Glutaricaciduria type 1 (GA1), and phenylketonuria.

³¹ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. Revision 2005 (p12)*

National alliances of patient organisations

There has been recent discussion amongst patient organisations concerning the creation of a national rare disease alliance.

Sources of information on rare diseases and national help lines

There are three new portals for patient organisations at the national level for health related information:

- the www.harvinaiset.fi portal provides rare diseases related information (an updated site will be launched in 2010);
- www.terveysuomi.fi;
- www.toimintasuomi.fi : a site providing patient organisation related information;
- the “Yksi ovi – monta ikkunaa” project’s web portal also provides rare diseases related information.

Possibilities for creating links between these portals will be discussed in 2010.

National rare disease events

Rare Disease Day 2009 was not celebrated nationally. A second joint meeting of patient organisations for rare diseases took place on 26-27 September 2009 in Helsinki. Swedish Orphan International, together with the Finnish Paediatric Society and the Finnish Society for Rheumatology, organised a Rare Disease Day conference on 9 October 2009 for Finnish doctors to increase their awareness and knowledge of rare diseases and orphan drugs and their status in the health care system.

Specialised social services

Patients with a rare disease, as well as all others with a severe disability, were given new possibilities 2009. The legislation for personal assistance was updated as of 1 September 2009. This update follows the principles of Independent Living Movement. Personal assistance for persons with a severe functional disability is free of charge. Besides the support in the daily living, work and education this now also includes assistance with participation in recreational activities, social activities and education. The service is financed by the municipalities.

B.1.9 FRANCE

B.1.9.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in France accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

France was the first EU country to put in place a comprehensive rare disease plan (2004-2008) with allocated funding. The axes of this plan were to:

- Increase knowledge of the epidemiology of rare diseases;
- Recognise the specificity of rare diseases;
- Develop information for patients, health professionals and the general public concerning rare diseases;
- Train professionals to better identify rare diseases;
- Organise screening and access to diagnostic tests;
- Improve access to treatment and the quality of healthcare provision for patients;
- Continue efforts in favour of orphan drugs;
- Respond to the specific needs of accompaniment of people suffering from rare diseases and develop support for patients’ associations;
- Promote research and innovation on rare diseases, notably for treatments;
- Develop national and European partnerships in the domain of rare diseases.

The first national plan provided for the official recognition and evaluation of centres of expertise (called Centres of Reference in France); new rare disease research networks and research projects are supported by a national call for proposals; information on rare diseases, orphan drugs and related fields was developed by Orphanet (established in 1997, but whose budget was increased significantly thanks to the Plan) and also by help lines and rare diseases identity cards. Several new information products were developed such as emergency guidelines and good practice guidelines for rare diseases (which are posted on the Orphanet website) and emergency cards to be kept by the patients in case of need.

Funding for this plan was provided within the general health system budget with ad hoc funding on the basis of rare disease projects. The funding allocated to rare disease actions is identifiable (over €100 million for the four year period).

A second plan under development, along 7 axes including "Health indicators and epidemiology", "Reimbursement and health care coverage", "Information and training", "Organisation of diagnosis and health care", "European and International cooperation", "Targeted medicines" and "Research and Development".

A separate plan is in place for cancers which includes rare cancers: the first ran from 2003-2007 and a second was announced on 2 November 2009 for the period 2009-2013. On 16 May 2008, the French Health Ministry announced a national plan for 2008-2010 aimed at improving the treatment of patients with autism, improving social care for patients and their families and better educating health professionals about this rare disease.

Centres of expertise

The National Rare Diseases Plan (2004-2008) introduced a structured organisation of health care for rare disease patients. A designation process was put into place to name centres of scientific and clinical excellence in the field of rare diseases. By the end of the plan, 131 "Reference Centres" in France were named. These centres have 6 main missions: to facilitate diagnosis and define a course of treatment; to define and publish treatment protocols in collaboration with the *Haute Autorité de Santé* (HAS) and the national health insurance bureau (CNAM); to coordinate research and participate in epidemiological surveillance in collaboration with the French Institute for Public Health Surveillance (InVS); to participate in training and information programmes for health professionals, patients and their families, in collaboration with the National Institute of Prevention and Health Education (INPES); to coordinate networks of health visitors and social workers; to be the contact point for patient organisations and social workers.

A second type of centre were designated in 2008: named "*centres de competences*" these qualified centres are identified by the reference centres and designated by Regional Hospital Agencies (ARH) whose aim is to assume responsibility for treatment and follow-up of the patient close to their home, and to participate in the entirety of the reference centres' tasks. These qualified regional centres ("*centres de competence*") take in charge patients from their region: 500 of these centres have been named corresponding to 1 competence centre per region in each of the large categories of centres of reference.

The reference centres are evaluated over time by the National Consultative Designation Committee (*Comité National Consultatif de Labellisation - CNCL*) first through self-evaluation after 3 years as a designated centre, with an external evaluation at 5 years. The centres have a double role: they are an expert centre for 1 or more diseases and they are a resource centre for patients referred to it.

The National Cancer Institute (*l'Institut National du Cancer - INCA*) published in June 2009 the list of the 11 adult 'rare cancer' Reference Centres designated in 2009. Rare cancers have been initially excluded from the national plan for rare diseases (2004-2008) as a national plan for cancer including measures for rare cancers was already in place.

There are also three designated reference centres for rare handicaps.

Registries

In December 2008, the National Rare Disease Registry Committee designated 6 registries, as part of Axe 1 'Improve Knowledge of Epidemiology of Rare Diseases' of the National Rare Diseases Plan. The Committee is working on how to also designate cohorts and observatories. France contributes to European registries including EUROCAT, EUROHISTIONET, EPI-EPNET, EURECHINOREG, the European central hypoventilation syndrome registry, EUROTRAPS, CHS, EURO CARE CF, ECFS, INFEVERS and TREAT-NMD.

Neonatal screening policy

A neonatal screening programme is in place in France and includes five rare diseases: phenylketonuria, cystic fibrosis, adrenal hyperplasia, sickle cell diseases (targeted screening) and congenital hypothyroidism.

National alliances of patient organisations and patient representation

The *Alliance Maladies Rares* (French Alliance for Rare Diseases) is the main umbrella organisation dealing with rare diseases and it plays a major role in organising working groups, communicating on rare diseases, offering support to patients and families and contributing to the development of the National Plan for Rare Diseases and the evaluation of the plan. This alliance played a role in the elaboration of the first and second national plan and the evaluation of the centres of reference.

The *Alliance Maladies Rares* and other patient organisations have also received some public funding during the first Plan for various support activities and awareness campaigns.

Sources of information on rare diseases and national help lines

In terms of public information measures, support for the Rare Diseases Platform (*Plateforme Maladies Rares*, established in 2001), and most particularly for the Orphanet portal on rare diseases, has been reinforced under the National Plan. Orphanet was established in 1997 and is the reference for all rare disease information in France: the team, hosted by the INSERM in Paris, is in charge of collecting data on services for rare diseases (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) for France, and of coordinating the activity of Orphanet's external teams across Europe as well as maintaining the encyclopaedia and inventory of rare diseases. A new more user-friendly version of Orphanet was launched in 2008 with additional features. Recent new Orphanet features include the encyclopaedia for patients in French, emergency guidelines and search by sign facility.

In addition to this, the French medicines agency's internet site (AFSSAPS) now publishes its list of clinical trials for rare diseases, its list of compassionate use authorisations (cohort use) from 1994 onwards and other general information on hospital preparations.

The help line *Maladies Rares Info Services* provides information on rare diseases. The AFM (*Association française contre les myopathies*) provides a help line for information on neuromuscular diseases.

Since June 2006, the French Health Directorate produces personal health care and information cards in close collaboration with health care professionals and patient organisations, within the scope of the French National Plan for Rare Diseases. These cards are distributed by health care professionals treating the patients concerned, and provide information for health care professionals about the patient and gives brief information on the disease.

In late 2008, the French Minister for Health introduced the outlines of the forthcoming Personal Medical Dossier (DMP). This facultative document, which will concern many rare disease patients (as it is primarily aimed at children, diabetics, those with a chronic illness), should improve the quality of coordination of treatment for both patients and health care professionals, and help information exchange.

National rare disease events

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

Every year in June Orphanet and the *Alliance Maladies Rares* organise jointly a one day meeting for all patient organisations to discuss themes of interest in the field of information and dissemination of good practices.

Hosted rare disease events

The EU presidency of France in 2008 provided a platform for meetings on theme of rare diseases, this included a conference on National Strategies and Actions for Rare Diseases in Europe (18 November 2008) on the theme of experience sharing and the elaboration of recommendations at European level.

Research activities and E-Rare partnership

Public funding is available for rare disease projects from the National Funding Agency for Research (ANR) (basic research) and Health Care Department (PHRC) (clinical research). In addition, some charities and private foundations provide funding for research, such as the AFM's *Téléthon*. The articulation between these funding sources should be improved under the second plan to make it easier to apply for funding for rare diseases.

The *GIS Maladies Rares* (Institute for Rare Diseases) was created in 2002 to coordinate and support research into rare diseases and to initiate and implement research on rare diseases at national and European levels. At national level, the GIS has been instrumental in implementing in the early 2000 research programmes (through yearly calls for research projects) on rare diseases (in particular networks), which have been later on entrusted to the French Funding Agency for Research in the context of the First French National Plan for Rare Diseases (2004-2008). Several targeted strategic actions are carried out by the *GIS Maladies Rares* to facilitate (and fund) access to technology platforms (i.e. genetically modified animal models, high throughput sequencing and drug-screening, etc.) for the French community of researchers on rare diseases. The GIS Maladies Rares is the coordinating partner of the E-Rare ERA-Net for Research Programmes on Rare Diseases, and organised the first joint transnational call in 2007³² for research on rare diseases, with the participation of 6 countries and a total of 13 consortia (French teams participated in each of these projects/consortia).

Participation in European projects

France participates in the following European Reference Networks for rare diseases: Dyscerne, EPNET/ EPI (main partner), EUROHISTIONET (main partner), NEUROPED, Paediatric Hodgkin Lymphoma Network, RBDD, and TAG (main partner). France participates in the following European research projects for rare diseases: ARISE, ANTEPRION, ANTIMAL, AUTOROME, BIOMALPAR, BIO-NMD, BRAINCAV, BNE, CARDIOGENET, CAV-4-MPS, CUREFXS, CLINIGENE, CONTICANET, CHEARTED, CRUMBS IN SIGHT, CUREHLH, CRANIRARE, ELAST-AGE, EPOKS, EMINA, ERMION, EVI-GENORET, EPINOSTICS, EUROBFNS, EuroGeBeta, ENRAH, EUNEFRON, EMSA-SG, EUMITOCOMBAT, EURAMY, EUREGENE, EUROCARE-CF, EUROAGENTEST, EUROGLYCANET, EUROPEAN LEUKEMIA NET, EUROWILSON, EUROAS, EURO IRON1, EURO-LAMINOPATHIES, EURORETT, EUROSCA, EURSPA, EUROTRAPS, ENCE-PLAN, EUSTAR, EPOKS, EURO-PADNET, EURIOFNET, FAD, GETHERTHAL, GENESKIN, GENOSTEM, HMA-IRON, HSCR, HAEIII, HUE-MAN, INHERITANCE, IMMUNOPRION, KINDLERNET, LEISHMED, LYMPHANGIOGENOMICS, MANASP, MILD-TB, MITOCIRCLE, MM-TB, MTMPATHIES, MPCM, MITOTARGET, MYASTAID, MYORES, MYELINET, NEUROBID, NEOTIM, NEUPROCF, NMD-CHIP, NOVSEC-TB, NM4TB, NEUROSIS, NEUROPRION, NOVELPID, NEMMYOP, NEUTRONET, NSEuroNet, OSTEOPETR, PODONET, PEMPHIGUS, RATSTREAM, RAPOSDI, RISCA, SKINTHERAPY, STEM-HD, SIOPEN-R-NET, RHORCOD, RDPLATFORM, TB CHINA, THERAPEUSKIN, WHIPPLE'S DISEASE and WHIMPath. France contributes to the following European registries: EUROCAT, EUROHISTIONET, EPI-EPNET, EURECHINOREG, European central hypoventilation syndrome registry, EUROTRAPS, CHS, EUROCARE CF, ECFS, INFEVERS, and TREAT-NMD. France contributes to the EUROPLAN project.

Orphan drug committee and incentives^{33,34}

Three institutions are involved in the field of orphan drugs on the French market: the French Agency for the Sanitary Security of Health Products (AFSAAPS - *Agence Française de Sécurité Sanitaire des Produits de Santé*), the High Health Authority (HAS – *Haute Autorité de Santé*), and the Ministry of Health.

Initiatives are in place to stimulate orphan drug development: research support is provided through national funding programmes: *GIS Maladies Rares*, the Hospital Clinical Research Programme (*Programme Hospitalier de Recherche Clinique*); during orphan drug development, free scientific advice is available from the AFSSAPS; and budgetary incentives (from 2001) are available in the form of a tax exemption from the national Health Insurance and AFSAAPS.

Fee waivers can be granted for drugs which fulfil the orphan drugs criteria but do not have orphan designation ("*medicament orphelin de fait*"). Free scientific advice is available for orphan medicines from the AFSSAPS.

Sponsors of orphan medicinal products are exempted from taxes to be paid by enterprises promoting pharmaceutical specialities or wholesale distributors under health and social legislation. These taxes are: the tax on the promotion of pharmaceuticals, based on the promotion costs of laboratories; the tax paid by the laboratories for the AFSSAPS; the safeguard clause for medicinal products; the tax on direct sales; the tax on the distribution of medicines.

The accelerated process for pricing has been reduced to 15 days.

³² http://www.e-rare.eu/images/stories/e-rare_final_list_of_funded_projects.pdf

³³ This section has been written using the *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp45-49)

³⁴ 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)

The Leem (French Pharmaceutical Companies Union) is a constituted professional organisation that represents the pharmaceutical industry in France, i.e. the companies whose mission is research, development, manufacturing and marketing of medicinal products. Rare diseases became priority action in the Leem's strategy in 2002: a rare disease work group made up of key stakeholders in the public and private sectors meets regularly to discuss: innovative therapies for rare diseases (and how to bring these therapies to patients), the provision of health care for rare disease patients, the communication of information on rare diseases and treatment, ways to create the correct conditions for optimal and innovative clinical treatment and ways to support the national plan for rare diseases. The LEEM organises a workshop dedicated to orphan drugs every year. Since 2001 the LEEM evaluates the advances made in clinical research in France, including clinical research in the field of rare diseases, based on criteria set by the High Health Authority (HAS).

Orphan drug availability^{35,36}

Compassionate use for individual patients takes the form of either cohort use (granted by the laboratory) or named patient supply (granted by the AFSSAPS). Patients can also be treated with drugs before these drugs have received MA through clinical trials and hospital preparations. Reimbursement measures are in place for compassionate use.

Innovative drugs are eligible for an ATU (Temporary Authorisation for Use) from the AFSSAPS if there is a public health need. The drug must fulfil the following criteria: the drug must treat a serious or orphan disease; no therapeutic alternative to the drug should be available; the drug must have a positive risk/benefit and the drug must be for temporary use. The aspect of the drug (quality, security and efficacy) and the medical environment (disease and alternatives) will be evaluated before receiving the ATU.

TTPs (Temporary Treatment Protocols) can also be implemented to extend licenced indications of medicines or devices.

The *KCE reports 112B: Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* highlights that “off-label use of an orphan or non-orphan drug is possible for a rare disease (as defined by the European Regulation 141/20005) if the medicinal product is listed in an advice or recommendation relating to a category of sick persons of the HAS (Article L162-17-2-1 of the Social Security Legal Code). Treatment and reimbursement is decided upon by decree of the Ministers of Health and Social Security and following advice of the National Union of the Sickness Funds. The specialities, products or services being the subject of the decree can be dealt with only if their use is essential to the improvement of the health of the patient or to avoid worsening of the condition. They must also be registered explicitly in the treatment protocol.”³⁷

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*³⁸, “particular prescribing conditions are in place for: drugs for hospital use, drugs with hospital prescription, drugs with initial hospital prescription, drugs with prescription only by specialists, drugs with a particular follow up during the treatment.”

In April 2008 a decree came into action concerning the exceptional coverage by the national insurance of certain pharmaceutical products or services. This decree will allow for the coverage of certain drugs, products or paramedical services for rare disease patients, for a 3-year renewable period.

Specialised social services

Respite care services are available for patients whose care is demanding on their relatives: this is only partially reimbursed for certain rare diseases (through the “*ticket modérateur*”). Therapeutic recreational programmes are available mostly within hospital organisations and patient organisations or local institutions and are mostly fully reimbursed. “*Centres communaux d'action social*” (CCAS) (Social assistance centres), social assistants within hospital structures and certain services provided by patient organisations all aim to assist the integration of rare diseases patients into daily life. These services are financed either by government budgets or patient organisations.

³⁵ This section has been written using the *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp45-49)

³⁶ 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)

³⁷ *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp47)

³⁸ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. 2005 Revision* (p14)

B.1.9.2 New initiatives and incentives in 2009

Evaluation of the First National Plan for Rare Diseases (2005-2008)

The first National Plan for Rare Diseases underwent intense scrutiny during its five-year term which concluded at the end of 2008. The overarching goal of the evaluation of the plan was to provide data to serve for the elaboration of the second version of the rare disease plan, due in 2010. An Evaluation Committee (Codev) consisting of health, economic and sociology experts, under the authority of the French Council for Public Health, thus measured the initial objectives of the plan against the corresponding actions undertaken during the past four years. An official report of the evaluation was rendered to the French Minister of Health on 7 May 2009. The document provides an analysis of the accomplishments, advances, and shortcomings of each of the ten axes of the plan. A series of propositions and recommendations was also provided for the elaboration of the future plan.

Throughout the evaluation, the committee underscores the satisfaction of the different stakeholders vis-à-vis the overall results accomplished. The objectives judged most pertinent – the access to information (particularly Orphanet and MRIS, the French rare disease informational service helpline), medical care (centres of reference), research funding, orphan product accessibility, and partnerships with European institutions – have benefited from corresponding actions that have satisfactorily fulfilled these goals. The need to sustain these actions was reiterated in the evaluation. However, certain objectives – specifically those concerning epidemiology, professional training for rare diseases, and screening and diagnostic programmes – were considered insufficiently developed. The strategies to meet these goals need to be reformulated taking stock of the difficulties encountered and defining tactics to overcome obstacles.

The tenth axis of the plan, “Develop national and European partnerships in the field of rare diseases” received an overall favourable evaluation with certain propositions presented to enhance and encourage European collaboration. Furthermore, the evaluating committee proposed the development of measures to bring non-European industrialised and developing countries into the fold. Indeed, throughout the evaluation of the plan, the necessity for European- and international-level coordination and resource-sharing is emphasised.

The evaluation³⁹, along with an additional report⁴⁰ drawn up by the Ministry of Health containing auto-evaluations from the plan’s pilot committee, and the testimonies of rare disease health professional, industry and patient organisation stakeholders who contributed actions to the first plan, were discussed at the final meeting of the Follow-up Committee for the first French National Plan.

The Second National Plan for Rare Diseases

On 21 October, 2009, a meeting took place in order to constitute the working groups and fix concrete objectives for each of the seven elements that will constitute the new four-year French National Rare Disease Plan scheduled to run from 2010-2014⁴¹. An inter-ministerial representative has been named to shepherd the plan over the next four years, and leaders have been appointed for each of the strategic axes. A toolbox is available on the website of the Ministry of Health to help stakeholders contribute to the elaboration of this plan⁴².

The final, detailed version of the plan was scheduled to be delivered to the French government by March 2010. France’s first national plan – which ran from 2005-2008 and was the first of its kind in the world – had ten strategic axes. After an intense period of evaluation of the first plan, the second plan has been streamlined to comprise seven defined priority areas for action.

The axes of the second plan are as follows: axis one “Organisation of diagnosis and health care” will pursue support for diagnostics and will tweak the actions taken vis-à-vis the centres of reference in order to meet any needs not currently covered in this area. Axis two, “Data collection, knowledge of rare diseases and their socio-economic and medical impact” will define a data collection strategy. The third axis, “Research” will seek an evolution of the GIS Maladies Rares, France’s main clearinghouse for calls for proposals in the field of rare disease research. Research will continue on the epidemiology and natural history of rare diseases, genetics, and psychopathological mechanisms. The development of therapeutic trials will be targeted. The fourth axis, “Targeted medicines” will address the development of specific products for rare conditions and will also focus on issues concerning price and commercialisation. Resources will be structured to implicate extra-

³⁹ http://www.hcsp.fr/docspdf/avisrapports/hcspr20090317_maladiesRares.pdf

⁴⁰ <http://www.orpha.net/actor/EuropaNews/2009/doc/DGSbilan.pdf>

⁴¹ <http://www.sante-jeunesse-sports.gouv.fr/les-maladies-rares.html>

⁴² <http://www.sante-jeunesse-sports.gouv.fr/boite-a-outils-pour-la-preparation-du-second-plan-national-maladies-rares.html>

hospital services as well as the country's rare disability schema recently adopted. The fifth axis "Reimbursements and health care coverage" will seek to better coordinate medicinal and related services usage and ensure equity. The sixth axis, "Information, training and patient organisation support" will reinforce support to Orphanet, improve information on disability by coordinating with appropriate national counterparts, and ameliorate rare disease training in France as well as helping patient associations with transversal and/or innovative actions. Finally, the seventh axis "European and International Cooperation" will seek enhanced collaboration with industrialised and developing countries in the areas of information, public/private partnerships, research, epidemiology, networks of expertise, etc.

It is important to remember that these elements identified for priority actions in the second plan build upon the groundwork of achievements accomplished in these and other areas during the first four years of the French plan.

A plan aimed at rare handicaps (of which rare diseases can be a cause) has been announced for the period (2009-2013). Measures include the creation of 300 additional places in care centres, regional relays, and two new resource centres. Cooperation between national resource centres for rare handicaps and the "reference centres" for rare diseases is planned.

Centres of expertise

In June 2009, The National Cancer Institute (*l'Institut National du Cancer - INCA*) published the list of the 11 adult 'rare cancer' Reference Centres designated in 2009.

National rare disease events

To mark the second Rare Disease Day, the French *Alliance Maladies Rares* organised an awareness campaign to highlight the number of people affected by rare diseases (www.malades-pas-si-rares.org). The Annual *Téléthon* organised by the AFM took place on the 4 and 5 December 2009 and raised over €90 million in donations. On the 5 December 2009 the *Alliance Maladies Rares* organised their annual march to coincide with the *Téléthon* and Orphanet France organised a fundraising music marathon concert. Orphanet and the *Alliance Maladies Rares* held their annual one day meeting for patient associations on 30 June 2009: this year's meeting focused on the theme of medical data in today's computerised world.

A symposium was organised by EuroBioMed on the theme of research and development in the field of rare diseases and orphan drugs in Montpellier (29-30 October 2009) which brought together over 200 stakeholders from the field and highlighted issues such as the cost of orphan drugs and reimbursement by the health system, centralisation of data for research, and public-private partnerships in the field.

Hosted rare disease events

Amongst the number of international rare disease events reported in *OrphaNews Europe* hosted by France in 2009 were: the ESH 11th International Conference on Chronic Myeloid Leukaemia (Bordeaux 11-13 September 2009), the ESH Conference on Myelodysplastic Syndromes (Mandelieu, 22-25 October 2009), the International Conference on Myasthenia (Paris, 1-2 December 2009).

Research activities and E-Rare partnership

France took part in the second E-Rare Joint Transnational Call and France is represented in 11 of the 16 consortia selected for funding in 2009, with funding totalling around €2 million. Also in 2009, different public bodies joined together to create the "*Plateforme Mutatio*" that aims to identify unknown mutations in rare diseases by means of high throughput sequencing technology.

B.1.10 GERMANY

B.1.10.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Germany accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

In the German health care system every patient is entitled to complete health care coverage consisting of preventive, diagnostic, therapeutic and rehabilitative measures. The medical care of patients is of high quality and the access to medical doctors and specialists is (independent of the disease's incidence) good. There is no national plan for rare diseases in Germany at the moment, and there are no specific funds allocated to rare diseases in the health care system, although ad hoc funding for rare disease projects does exist. However, the first steps are being made to establish a national plan for rare diseases: a study entitled 'Strategies for improving the health care situation of patients with rare disease in Germany' has been commissioned by the Federal Ministry of Health. Its goal is to focus on existing measures and to refine them by involving all key bodies and organisations of the German health care system.

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): at this level, centres of expertise have not yet been established.

Hospitals are entitled to provide outpatient care for rare diseases patients if they have received prior authorisation by the competent Land authority (Social Code V, Section 116b): however this applies only to certain rare diseases according to a list which has been stipulated by law (Social Code V, Section 116b). The Federal Joint Committee (*G-BA*) can extend this list. 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 Germany. 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 that are necessary for safeguarding medical service provisions. The latter aims to ensure that medical services for persons insured 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 (*GKV*) covering about 70 million people. The *G-BA* is responsible for reimbursement decisions in the statutory health insurance (*GKV*). 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 hospitals as well as the cross-institutional measures for quality assurance. In this context, for the purpose of ensuring the quality of treatment, the *G-BA* may also lay down certain minimum numbers of patients treated per year in a certain 'Section 116b centre'.

In addition to the so-called 'Section 116b centres', other centres like social-paediatric centres (Social Code V, Section 119) or university clinics for outpatient care (Social Code V, Section 117) may also be involved in the treatment of rare disease patients.

Legislation provides the basis for the contracting of *Hochspezialisierte Versorgung* (highly specialised care) for a limited number of diseases (see above), some of which are rare.

Registries

There are few registries for rare diseases in Germany. An analysis based on the Orphanet database identifies about 50 registries, most of them belonging to academic institutions. A minority of these registries are implicated in international networks or covers the whole European region. There is no public central clinical trial registry dedicated solely to rare diseases: the German Clinical Trials Register (DRKS) is funded by the BMBF and is open access for rare disorders. Germany contributes to European registries such as EUROCAT, TREAT-NMD, EBAR, EHDN, EurIPFnet, EURIPEDES, European Alport registry, EUROSCA-R, EUTOS, and RegiSCAR.

Neonatal screening policy

Since 2005 there is a mandatory legalised screening program covering fourteen conditions: phenylketonuria, biotinidase deficiency, galactosaemia, MCAD deficiency, VLCAD deficiency, LCHAD deficiency, CPT1, CPT2, CAT deficiencies, maple syrup urine disease, glutaric aciduria type 1, isovaleric acidaemia, adrenogenital syndrome and congenital hypothyroidism.

National alliances of patient organisations and patient representation

In Germany, the German National Alliance for Chronic Rare Diseases (ACHSE) regroups more than 70 patient organisations. Through ACHSE, rare disease patient organisations support each other, exchanging know-how so as to strengthen their influence in the political arena.

In Germany, health-related self-help is eligible for financial support from the statutory health insurance funds since 2000. A legislative reform (1 January 2009) has made access to funding easier and the distribution of the funding ear-marked by the statutory health insurance funds is guaranteed.

The Ministry of Health currently supports different projects concerning the participation of patients with rare diseases at the Charité Berlin. One of these projects deals with the "Contribution of self-help groups/patient organisations to the organisation of interfaces within the health care system", aimed at improving patient participation and orientation.

An important role is played in the regulation of the medical services of the German health care system by self-governing bodies such as patient associations: since 2004, national groups representing patients participate in the consultations of the Federal Joint Committee.

Sources of information on rare diseases and national help lines

The Orphanet portal on rare diseases is available in German⁴³ and is widely used as a major information source on rare diseases in Germany. Since 2001 there is a dedicated Orphanet team in Germany, currently hosted by the Human Genetics department of the Medizinische Hochschule Hannover. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

All medicinal products, including orphan drugs, are included in a database called AMIS, run by the German Institute of Medical Documentation and Information (DIMDI)⁴⁴ ensuring public information in the field.

The ACHSE website⁴⁵ provides a platform for information on rare diseases. This platform is a validated and patient-orientated source of information. It encourages patient organisations to improve their information continuously. ACHSE has also established a help line to inform patients and their families in particular those without a diagnosis or an established patient organisation.

The KINDERNETZWERK⁴⁶ offers a service line for patients with rare diseases together with patient oriented online diseases descriptions. The KINDERNETZWERK additionally holds a database for registering parents with children suffering of rare diseases. Information on patient groups can also be found at the NAKOS website⁴⁷ (The National Clearing House for the Encouragement and Support of Self-Help Groups). Other non-rare disease specific help lines are available to help patients understand the health care system.

National rare disease events

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. ACHSE organises meetings for patient organisations twice a year.

Research activities and E-Rare partnership

In 2003, the Federal Ministry for Education and Research (*Bundesministerium für Bildung und Forschung, BMBF*) funded ten networks of national academic groups, clinical centres, specialised laboratories and patients organisations for basic and clinical research for an initial three years. After a successful interim evaluation, nine of the networks for rare diseases were funded for another two years. The budget of this rare disease research programme was €31 million.

In 2007, the BMBF opened a new funding programme on rare diseases research with a substantial increase in budget to €24 million for a 3 year period and an extension of the maximum funding duration to 3 times renewable 3 year periods for new networks. Starting in October 2008, 16 networks are now being funded. Six of these are extensions of previously funded networks, while the other 10 networks are new. These activities are funded within the research programme entitled 'Health Research Scientific Research for the People'. In co-operation with the Federal Ministry of Health, the BMBF assumes responsibility for the programme which is financed with funds from the BMBF.

Germany is a partner of the E-Rare project, represented by the BMBF and the Project Management Agency of the German Aerospace Centre (*Projekträger im Deutschen Zentrum für Luft- und Raumfahrt, PT-DLR*). Germany participated in the first E-Rare joint transnational call in 2007 and funds the participating German research groups of 10 transnational research projects with a total €3.3 million funding.

⁴³ www.orphanet.de

⁴⁴ www.dimdi.de/static/de/amg/amis/index.htm

⁴⁵ www.achse.info

⁴⁶ www.Kindernetzwerk.de

⁴⁷ www.nakos.de

In addition, the BMBF has funded research on rare diseases in several other funding initiatives like the National Genome Research Network (NGFN), the Competence Networks for Medicine, Innovative Therapies, Clinical Trials and others.

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

Regional sources of funding are also available.

Participation in European projects

Germany participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN-CF (main partner), ENERCA, EPI, EPNET, EUROHISTIONET, NEUROPED, Paediatric Hodgkin Lymphoma Network (main partner), PAAIR, and RBDD. Germany participates in the following European research projects for rare diseases: AUTOROME, ANTEPRION, BIOMALPAR, BNE, CAV-4-MPS, CRANIRARE, CURE-FXS, CHD PLATFORM, CILMALVAC, CUREHLH, EMVDA, ENRAH, ENCE-PLAN, EURADRENAL, EUCILIA, EUNEFRON, EURIPFNET, EUROBONET, EUROBFNS, EURODS, EURO-LAMINOPATHIES, EUROPEAN LEUKEMIA NET, EUROSCA, EUROTRAPS, EURORETT, EUROSPA, ERMION, EuPAPNet, EUBNFS, EURO-CGD, ELA2-CN, EMINA, EPINOSTICS, EUREGENE, EUROPEAN LEUKEMIA NET, EMSA-SG, ESDN, FASTEST-TB, GETHERTHAL, HMA-IRON, HAE III, HDLOMICS, HUE-MAN, HMANASP, INTHER, KINDLERNET, LEISHDRUG, MANASP, MITOTARGET, MYORES, MIMOVAX, MOLDIAG-PACA, NEUROSI, NSEuroNet, NEUTRONET, NEMMYOP, NEWTBDRUGS, PULMOTENSION, OVCAD, OSTEOPETR, PODONET, PEMPHIGUS, RD PLATFORM, RevertantEB, RHORCOD, RATSTREAM, RISCA, WHIPPLE'S DISEASE and TB-VIR. Germany contributes to the following European registries: EUROCAT, TREAT-NMD, EBAR, EHDN, EurIPFnet, EURIPEDES, European Alport registry, EUROSCA-R, EUTOS and RegiSCAR. Germany contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

Once authorised, all orphan drugs are fully reimbursed by the statutory health insurance (*GKV*). Due to the specific characteristics of several drugs the German Joint Federal Committee decided in October 2008 to implement additional requirements for the prescription procedure concerning the qualification of the physicians and the documentation of the therapy. Up to now, these requirements apply to one rare disease (pulmonary arterial hypertension).

Irrespective of the prevalence of the disease, the off-label use of drugs is reimbursed by the statutory health insurance (*GKV*) on the following conditions: the drug will be used to treat a life-threatening or fatal disease; there is an absence of state-of-the-art therapy; and there is scientific evidence of positive therapeutic effects. Three expert-groups (oncology, HIV/AIDS, neurology) were established by the German government in 2005. The *G-BA* commissioned these expert groups to develop recommendations for the off-label use of a specific drug in a specific off-label-indication. On this basis the *G-BA* regulates reimbursement modalities in its directives.

In 2005, on the basis of the Regulation (EC) No 726/2004 the German government implemented rules for providing such medicinal products in form of so-called Compassionate Use Programmes. Section 21 sub-section 2 no.6 of the German Medicinal Products Act states that the provision of a medicinal product in such cases has to be free of charge.

Specialised social services

No specific activity reported.

B.1.10.2 New initiatives and incentives in 2009

National plan for rare diseases and related actions

An in-depth evaluation of the situation of patients affected by rare diseases in Germany was published by the Federal Ministry of Health in August 2009. The study is entitled "Maßnahmen zur Verbesserung der gesundheitlichen Situation von Menschen mit Seltenen Erkrankungen in Deutschland" ('Strategies for improving the health care situation of patients with rare disease in Germany'). The study analyses the current

situation of care for persons with rare diseases in Germany from the perspective of various actors in the health care system by evaluating the perspective of public organisations, service providers and patient organisations on the basis of quantitative and qualitative surveys in the form of questionnaires, individual interviews and group discussions. In the process, the priority spheres for action in the areas of the general care situation, specialised forms of care, diagnosis, therapy, exchange of information and experience as well as research, are identified. This provides the basis for discussions regarding the first implications of implementing a national action forum as well as a national action plan for rare diseases in Germany. Subsequently, possible solutions for individual areas will finally be developed in co-ordination with existing and planned activities at EU level.

National rare disease events

The Orphanet-Germany team organised a balloon-release and a stand for International Rare Disease Day, in Hanover on 28 February 2009. Team members informed patients, families and the public about Orphanet and rare diseases in general.

Additional events took place at the Rare Disease Day 2009. In several cities members of patients associations gathered to create awareness for rare diseases in society. These events took place in Cologne, Hamburg, Hanover, Berlin, Würzburg, Bielefeld und Stuttgart.

The *Eva Luise and Horst Köhler Stiftung für Menschen mit Seltenen Erkrankungen* in cooperation with ACHSE e.V. awarded a prize on 2 March 2009 for a research project on a rare disease. ACHSE also organised a conference in Bonn in October 2009 gathering representatives from patient organisations, the health ministry, doctors and researchers on different topics concerning rare disease information collection (such as registries and classification of diseases). The results of the Ministry study "Measures for improvement of the health situation for people living with a rare disease" were presented and there was a consensus that the German health care system could provide specialised services for rare diseases. ACHSE presented two position papers "Improving Information" and "Shortening the Route to Diagnosis" and called for a National Plan.

Hosted rare disease events

The 22nd Annual Meeting of the European Musculo-Skeletal Oncology Society was held in Stuttgart (13-16 May 2009). The 12th International Congress on Neuronal Ceroid Lipofuscinoses was held in Hamburg on 3-6 June 2009. The OI in Motion: Rehabilitation and Physiotherapy in Osteogenesis Imperfecta conference was held in Rheinsberg (20-22 November 2009).

Research activities and E-Rare partnership

The BMBF continues to fund the 16 networks for rare diseases research, the last having started in July 2009. Additional funding of rare disease research is ongoing in other funding initiatives of the BMBF with about €20 million in 2009.

Germany, as a partner of the E-Rare project represented by the BMBF and the PT-DLR, participated in the second transnational call in 2009. PT-DLR managed the joint call secretariat for this second call. The BMBF intends to fund the participating German research groups of 14 transnational research projects with approximately €3 million.

B.1.11 GREECE

B.1.11.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Greece accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

A commission composed of government officials, health professionals and patient representatives was formed in 2007 to help draft the Greek National Plan for Rare Diseases. An outline for this National Plan of Action for

Rare Disorders (to run over the period 2008-2012⁴⁹) was presented by the Greek Minister for Health in February 2008: this document identified and outlined eight strategic priorities:

- Acknowledgement of the specificity of rare diseases (registration on the list of chronic long-term disorders),
- Increase the knowledge of the epidemiology of rare diseases and establish a National Registry of Rare Disorders,
- Develop information for patients, health professionals and the general public concerning rare diseases,
- Upgrade services for diagnosis, therapy and rehabilitation of rare diseases patients (training for health care professionals to improve diagnosis and access to quality health care),
- Organise screening and access to diagnostic tests,
- Promote research and innovation regarding rare diseases and specifically effective new therapies,
- Respond to the specific needs of people living with rare diseases,
- Generation of an integrated platform for action in the field of rare diseases at a national level and the development of European partnerships.

The plan has a total budget for the period of €27,703,834 and intends to obtain €16,335,734 of EU funding by declaring the plan as a priority in their National Strategic Reference Framework. Current actions prior to the plan are targeted to specific diseases, and it is not possible to identify a budget allocated to rare disease actions in Greece.

Centres of expertise

Greece is working to provide better access to treatment of rare disorders, including accreditation for expert centres for rare disorders. There are currently four official centres of expertise for rare diseases in Greece: the National Centre for Thalassaemia and Haemoglobinopathies, the Paediatric Immunology and Rheumatology Referral Centre, the “Choremio” Laboratory of Medical Genetics, University of Athens and the Institute of Child Health for Rare Genetic Diseases.

Registries

Greece contributes to the European registries EUROCARE CF and EUROWILSON.

Neonatal screening policy

Neonatal screening is provided by the Institute of Child Health, Athens, for familial hypothyroidism, phenylketonuria and G6PD deficiency.

A National Programme of Haemoglobinopathies is in place (covering thalassaemia, sickle cell anaemia, etc.) which includes carrier detection, prenatal diagnosis and patient diagnosis.

National alliances of patient organisations and patient representation

In Greece, PESPA (the Greek Alliance for Rare Diseases) is an umbrella non-profit organisation established in 2003, established by health professionals and presidents of rare disease patient associations with the help of Eurordis. There are currently no public funding schemes to support patient organisation activities in Greece.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Greece, currently hosted by the Institute of Child Health's Department of Genetics (from 2009). This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no official information centre for rare diseases in Greece apart from Orphanet. The PESPA website offers information on rare diseases and a list of some rare diseases in Greek. There is currently no official help line for rare disease information in Greece, but some services are provided on an amateur level with volunteers from the Greek Alliance and other patient organisations who provide psychological support and general information to callers.

National rare disease events

No specific activity reported.

⁴⁹ http://www.ygeianet.gov.gr/HealthMapUploads/Files/SPANIES_PATHISEIS_TELIKO_LOW.pdf

E-Rare partnership and research activities

Some research programmes exist for rare disease research, and are often sponsored by pharmaceutical companies and patient associations. Up till 2009, Greece was not a partner of the E-Rare project, and in 2009 they joined the second transnational call.

Participation in European projects

Greece participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, ENERCA, EUROHISTIONET, RBDD and TAG. Greece participates in the following European research projects for rare diseases: BIOMALPAR, BNE, EPINOSTICS, EUROGLYCANET, EUROPEAN LEUKEMIA NET, EVI-GENORET, GEN2PHEN, GETHERTHAL, HDLOMICS, ITHANET, MYASTAID and NEUROPRION. Greece contributes to the following European registries: EUROCARE CF registry. Greece contributes to the EUROPLAN project.

Orphan drug committee and incentives

The Greek National Organisation for Medicines (EOF) ensures the public health and safety of all medicinal products, including Orphan Drugs.

Orphan drug availability

The goal of the Greek Ministry of Health is to improve the access of the patients to orphan drugs, including reimbursement from the public insurance system. There are currently no programmes to facilitate access to Orphan drugs. The Greek Alliance has put in place some awareness raising campaigns concerning orphan drugs. Some orphan drugs for patients with rare diseases are available from the Hellenic Drug Organisation (EOF) and the Institute of Pharmacological Research and Development (IFET): fabrazyme, replagal, gliver, tracleer, trisenox, aldurazyme, ventavis, myozyme, and siklos.

Specialised social services

Patients have limited access to respite care services, but these are not specifically for rare disease patients. The patients sometimes have to financially contribute to these services which are run by national institutions, patient associations and non-governmental organisations. A few therapeutic recreational programmes are available, organised by the same types of organisations, and the patient must also financially contribute to this. Limited help with household chores, psychological support, help with shopping and mobility assistance can be sought by patients with special needs (suffering from rare diseases or not) and are provided by local authorities or NGOs.

B.1.11.2 New initiatives and incentives in 2009**National rare disease events**

PESPA, the Greek Alliance, launched an awareness campaign including a TV commercial broadcasted on many different Greek TV channels on the they had put together and was broadcast on Greek TV on the days leading up to Rare Diseases Day 2009.

Hosted rare disease events

Athens hosted the Eurordis Annual Conference (8-9 May 2009). On the 11-12 December 2009 a conference entitled "Rare Diseases involving the Hemopoietic System – News on therapeutic approaches" was organised.

Research activities and E-Rare partnership

Greece joined the second transnational call of the E-Rare project in 2009, and Greece participates in 1 of the 16 consortia projects selected for funding with a total of around €140,000.

B.1.12 HUNGARY

B.1.12.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Hungary accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

A decree of the Ministry of Health established the National Rare Disease Centre (NRDC) in Hungary on 11 November 2008 as a part of the National Centre for Healthcare Audit and Inspection by modifying its foundation deed. The National Centre for Healthcare Audit and Inspection is a part of the National Public Health Institute, and is empowered to investigate quality related issues in health care, public health consequences of health care operation, and to initiate interventions if needed. The NRDC's rules and regulations describe the fields which this agency is responsible for:

- it elaborates its own data collecting technology and co-operates with other agencies in order to obtain rare diseases related data and to prepare these indicators;
- it defines public health indicators for rare diseases;
- it initiates the elaboration of rare diseases guidelines and carries out the audit projects;
- it maintains the national database of rare diseases specialised health care providers;
- it contributes to the assignment of national centres of expertise and their participation in European networks;
- it facilitates the establishment and operation of the quality management programs for the Hungarian rare diseases laboratories;
- it facilitates the application of e-health in rare disease related care;
- it initiates the rare diseases teaching programs launching in the universities;
- it participates in the work of national agencies responsible for orphan drug and orphan medical device legislation;
- it supports the improvement of the availability of special social services for rare disease patients;
- it supports the effective primary preventive program;
- it evaluates the efficacy of the rare diseases screening programs;
- it facilitates the rare diseases research projects, the international co-operations;
- it contributes to the development of collaboration between governmental bodies, providers and patient organisations;
- it supports the Hungarian participation in the European rare diseases projects;
- it initiates programs, which contribute to the improvement of the perception of rare diseases among the general public;
- it co-ordinates the elaboration and monitoring of national policy on rare diseases;
- it reports on the Hungarian achievements regularly.

The NRDC is supported by an advisory group established by the Chief Medical Officer. Its members are from medical universities, governmental institutions and patient organisations. This advisory group supports strategic planning and program management.

The NRDC makes use of the National Centre for Healthcare Audit and Inspections' IT centre facilities for the systematic analysis of the hospital and outpatient discharge records of rare diseases patients (for rare diseases which have their own ICD10 code), as well as laboratories, research programmes and patient groups.

The NRDC also works with the Rare Disease Research Coordination Centre which is outsourced to Pecs University.

The NRDC cooperates with the National Board for Genetics, and with the officials responsible for rare diseases policy at the Ministry of Health, and at the National Institute of Pharmacy. Project based collaboration has been established with universities' internal rare disease coordination units, sociological centres (for studying sociological characteristics of the patient groups), the National Foundation for Disabled Persons (multi-sector conference organisation), the National Centre for Statistics (for studying the mortality trends of rare diseases).

Centres of expertise

There are currently no officially approved centres of expertise in Hungary. In Hungary, a committee on the treatment of rare conditions has been set up within the Scientific Health Council (*Egészségügyi Tudományos Tanács*). It ensures, *inter alia*, that people suffering from such conditions receive adequate care in all cases. People suffering from rare conditions in Hungary are registered at the various treatment centres.

Registries

The clinical centres of rare disease have registry of cared patients. These registries do not report their cases to a national data collecting system, and their registration methodology is developed according to the local need of care management and to the research requirements. All of these registries are in line with the Hungarian laws on genetic data handling and on the personal data protection. Congenital anomalies are registered in the whole country according to the EUROCAT protocol. Hungary contributes to European Registries such as TREAT-NMD and EUROCARE CF.

Newborn screening policy

A compulsory, government-financed newborn screening program covering the whole country has been running since 1975, and now includes 26 diseases, amongst which phenylketonuria, hypothyroidism, galactosaemia and biotinidase deficiency. Two centres are responsible for the operation of this nationwide system.

National alliances of patient organisations and patient representation

The Hungarian Federation of People with Rare and Congenital Diseases (HUFERDIS) is the national alliance of rare disease patient organisations in Hungary, affiliated with Eurordis. HUFERDIS is currently encouraging the creation of a Hungarian Rehabilitation Centre for Rare Disease Patients. HUFERDIS represents rare diseases patients in the Council of National Alliances (CNA).

Patient organisations provide information and act as contact points for rare disease patients and organise conferences. Non-medical services for rare disease patients are currently available at local level or by non-profit organisations. Patient organisations are partly supported by the '1% Law' which allows taxpayers to transfer 1% of their previous year's taxable income to a non-profit organisation (which may be a patient organisation), without loss of income. Grants from the National Civil Fund are also available to patient organisations. There is no regular, direct governmental support for rare disease self help groups, but there are many indirect governmental financing mechanisms: 25% of the civil budget is from governmental sources.

Following a collaboration established between HUFERDIS, NRDC and the Hungarian Orphanet team, the EurordisCare3 survey was carried out implemented in Hungary. It was the first occasion when Hungary joined a European study concerning patient experiences.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Hungary, currently hosted by the University of Pécs. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. The Orphanet website (www.orpha.net) is widely used by professionals.

There is currently no official information centre for rare diseases in Hungary apart from Orphanet. But scientific societies (www.humangenetika.hu), HUFERDIS (www.rirosz.hu), non-governmental expert groups (www.betegmagzat.hu) and market-based organisations (www.webdoki.hu) have web based services for patients.

Guidelines

Guidelines related to rare diseases are produced by the Ministry of Health and are available for: autism spectrum, cystic fibrosis, diagnosis of the inherited metabolic diseases, genetic counselling, haemophilia, investigation of familial clustering of anomalies, investigation of multiple congenital anomalies, Legg-Calve-Perthes disease (Perthes disease), multiple sclerosis, myasthenia gravis, Osgood-Schlatter disease, prenatal screening of Down syndrome, Scheuermann disease, systemic lupus erythematosus, Tibial hemimelia, clubfoot. Some guidelines have been developed in collaboration with patient organisations and specialised clinics (e.g. Williams syndrome).

National rare disease events

The Orphanet Team and the NRDC are involved in Rare Disease Day events, which are organised by HUFERDIS.

A symposium was organised (6 October 2007) at the Pecs University Faculty of Health Sciences on the "Life quality of Down children". The Down syndrome as a model had been applied to explore the factors influence the life quality of children with rare diseases.

A symposium was organised (22 November 2008) at the Pecs University Faculty of Health Sciences on "Patient organisations as a resource of life quality improvement for those with a rare disease". The symposium disseminated the results of a research program which investigated the sociological properties of the Hungarian patient organisations.

A national workshop on centres of expertise was organised at the Hungarian Parliament on 19 March 2008 and hosted by SZILI Katalin, president of the Hungarian Parliament.

Hosted rare disease events

The 1st Central and Eastern European Summit on Preconception Health and Prevention of Birth Defects (27-30 August 2008) was organised by the NRDC in collaboration with the CDC and March of Dimes. This Summit provided a platform for review, analysis and discussion of the promotion of women's health before, during and after pregnancy, and the role of preconception health and health care in the prevention of birth defects in the Central and Eastern European region.

Research activities and E-Rare partnership

Research funds for rare diseases are available from the Hungarian Scientific Research Fund for Rare Disease Research.

In Hungary, the Ministry of Health announces its health related research grants through the Scientific Health Council (ETT), Department of Research Coordination every three years. In the last evaluated period (2004-2006) €3 million went to support research grants. Rare diseases are not among the priority areas, but many rare diseases related grants had been financed. (e.g. governmental supported the project on the periconceptional folate status and on attitude towards different supplement programs).

A multidisciplinary centre had been established in the Semmelweis University (Budapest) on the rare neurological disorders. The centre organises its work according to the principals published in the Communication from the European Commission on Rare Diseases. The centre has a patient registry, a diagnostic department, a multidisciplinary care providing network, research projects, and a teaching program⁵⁰.

Hungary is not currently a partner of the E-Rare project.

Participation in European projects

Hungary participates in the following European Reference Networks for rare diseases: EPNET/EPI and RBDD. Hungary participates in the following European research projects for rare diseases: BNE, EURO BONET, EURO GENTEST, EUROPEAN LEUKEMIA NET, EUROSCA, EUROWILSON, GENESKIN, NMD-CHIP, TREAT-NMD, SCRIN-SILICO and SIOPEN-R-NET. Hungary contributes to the following European registries: EURO CARE CF, EURO CAT and TREAT-NMD. Hungary contributes to the EUROPLAN project.

Orphan drug committee and incentives⁵¹

The holders of marketing authorisations for orphan medicinal products (or their representatives in Hungary) cooperate with the medical profession and the OEP (The National Health Insurance Fund - *Országos Egészségbiztosítási Pénztár*).

Orphan drug availability

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal product*, "the Hungarian Government promotes the use of orphan medicinal products for specific patients by means of special financial arrangements". In addition "some rare conditions (such as Fabry disease or adult-type chronic myeloid leukaemia - CML), the National Health Insurance Fund (OEP) provides standard price-support for the medicinal products in a predetermined manner. In this case the patient's contribution is negligible or 0%. In other cases, support for the orphan medicinal products imported for patients' treatment can be provided on application under a special

⁵⁰ <http://www.molneur.eoldal.hu/cikkek/english>

⁵¹ 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)

*equity procedure laid down by law. The OEP pays the price-support for the necessary medicinal products from earmarked resources in the outpatients' equity fund"*⁵².

Specialised social services

No specific activity reported.

B.1.12.2 New initiatives and incentives in 2009

Research activities and E-Rare partnership

To ensure the scientific expertise for NRDC, the general director of the National Centre for Healthcare Audit and Improvement and the rector of Pecs University signed the detailed agreement which established the Hungarian Coordinating Research Centre for Rare Diseases on the 21st April 2009. The Medical Faculty, Faculty of Health Sciences and the Faculty of Special Pedagogy are involved in this cooperative project. The experts employed by these faculties come from the fields of medicine, paramedicine, social services and education. The new working environment is expected to improve the Hungarian teams' ability to contribute to the work of European organisations.

All Hungarian Medical Faculties will establish their own coordinating centres to harmonise their rare diseases related activities.

The IT centre of the NRDC elaborated the on-line registration system for health care providers, laboratories, research programs and patient groups related to rare diseases. This data collection is in line with the Orphanet data collection standards. The system has been launched and the primary database will be used to contribute to the Orphanet database.

National rare disease events

The NRDC supported the HUFERDIS meetings related to Rare Disease Day in 2009, an event which has an important media impact in 2009. A conference on Montessori pedagogy for handicapped children, "Every child is unique", was held on 5-6 June 2009 which was widely covered in the media.

Education and training

In 2009, the Medical Faculty of Debrecen University organised a PhD course on rare diseases and a postgraduate teaching program for health professionals on diagnostic specialities for rare diseases in general practice.

B.1.13 IRELAND

B.1.13.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Ireland accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Ireland, but lobbying is underway by the Genetic and Rare Disorders Organisation (GRDO).

⁵² *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. 2005 Revision (p15)*

Centres of expertise

Currently, the Irish Department of Health and Children has no specific list of national centres of expertise, nor does it set standards for specific units to be considered “national”. However, the department does recognise that particular centres have particular expertise, and would give specific funds to support those specialist services. The Health Service Executive is responsible for these services and supports centres of expertise and laboratories, including 8 cancer centres and a national centre for medical genetics.

Registries

There are 9 patient registries for rare diseases registered with Orphanet: four of these contribute to the EUROCAT registry. The Medical Research Charities Group (MRCG) has created a Steering Group involving the MRCG, Health Services Executive (HSE), HRB and the Health, Information and Quality Authority (HIQA) to oversee research into the area of patient registries in Ireland. The aim is to identify existing patient registries in Ireland, to describe these in detail (functions, methodologies, standards, funding mechanisms) and also to identify best practice and guidelines for quality standards in this area. This research will also shed some light on the existence and quality of rare disease patient registries in the country. Ireland also contributes to other European registries, such as EURO CARE CF.

Neonatal screening policy

In neonatal screening is in place for galactosaemia, hypothyroidism, phenylketonuria, homocystinuria and maple syrup urine disease. Neonatal screening for cystic fibrosis is expected for the end of 2010.

National alliances of patient organisations and patient representation

The Genetic and Rare Disorders Organisation (GRDO) is a non-governmental organisation created in 1988 which acts as an umbrella group for rare disease patient organisations. GRDO was initially founded in 1988 with a view to lobbying for the establishment a National Centre for Medical Genetics. In 1992 this Centre was established by Government. The organisation is run by volunteers and has since 1988 acted as an advocate for the voluntary sector concerned with genetics. This has been achieved by creating awareness and providing information on genetic disorders to policy makers and health officials in order to achieve a high quality of services for those directly affected by genetic conditions and their families. GRDO also acts as a watchdog in relation to legislation concerning disability to ensure that the rights of people with genetic conditions are protected: the organisation was involved in the consultation process for the Disability Act, 2005 resulting in the inclusion in the Act of provisions regarding genetic tests.

Sources of information on rare diseases and national help lines

Since 2004, there is a dedicated Orphanet team for Ireland and the UK, hosted by the University of Manchester in the UK. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in Ireland and the UK for entry into the Orphanet database.

There is no official information centre of rare diseases in Ireland other than Orphanet. Public information about rare diseases is also provided by patient organisations and the GRDO. The MRCG supports smaller patient groups in securing research funding for rare diseases. IPPOSI provides web-based information and policy support to patient groups. IPPOSI and MRCG are funded partly by the government and membership fees.

In 2008, a report funded by Ireland’s Health Research Board discovered an urgent need for information and support resources for both patients and medical professionals encountering rare disease patients in their practice. The report, *An investigation into the social support needs of families who experience rare disorders on the island of Ireland*, is published by Rehab Care, a unit of independent non-profit organisation Rehab Group⁵³. Amongst the findings, 73% of general physicians admit to difficulties in providing patients and families with appropriate information; some 60% of physicians access rare disease information via the internet; and patients need a reliable resource that does not present a worst-case scenario leading to additional stress and worry. The report recommends developing a centre of excellence in Ireland dedicated to rare diseases that could support health professionals and also provide materials suitable for patients and their families. The authors recommend that Orphanet, as a freely-accessible information resource for professionals and patients, receive a high profile in Ireland, along with UK charity Contact a Family⁵⁴.

⁵³<http://www.rehab.ie/index.aspx>

⁵⁴<http://www.cafamily.org.uk/index.php?section=861>

National rare disease events

IPPOSI holds 2-3 conferences annually to tackle various questions in the field of rare diseases and orphan drugs.

Research activities and E-Rare partnership

The Medical Research Charities Group (MRCG) was formed in 1998 to inform and support charities in Ireland in the development of their medical research. As an alliance promoting medical research, the MRCG works to raise the profile of medical research, increase funding, and ultimately alleviate suffering and mortality caused by illness. Since 2006 the MRCG charities have been co-funding research projects with the Health Research Board (HRB). This is made possible by an allocation to the HRB from the Department of Health and Children. While the scheme does not focus solely on rare diseases a number of research projects in the area have been funded. Since the Scheme was put into action in 2006, 44 projects (covering rare and non rare conditions/diseases) have been supported. In this joint funding scheme the Department of Health and Children provides an ongoing allocation of €1 million to the HRB which is matched by the research charities. Total investment for the three years 2006, 2007, 2008 was €6 million of which €3 million was provided by the Department of Health.

In addition to the joint funding scheme activities, the MRCG also has a working group on rare diseases and has prepared a policy paper on rare diseases entitled "It's not rare to have a rare disease".⁵⁵

Ireland is not currently a partner of the E-Rare project.

Participation in European projects

Ireland participates in the following European Reference Networks for rare diseases: Dyscerne, HodgkinEPNET, EPI and the Paediatric Hodgkin Lymphoma Network. Ireland contributes to the following European rare disease research projects: AUTOROME, EPOKS, EURAPS, EUROPEAN LEUKEMIA NET, EVI-GENORET, GENESKIN, MANASP, MOLDIAG-PACA, NEUROPRION and NOVSEC-TB. Ireland contributes to the following European registries: EUROCAT and EURO CARE CF. Ireland contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

No specific information provided.

Specialised social services

No specific activity reported.

B.1.13.2 New initiatives and incentives in 2009**National plan for rare diseases**

GRDO and IPPOSI met with the Irish Minister for Health and Children, Mary Harney TD, in July 2009 to progress the issue of implementing the EU Council Recommendation on Rare Diseases. The IPPOSI/MRCG/GRDO Report "Rare Diseases in Ireland - What is the National Plan?" was planned for publication in Autumn 2009.

National rare disease events

To mark the second Rare Disease Day, the Irish Platform for Patients' Organisations, Science and Industry (IPPOSI), the Genetic and Rare Disorders Organisation (GRDO) and the Medical Research Charities Group (MRCG) held a meeting on 25 February 2009 entitled 'Focus on Rare Disease in Ireland – What is the National Plan?' bringing together speakers from all sectors in Ireland and Europe to look at diagnosis, treatment and access to medicines for people with a rare disease in Ireland and to consider a national plan of action. The meeting highlighted how important it is for all the stakeholders in the Rare Disease community in Ireland to work together and a commitment was given to do so by the Health Service Executive (HSE) and all parties on the day.

⁵⁵IPPOSI Information Document on Rare Diseases – 19 February 2009
<http://www.ipposi.ie/index.php/information-centre/rare-diseases>

On 28 February 2009, a family day was organised to mark the second Rare Disease Day, where many Irish rare diseases patient organisations were present to provide information to families.

B.1.14 ITALY

B.1.14.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Italy accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

Although there is no specific national plan for rare diseases in Italy, rare diseases have been designated since 2001 as a health care priority in the context of the 3-year national health plans, which are intended by the national government as directions for actions at a national level, whilst the responsibility for actual implementation of measures is attributed to the regional governments. A coordinated and comprehensive framework of actions has been set up by the Ministry of Health Decree 279/2001, which established a national network for the prevention, surveillance, diagnosis and treatment of rare diseases, a National Registry of Rare Diseases, and a waiver for the cost of medical care, diagnostic work up and therapy for patients with suspected, or recognised, as affected by one of rare diseases included in an identified list. Provision of services for rare diseases and orphan drugs follows the distribution of responsibilities described above. A Committee ensures the Interregional Coordination for Rare Diseases between the Ministry of Health, the *Istituto Superiore di Sanità* (National Institute for Health), and all Italian regions. This Committee has several aims, which include harmonisation of the regional networks for rare diseases, the implementation of the National Registry for Rare Diseases and the management of the list of rare diseases for which patients can obtain free diagnosis and treatment. Based on the work of this Committee, Ministerial Decree 279/2001 established a list (*Livelli Essenziali di Assistenza - LEA*) of rare conditions (284 single rare diseases and 47 groups of diseases) which receive specific cost exemption. These diseases are assessed as being chronic, debilitating and requiring a high cost treatment. Decree 279/2001 provides for a regular update of such list. In four regions of Italy regional legislative acts extend the number of rare diseases in this list. The implementation of the regional actions on rare diseases receives funding from the Ministry of Health. Rare diseases costs are included in the national health care budget and dedicated funds are available for the implementation of projects aimed at strengthening regional networks (€30 million for 2008 with €5 million for the following years).

In 2008 the National Centre for Rare Diseases was established, with the mission of promoting and developing scientific research and public health actions as well as providing technical expertise and information on rare diseases and orphan drugs, aimed at the prevention, treatment and surveillance of these diseases. This Centre takes over the activities carried out for many years by *Istituto Superiore di Sanità* (ISS) to tackle rare diseases.

Centres of expertise

In 2001 Ministerial Decree (279/2001) set up a national network for rare diseases (*Rete Nazionale Malattie Rare*), made up of hospitals and referral centres for around 500 rare diseases, selected on the basis of their documented experience in the diagnosis and treatment of rare diseases, their technical equipment and suitable service availability. Since 2001, over 250 Regional Centres have been designated by official regional decisions. Soon after the delivery of the Ministerial Decree, the Italian Constitution was changed and health programmes and their organisation were delegated to the regions. Because of their autonomy, the 21 regions used different criteria to identify centres for rare diseases and adopted different models to organise the regional network.

In each region a Regional and Interregional Coordination Centre has been (or should be) created in order to coordinate the activities of referral centres, the exchange of information between them, and the provision of expertise and data to the regional rare disease registries. Following a diagnosis in a designated hospital, patients can obtain free treatment (Ministerial Decree 279/2001).

Registries

The National Registry of Rare Diseases was created by ISS in 2001 in accordance with article 3 of Ministerial Decree 279/2001 which provides for the collection of clinical, biochemical, demographic, risk factors, lifestyle and other useful data for scientific study and research in the epidemiologic, medical and biochemical fields. Its general goals are to supervise the situation of rare diseases and to support National and Regional planning of interventions for rare diseases patients.

The Registry aims to obtain epidemiologic information (in the first place, the number of cases of a specific rare disease and the related distribution on National territory), and other useful information to evaluate problems in the field of rare diseases; it is also a useful tool to evaluate delays in diagnosis and patient migration, to support clinical research and to promote discussion amongst health workers regarding the definition of diagnosis criteria.

The Regions have developed independent registries. The model established by the Veneto region has been also adopted by other regions including Friuli Venezia Giulia, Trentino Alto Adige, Emilia Romagna and recently Liguria. The Veneto model is based on an informatics infrastructure acting as a network connecting different centres involved in the management of patients with rare diseases. All the steps concerning diagnosis, clinical follow-up and treatment are linked by a unique information system shared by all those involved in patient management.

In 2007 the National Centre for Rare Diseases (*Centro Nazionale Malattie Rare* - CNMR) put into action a new method of data collection which includes new software which can be used both by separate medical centres/ centres qualified to diagnose and treat rare diseases patients, and by those in charge of Regional Centres of Coordination that coordinate activities and provide the liaison between the CNMR and separate medical centres.

The registry is linked to other interregional, regional and international registries. The regional registries are updated and they not only report information on diagnoses, but also on distributed orphan drugs.

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

Neonatal screening policy

In Italy, neonatal screening is mandatory for cystic fibrosis, congenital hypothyroidism and phenylketonuria. Some regions perform screening of additional diseases including adrenal hyperplasia, biotinidase deficiency, maple-syrup urine disease and galactosaemia.

Some regions, including Tuscany, Sicily and Emilia Romagna have adopted larger neonatal screening programs to include a wider number of metabolic disorders, based on the guidelines developed by some scientific societies.

National alliances of patient organisations and patient representation

In Italy, UNIAMO (*Federazione Italiana Malattie Rare*)⁵⁷ is the national alliance of rare disease patient organisations. Established in 1999, UNIAMO regroups over 85 patient organisations dedicated to over 600 rare diseases. UNIAMO publishes a newsletter and organises regular meetings and conferences. Its goal is to create a national reference body which guarantees the coordination among rare diseases organizations, the protection of patients' rights and the life quality improvement for people affected by rare diseases. UNIAMO is a member of Eurordis.

There is no public funding scheme for the activities of patient organisations, but government institutions are sometimes requested to support specific initiatives by providing necessary means such as meeting places and patient organisations may apply for funding for activities listed as eligible for funding by the Welfare Ministry and local governmental institutions. Grants for activities of patient organisations come mainly from private sponsorship, charities and income tax donations.

The ISS hosts the activities of the National Council for Rare Diseases (the "*Consulta*"), established in September 2006 by a Directorial Decree of the Ministry of Health and Welfare: the Council is a national independent representative body, which collaborates with the National Centre for Rare Diseases. It was originally composed of 34 members (one for each participating rare disease organisation), but now the number of members is limited to 28 and these members are elected from the 264 rare diseases patient organisations' representatives. Its goals are to determine priorities in the field of rare diseases, to define the problems and to identify possible solutions for patients and their families. It is also important for the Council to involve rare

⁵⁷<http://www.uniampo.org/>

diseases patients in the legislative bodies' decisions and to strengthen the links between rare diseases organisations and civil society. Patients' opinions are not binding, but are taken into account in decisions taken at national level. No financial support is available for patient representatives to attend these meetings.

Sources of information on rare diseases and national help lines

Since 2001, there is a dedicated Orphanet team in Italy, currently hosted by the Mendel Institute in Rome. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. The Orphanet portal is available in Italian.

A specific service is run by the Italian National Centre for Rare Diseases (based at the ISS) which provides information to patients, families and health professionals by means of a dedicated website and a telephone helpline. The information provided includes information on the education of health professionals; elaboration of specific guidelines; elaboration of a database containing Orphan Drugs available in the country; and collaboration with patient organisations (quality of life, access to social and health services, etc.). Information for patients is also provided by websites run by the Regional Centres for Rare Diseases which are present in some Italian Regions.

The official website of the Ministry of Health provides information about legislative and administrative issues. Regional website information is also available. Other services are run by patient organisations and are largely heterogeneous in their coverage, either of a single rare disease or a group of rare diseases.

To mark the first Rare Diseases Day (29 February 2008) a rare diseases helpline (*Telefono Verde Malattie Rare*) was put into place by the National Centre of Rare Diseases at the ISS. Some regional toll free numbers are available and information lines are sometimes provided by patient associations.

Guidelines

The Ministry of Health and NIH are involved in the National Guidelines System which is officially entitled to issue guidelines and to make available any other documents drawn up by Consensus Conferences carried out by the National Guidelines System. The list of procedures for treatment and diagnosis of rare diseases (as listed by Decree 279/2001) is updated and includes laboratory procedures for metabolic diseases diagnosis. In 2007 the "Multidisciplinary Guidelines for the Integrated Assistance to Down's Syndrome Patients and their Families" were published by CNMR as part of the National Guideline System.

National rare disease events

Since February 2008, UNIAMO, the Italian national rare diseases alliance, coordinates Rare Disease Day. This activity is supported by private funding (FARMINUSTRIA and Cesare Serono Foundation). The CNMR ISS also organises an annual international rare disease meeting and several national meetings each year. Telethon-Italy organises a fundraising event every year to promote research on genetic diseases.

Research activities and E-Rare partnership

In Italy, there are efforts to co-ordinate research between the regions, the Italian Drug Agency (AIFA⁵⁸), the Ministry of Health and the Istituto Superiore di Sanità (ISS). Funds for research into rare diseases are provided by the Ministry of Health, the ISS, the AIFA and the Ministry of Education, Universities and Research, as well as the Telethon. The last Health Ministry call for projects for rare diseases⁵⁹ had a total budget of €8 million.

The AIFA (the Italian Drug Agency) has issued over previous years calls to fund independent research projects on the development of orphan drugs. In particular, the AIFA financed a three year initiative, launched in 2005, to support clinical research on drugs of interest to the national health service and where commercial support is normally insufficient: one of the concerned areas was the field of rare diseases and orphan drugs. Three topics were included in the clinical research area concerning rare diseases: firstly the benefit-risk profile of orphan drugs designated by the EMA, secondly the benefit-risk profile of off-label drug use (and in particular generics), and thirdly the benefit-risk profile of drugs for non-responders to standard treatments. Projects in these topic areas were funded for up to a maximum of 300'000€ with the cost of therapies funded separately.

Foundations and associations promote campaigns to fund genetic research (such as the Telethon) or research on specific diseases. Voluntary funds can be collected through general taxation.

Italy, represented by the ISS, is a partner of the E-Rare project and has participated in the last two Joint Transnational Calls. Italy participated in 12 of the 13 consortia selected for funding by the first call.

⁵⁸ <http://www.agenziafarmaco.it/section8983.html>

⁵⁹ http://www.salute.gov.it/bandi/documenti/Bando_malattie_rare.pdf

Participation in European projects

Italy participates in the following European Reference Networks for rare diseases: Dyscerne, ENERCA, EPNET, EPI, EUROHISTIONET, NEUROPED, PAAIR, RBDD (main partner) and TAG. Italy participates in the following European research projects for rare diseases: AAVEYE, ADIT, ANTIMAL, BIG HEART, BIOMALPAR, BIO-NMD, CARDIOGENET, CUREHLH, CUREFXS, CLINIGENE, CONTICANET, CSI-LTB, ENRAH, EURADRENAL, EUCILIA, EUCLYD, EMSA-SG, EUROBONET, EUROGROW, EURO-LAMINOPATHIES, EUROPAPNET, EUROBNFS, EURO-CGD, EUROTRAPS, EURPIFNET, EUROSD, EPINOSTICS, ERMION, EUROGEBETA, EURORETT, EUROPSPA, EUMITOCOMBAT, EURAMY, EURAPS, EUREGENE, EUROCARE-CF, EUROPEAN LEUKEMIA NET, EUROSCA, EUROWILSON, GENESKIN, INHERITANCE, HAE III, HMA-IRON, HSCR, KINDLERNET, MTMPATHIES, LEISHMED, LIGHTS, MALARIA AGE EXPOSURE, MANASP, MITOCIRCLE, MOLDIAG-PACA, MCSCS, MILD-TB, MM-TB, MYELINET, MYORES, NANOMYC, NEUROKCNQPATHIES, NEUROPRION, NEUROPROMISE, NEUROSIS, NMD-CHIP, NSEURONET, OSTEOPETR, PEROXISOMES, PNSEURONET, PROTHETS, PODONET, PEMPHIGUS, RD PLATFORM, RISCA, READ-UP, SIOPEN-R-NET, SPASTICMODELS, SME MALARIA, STEM-HD, TAMAHUD, TARGETHERPES, VITAL, WHIPPLE'S DISEASE and WHIMPAT. Italy contributes to the following European registries: EUROCAT, TREAT-NMD, HAE-registry, RBDD, AIR and EUROCARE CF. CNMR (ISS) coordinates the EUROPLAN project and a service project for the Evaluation of Neonatal Screening practices in EU Member States.

Orphan drug committee and incentives^{60,61}

The Italian Medicines Agency (AIFA - *Agenzia Italiana del Farmaco*) is the main body in charge of the introduction of orphan drugs on the Italian medicine market. The AIFA has established an innovative funding scheme (*Fondo AIFA 5%*) which requires Italian pharmaceutical companies to donate 5% of their promotional expenditure to an independent research fund. The fund collects €45 million a year: half of this is used for the reimbursement of orphan and 'life saving' drugs and the other half is aimed at supporting independent research, drug information programs and pharmacovigilance. This funding program for independent clinical research on drugs is open to researchers working in public and non profit institutions. One of the research areas of the program is dedicated to orphan drugs for rare diseases. At the start of 2009, three calls for proposals (2005-2007) had been finalised and 69 studies had received funding in the area of rare diseases.

The National Registry of Orphan Drugs includes data on the diagnosis and follow-up of patients treated with orphan drugs. These drugs are authorised at central level by the EMA (European Medicines Agency) and reimbursed by the National Health Service (NHS). The National Registry of Orphan Drugs, established by the AIFA and managed in collaboration with the ISS, has survey forms for each rare disease and its related drugs, and collects, checks and analyses data sent by Regional Centres authorised to distribute drugs. The goal of this registry is to have nationwide coverage, in other words, to address all Italian Centres qualified to distribute drugs and to prescribe orphan drugs.

Since 2005, orphan drug research in Italy has benefited from the "*Fondo AIFA 5%*", which also finances compassionate use of Orphan Drugs. In 2006, for example, some 30 independent research protocols in the area of rare diseases and orphan drugs were selected for funding by the AIFA through this unique initiative. In 2008, however, rare disease and orphan drug research did not figure amongst the areas given priority.

Orphan drug availability

Reimbursement is based regionally and is granted for all orphan drugs which follow centralised marketing authorisation procedure. Italy also has an off-label, compassionate use, procedure regulated by Law 648/96⁶² (a list of eligible drugs is annexed to this law). The Technical Committee of the AIFA can include a given medication in the official list allowing it to be prescribed at the NHS's (National Health Service) charge, if for a specific disease there is no therapeutic alternative. There are three types of medical products that can be included: innovative drugs for which the sale is authorised abroad, but not in Italy; drugs which have not yet

⁶⁰ This section has been written using the *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp49-53).

⁶¹ 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* (pp15-16)

⁶² Law 23-12-1996 n. 648. *Conversione in legge del D.L. 21 October 1996, n. 536, recante misure per il contenimento della spesa farmaceutica e la rideterminazione del tetto di spesa per l'anno 1996* (published in *GU* 23 December 1996, n. 300).

received authorisation but which have undergone clinical trials; and drugs to be used for a therapeutic indication other than the one which has been authorised⁶³.

The off-label use of a drug on the costs of the National Health Service can also be decided by a doctor, as envisaged by article 3, paragraph 2 of DL 23/1998⁶⁴ provided that this decision is made on a named patient basis and documented evidence is provided and no other treatment is possible. A Ministerial Decree of 8 May 2003⁶⁵ allows for the prescription (paid for by the producer) of drugs which are not yet authorised but are subject to phase II or III clinical trials for the same therapeutic indication and for which the likely result is a favourable evaluation of efficacy and safety.

Specialised social services

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

Therapeutic recreational programmes are provided by local authorities’ social services under the administration of the municipalities. At government level the competence is that of the Ministry of Social Policies. Some municipalities assure public services, but more often services are run by private bodies (companies or patient organisations) commissioned by social authorities. Some summer camps are informally or formally organised by patient organisations. These services are sometimes fully reimbursed, or there is a partial contribution according to family income.

Additional social and/or financial support is available for families and patients with disabilities (Law Decree n.509, 23 November 1988). Services promoting social integration of patients with disabilities in schools and the workplace are provided by the government.

B.1.14.2 New initiatives and incentives in 2009

National plans and actions in the field of rare diseases

On the occasion of the “*Conferenza Stato-Regioni*” on 26 February 2009, the State Secretary for Health (and now Minister of Health), Ferruccio Fazio, communicated that €8 million will be allocated to Rare Diseases: €5 million from Ministry of Welfare and €3 million from AIFA.

During the Second Rare Disease Day 2009, Ferruccio Fazio promised to include 109 additional rare diseases in the LEA (*Livelli Essenziali di Assistenza*). The *Livelli Essenziali di Assistenza* lists services provided by the National Health System to citizens, they can be free or provided after paying a prescription charge. The services included in LEA represent the ‘essential’ services granted to all Italian citizens. The problem is that only a few rare diseases are included in LEA and updates of this disease list are infrequent.

Registries

The State Secretary also announced in 2009 that the National Registry for Rare Diseases (*Registro Nazionale Malattie Rare – RNMR*) will be soon updated: in the last year, the registry received around 50,000 new notifications of diagnoses which covered about 60% of the national territories. The coverage of the national territory by the RNMR will soon be extended with the areas of Veneto Region and Emilia Romagna Regions.

National alliances of patient organisations and patient representation

The Council for Neurodegenerative Diseases was established by the Ministry of Labour, Health and Social Affairs, by a Ministerial Decree (27 February 2009). The Council brings together organisations of neurodegenerative rare diseases, such as the organisations representing Amyotrophic Lateral Sclerosis, Muscular Dystrophy, Spinal Atrophy, Advanced Stage Muscular Dystrophy and Locked-in syndrome.

⁶³ *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (p50).

⁶⁴ D.L. 17-2-1998 n. 23 *Disposizioni urgenti in materia di sperimentazioni cliniche in campo oncologico e altre misure in materia sanitaria*. (published in GU 17 February 1998, n. 39).

⁶⁵ Ministerial Decree 8 May 2003 *Uso terapeutico di medicinale sottoposto a sperimentazione clinica* (published in GU 28 July 2003, n. 173).

Sources of information on rare diseases and national help lines

In order to improve the classification of rare diseases and to codify them to the highest degree of accuracy, completeness and consistency, an Italian Working Group, coordinated by the National Centre for Rare Diseases (CNMR) has been established. The aims of the working group are the following: to evaluate the accuracy of the coding of rare diseases in the ICD 10 and ICD 9CM classification system; to harmonise the terminology of rare diseases; to develop coding procedures; and to identify problem areas regarding coding process of rare diseases. This Working Group includes: national experts on coding of mortality data (ISTAT), hospital discharge data (Ministry of Health), rare tumours data, and of congenital malformation data; regional representatives involved in activities related to rare diseases from Lombardy, Piedmont, Apulia and Latium. A web-based system, elaborated by the CNMR, is designed to facilitate exchanges between the experts in the working group. For each rare disease, members can make proposals in a structured and organised manner.

Education and training

In spring 2009 a 'Learning at Distance Course' has been issued by CNMR, targeted to improve the knowledge of health professionals concerning primary prevention with folic acid.

In July 2009, UNIAMO, SIP (*Società Italiana di Pediatria*), FIMP (*Federazione Italiana Medici Pediatri*), SIMGEPED (*Società Italiana Malattie Genetiche Pediatriche e Disabilità Congenite*), SIGU (*Società Italiana di Genetica Umana*) and *Farmindustria* signed a memorandum highlighting the need to develop an education and training program on rare diseases for medical practitioners. The principal goal of this agreement is to reduce waiting times for diagnosis. The parties committed themselves to a work of awareness-raising and education at regional level, in order to improve diagnosis and health care management of rare diseases patients and their families. The education will be provided through seminars, organised in different Italian regions.

Guidelines

The National Centre for Rare Diseases published in March 2009 the "Guidelines for the care of patients affected by alternating hemiplegia and their relatives", within the National Guidelines System. Guidelines for the Hereditary Epydermolysis Bullosa, Aniridia and Multiple Hereditary Exostosis are in preparation. Experts from Italy have collaborated on the guidelines for Williams syndrome and Kabuki syndrome, delivered by the Dyscerne project.

National rare disease events

UNIAMO organised the Second Rare Disease Day 2009 on 28 February 2009 in Italy: a two-day seminar ("*Conoscere per assistere*") was organised on the theme of rare diseases and patient care in Rome where expert speakers from the field approached the subject from different perspectives. In 2009, the national male volley-ball team joined UNIAMO to celebrate Rare Disease Day. The Barbareschi Foundation, in collaboration with ISS, Orphanet, Dossetti Association, UNIAMO Onlus and with the support of *Farmindustria*, promoted the event, "*Figli di un Male Minore*". In addition to well-known actors Gigi Proietti and Lino Banfi, the Minister Maurizio Sacconi attended the event. Through UNIAMO intermediation, the Minister of Labour, Health and Social Affairs became acquainted with the requests of Italian rare diseases patient organisations, who asked that the same benefits and incentives be available for all rare diseases.

In Turin, Rare Disease Day 2009 was a three day event with different meetings and informative actions. There were also booths representing Piedmont's rare diseases organisations in the town, and one discussion dealt with ethical and social aspects of rare diseases. In Milan, the Lombardy region organised an open conference for doctors and patients. The Sardinia region created a special postcard for the occasion. Other concerts, conferences and booths were organised in Palermo, Catania, Messina, Reggio Calabria, Monsummano Terme, Pesaro and Casale Monferrato.

Rare Disease Day 2009 also involved schools: in Formia, Gaeta and Modena children had the opportunity to attend lessons on rare diseases. In Levanto di Deiva Marina, students learned more about rare diseases, taking part in a treasure hunt.

Within the framework of the manifestations for the National Rare Disease Day, CNMR organised a literary and fine arts competition ("*The Flight of Pegasus*"): the subjects were related to rare disease patient conditions, with the aim of reducing the cultural barriers towards the "unknown" and the different. The competition was a success and will be repeated.

Hosted rare disease events

In 2009 several congresses were hosted in Italy concerning rare diseases and orphan drugs: the International Conference on Rare Diseases and Orphan Drugs (ICORD 2009)⁶⁶ was held in Rome on the 23-25 February 2009. The 3rd International Congress on Rare Pulmonary Diseases and Orphan Drugs was held on 20-21 March 2009. The Molecular Mechanisms of Neurodegeneration symposium was held on 8-10 May 2009⁶⁷. The Narrative Medicine Conference was held in June 2009: this workshop aimed to promote the knowledge of narrative medicine as a functional tool in the management of patients with rare diseases: narrative medicine aims to fill the gap between the physician's bedside clinical knowledge and the patient's subjective experience. The 1st European Congress on Rett Syndrome was held on 5-7 June 2009⁶⁸. An international conference on DiGeorge/Velocardiofacial syndrome was organised by Aidel 22 association in Rome (3-5 July), while UNIAMO celebrated its 10th anniversary in Venice. The Rare Neurometabolic and Neurogenetic Disease in adults joint French-Italian workshop, was held on 10-11 September 2009⁶⁹. The European Working Group on Rett Syndrome 2009 Meeting was held on 17-18 September 2009. The Adaptive Immunity and the Pathogenesis of Rheumatic Diseases – A Translational Research in Paediatric Rheumatology Conference was held on 24–27 September 2009⁷⁰. The national conference on the National Network for Rare Diseases (which deals with national and the regional registers) was held on 7 October 2009. The 1st Meeting of the National Coordination of Congenital Malformations was held on 8 October 2009. The Annual Meeting of the Italian Network for the promotion of Folic Acid and the prevention of congenital defects was held on 9 October 2009⁷¹.

Research activities and E-Rare partnership

Italy, represented by the ISS, participated in the second E-Rare transnational call and Italy participates in 8 of the 16 consortia/projects selected for funding with a total funding of around €1 million. A specific call to fund research projects on rare diseases has been issued by the Ministry of Welfare In 2009. AIFA funded rare disease and orphan drug research until 2007, from 2008 onwards rare disease and orphan drug research is being funded by the Ministry of Health, within the general health research call with a specific budget reserved for rare disease research. The Annual Telethon was able to fund 36 out of the 48 selected research projects on genetic diseases thanks to fund raising activities.

B.1.15 LATVIA

B.1.15.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Latvia accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals, although there is no official definition of rare diseases in laws and regulations.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Latvia. The costs related to rare diseases are included in the national health care budget.

Centres of expertise

There are currently no official centres of expertise for rare diseases in Latvia, but the Latvian State University Children's Hospital provides genetics services.

⁶⁶ http://www.icord.se/rome_2009.php

⁶⁷ <http://users.unimi.it/triplet/2009/>

⁶⁸ <http://www.aimgroup.it/2009/airett/>

⁶⁹ http://www.xerver.it/maillinglist/allegati/SIN%20italofrancese_22062009%20%204.pdf

⁷⁰ http://www.sispge.com/tripr/EVI_Generalinfo.asp

⁷¹ http://www.sispge.com/tripr/EVI_Generalinfo.asp

Registries

Latvia contributes to the EUROCARE CF European registry and the UK DMD registry.

Neonatal screening policy

In Latvia, newborns are screened for phenylketonuria and congenital hypothyroidism. All activities connected with the evaluation of these tests and quality control are carried out under the supervision of the International Society of Neonatal Screening.

National alliances of patient organisations and patient representation

Before 2009 there was no alliance of patient organisations in Latvia although there are patient organisations representing individual rare diseases. In 2009 the Latvian Rare Disease organisation “Caladrius”⁷² was launched.

Sources of information on rare diseases and national help lines

Since 2006, there is a dedicated Orphanet team in Latvia, currently hosted by the Medical Genetics Clinic of the Latvian State at the Children’s University Hospital, Riga. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no information centre for rare diseases in Latvia other than Orphanet. Web based information is available for a limited number of diseases (rare and non-rare) and certain information is maintained using a state budget. There are non-rare disease specific help lines run by the state, some with a state budget, to help patients access health care and psychological support.

National rare disease events

No specific activity reported.

Hosted rare disease events

No specific activity reported.

Research activities and E-Rare partnership

Funding is available for rare disease projects (through state budget, charities and pharmaceutical companies) although funds are not specifically earmarked for rare disease research. Latvia is not currently a partner of the E-Rare project.

Participation in European projects

Latvia participates in the following European Reference Networks for rare diseases: Dyscerne and PAAIR. Latvia contributes to the following European registry: EUROCARE CF. Latvia contributes to the EUROPLAN project.

Orphan drug committee and incentives

The Latvian State Agency of Medicines regulates orphan drug availability.

Orphan drug availability

The *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products* reported that in Latvia “the State Agency of Medicines is entitled, due to considerations of health protection, to make a decision (after discussion with the Minister for Health) regarding the fee exemption or reduction for activities associated with the evaluation, registration or re-registration of a medicinal product if the medicinal product (with or without orphan designation pursuant to Regulation 141/2000) is intended for the treatment of a rare disease.

“The State Agency of Medicines may issue importation and distribution authorisation for medicinal products not registered in Latvia if the medicinal product is intended for treatment of a rare disease (for an individual patient on the basis of prescription or for use in a health care institution on the basis of a written request).

“1% of reimbursement budget is intended for reimbursement of medicinal products used for treatment of rare diseases ([which are] not always those drugs [having an] orphan designation).”⁷³

⁷² www.caladrius.lv

⁷³ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (pp16-17)

Specialised social services

Respite care services are available and the categories of patients eligible for reimbursement are described in the “Procedures for the Organisation and Financing of Health Care” (Regulation of the Cabinet of Ministers No. 1046, adopted on 19 December 2009). Therapeutic recreational programmes are also available and costs are included in the national health care budget. There are existing government-run services promoting social integration of those with handicaps, including the school environment and work place.

B.1.15.2 New initiatives and incentives in 2009**National plan for rare diseases and related actions**

A National Cancer Control Programme (2009-2015) was adopted through order No.48 of the Cabinet of Ministers of the Republic of Latvia on the 29 January 2009 by the Cabinet of Ministers: rare cancers are covered by this programme. In August 2009 a regulation was introduced which allows for compensation of up to 700'000 Ls a year for children with rare diseases. In November 2009, drugs for MPS II were available for children with this disease as part of the programme.

National alliances of patient organisations and patient representation

In 2009 the Latvian Rare Disease Organisation Caladrius⁷⁴ was launched on the occasion of the 2nd Rare Disease Day. The mission of the organisation is to provide patients with the relevant information and support and to represent patients. Association representatives also presented Caladrius at the Latvian Parliament *Saeima* Social and Employment Matters Committee, and a press conference was organised in Riga.

B.1.16 LITHUANIA **B.1.16.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in Lithuania accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Lithuania. There is no budget currently dedicated to rare diseases in Lithuania.

Centres of expertise

There are no official centres of expertise in Lithuania, but two centres (Centre for Medical Genetics in Vilnius University Hospital Santariškių Clinics and the Hospital of Kaunas University of Medicine) provide genetics services and diagnostic services for rare diseases to the Lithuanian population.

Registries

Lithuania contributes to the EURO CARE CF registry.

Neonatal screening policy

Newborn screening programmes are in place for phenylketonuria and hypothyroidism (Order No. V-865 of the Healthcare Minister of Lithuania of 6 December 2004 “Regarding the Approval of Universal Screening of Newborns for Inborn Metabolism Disorders Procedures”).

⁷⁴ www.caladrius.lv

National alliances of patient organisations and patient representation

There is currently no umbrella organisation for patient organisations in Lithuania. There are several separate patient organisations for patients with rare diseases, including phenylketonuria, cystic fibrosis, rare oncological diseases, Alpha-1-antitrypsin insufficiency disease and haemophilia. Patient organisations receive funding mainly from private sponsorship, donations and income tax donations. Patient organisations are represented at the Compulsory Health Insurance Council, and at the Council of Representatives of Patients' Organisations under the Ministry of Healthcare as of April 2009.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Lithuania, currently hosted by the Department of Human and Medical Genetics at the University of Vilnius. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no official information centre on rare diseases in Lithuania other than Orphanet. Lithuania is a partner in the ECORN-CF project which maintains a website and forum for patients with cystic fibrosis, their relatives and any other interested parties where they can ask questions and obtain answers from experts. There is currently no help line dedicated to providing information on rare diseases, but other general help lines (e.g. providing psychological support) exist.

National rare disease events

The International Rare Disease Day 2008 was publicised in Lithuania.

Hosted rare disease events

No specific activity reported.

E-Rare partnership and research activities

There is no specific programme for rare disease research in Lithuania, though funding is available for fundamental research and research concerning medicinal products: this second area of research is in particular targeted by the European Union Structural Assistance Operational Programme 2007-2017 for Economical Growth and research projects for rare diseases may receive financial support by taking part in tendering processes. Additionally, in 2007 the Government of the Republic of Lithuania adopted the Lithuanian Research and Development Priorities for 2007-2010 (Governmental Decree No. 166, 7 February 2007) which also includes as a priority the development of medicinal products, including those targeting rare diseases. Lithuania is not currently a partner of the E-Rare project.

Participation in European projects

Lithuania participates in the following European Reference Networks for rare diseases: ECORN CF, and PAAIR. Lithuania participates in the EUROPEAN LEUKEMIA NET research project. Lithuania contributes to the following European registry: EUROCARE CF. Lithuania contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products concerning Lithuania*, "compensation for orphan medicinal products and medicinal products for rare diseases and conditions is paid for out of the funds earmarked for that purpose in the budget of the compulsory health insurance fund (Ministry of Health Decree No 151 of 20 March 1998; Official Gazette, 1998, No 33-894; 1999, No 7-159). A list of reimbursed medical products is available (the last update is dated 2 February 2009, Healthcare Ministerial Order No v-52, regarding the amendment of Order No.49 of 28 January 2000 "Regarding the Approval of the List of Reimbursed Medicinal Products"). Individuals are compensated for the purchase of medicinal products for rare diseases and conditions on presentation of specialist doctors' reports, following a decision by the committee, set up by the Health Ministry's State Patient Fund, responsible for taking decisions on medicines and medical treatment for very rare diseases and conditions and on cases for which no provision has been made (Decree of the Health

Ministry's State Patient Fund Directorate No 1K-149 of 22 November 2005; Official Gazette, 2005, No 139-5037)."⁷⁵

Specialised social services

Respite care services are available and are organised by municipalities and hospital clinics: the Kaunas Children's Development Clinic, the Centre of Children's Development at Vilnius University Children's Hospital and day care centres for mentally disabled patients at municipal level. Therapeutic recreational programmes are available and are provided by local authorities under the administration of municipalities and directed at government level by the Ministry of Social Security and Labour. Some municipalities provide public services but these services are mostly run by private bodies (either companies or patient groups) commissioned by the social authorities. Educational camps are available for children, organised by the Ministry of Education. Rehabilitation issues are regulated by Healthcare Ministerial Order No. V-50 (17 January 2008) "Regarding the Organisation of Medical Rehabilitation and Sanatorium". Governmental services are available to promote social integration including integration in schools and the work place of patients with disabilities: this includes personalised secondary training syllabi and a special integration programme for sick and disabled persons for the labour market.

B.1.16.2 New initiatives and incentives in 2009

National plan for rare diseases and related actions

The Ministry of Health Decree Nr.V-239 of 31 March, 2009, established an Action Group for the development of a National Plan for Rare Diseases in Lithuania. Among the members of this group are Orphanet Lithuania National Advisory Committee members Prof. Milda Endziniene and Dr. A.Utkus.

National alliances of patient organisations and patient representation

A new measure is in place to promote the active involvement of non-governmental organisations in the formation of implementation of health policy and public awareness raising (Programme for the Promotion of NGO Involved in Wellness Activity – Healthcare Ministerial Order No. V-318 24 April 2009). This measure will receive funding. The Council of Representatives of Patients' Organisations under the Ministry of Healthcare was established in April 2009 and includes representation of a rare disease patient organisation (Association of People Sick with Haemophilia): this body is expected to become an important mechanism for co-operation between policy makers and patients through working groups and meetings with patient organisations.

National rare disease events

A special session dedicated to rare disease related problems was held during the 9th Baltic Children's neurology Conference in Vilnius, on 22 May 2009.

B.1.17 LUXEMBOURG

B.1.17.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Luxembourg accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

The Task Force on Rare Diseases Luxembourg ("*Groupe de travail maladies rares*") was created in 2005 to analyse the needs of rare disease patients in the country. This Task Force will soon propose a national plan for rare diseases based on the results of a survey analysing the strengths and weaknesses of the healthcare system and the experiences of rare disease patients.

⁷⁵ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision) (p17)*

Centres of expertise

There are currently no official centres of expertise for rare diseases in Luxembourg.

Registries

Luxembourg contributes to the EURO CARE CF European registry.

Neonatal screening policy

A neonatal screening programme is in place in Luxembourg.

National alliances of patient organisations and patient representation

The Luxembourg Association for Neuromuscular and Rare Disorders (ALAN absl.) was established in 1998 to represent patients with rare diseases: the association organises informative events, counselling, guidance and self-help groups and is involved in the work of the Task Force on Rare Diseases Luxembourg.

Sources of information on rare diseases and national help lines

Since 2006, there is a dedicated Orphanet team in Luxembourg, currently hosted by the Ministry of Health. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in Luxembourg for entry into the Orphanet database.

Before 2009 there was no official centre for information on rare diseases in Luxembourg apart from Orphanet.

National rare disease events

No specific activity reported.

Hosted rare disease events

The European Commission at Luxembourg hosts the meetings of the Rare Disease Task Force, and also hosted the First European Conference on Rare Diseases (21-22 June 2005).

Research activities and E-Rare partnership

An annual rare disease telethon, organised by the Lions Club, raises money and pools this with that of the AFM (*Association française contre les myopathies*) which then redistributes these funds to research projects in Luxembourg. Luxembourg is not currently a partner of the E-Rare project.

Participation in European projects

Luxembourg does not currently participate in European Reference Networks for rare diseases. Luxembourg contributes to the following European registry: EURO CARE CF. Luxembourg contributes to the EUROPLAN project.

Orphan drug committee and incentives

The Task Force also aims to create a national medical commission to consult on issues regarding access to and reimbursement of Orphan Drugs.

Orphan drug availability

No specific activity reported.

Specialised social services

No specific activity reported.

B.1.17.2 New initiatives and incentives in 2009**Neonatal screening policy**

As of 1 January 2009, Luxembourg has broadened its newborn screening programme to include medium chain acyl CoA dehydrogenase deficiency (MCAD), an autosomal recessive disorder characterised by acute episodes of hypoketotic hypoglycaemia with hepatomegaly (pseudo Reye syndrome), triggered by fasting or infections.

National rare disease events

ALAN was involved in the organisation of Rare Disease Day 2009 in Luxembourg.

Hosted rare disease events

The Second ELA Research Foundation Congress was held on the 26-27 June 2009: this congress examined the therapeutic challenges linked with leukodystrophies and myelin diseases.

Sources of information on rare diseases and national help lines

The Task Force will soon put into place a national rare diseases platform which offers medical and social services, a rare disease hotline, counselling, self-help groups, specialised information on rare diseases and guidelines of best practices. A guide to all medical, paramedical and social services available to rare disease patients and their family should be available online in 2009.

B.1.18 MALTA **B.1.18.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in Malta accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Malta. A Committee will soon be established to develop a national plan for rare diseases in response to the Council Recommendation.

Centres of expertise

There are currently no official reference centres of expertise for rare diseases in Malta. Assistance by local government for treatment abroad (namely in the UK) is possible through a bilateral health agreement between the two countries.

Registries

Malta contributes to the EUROCAT European registry.

Neonatal screening policy

Neonatal screening is available for haemoglobinopathies and hypothyroidism. Genetic studies (karyotyping and molecular genetic studies) in foetuses and neonates born with congenital malformations or rare syndromes are also available.

National alliances of patient organisations and patient representation

Malta does not currently have a national alliance of rare diseases patient organisations.

Sources of information on rare diseases and national help lines

There is no official information centre on rare diseases in Malta. Although there is no official help line for rare diseases, the agency Sapport provides support by telephone to all disabled people and is funded by the government.

National rare disease events

No specific activity reported.

Research activities and E-Rare partnership

Funding for research into haemoglobinopathies is available through various sources (including the Italian Protocol, Ithamet and the University of Malta). Malta is not currently a partner for the E-Rare project. According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing,*

development and availability of orphan medicinal products, “measures [...] are being taken to promote research and development in Malta. Enterprises carrying out research and development are entitled to various tax credits according to the nature of the specific investments. These tax credits are in addition to the standard 100 % deductions allowed under the Income Tax Act (Cap. 123). These credits are granted under a general framework, which applies to all Research and development initiatives and not exclusively to the pharmaceutical sector⁷⁶”.

Participation in European projects

Malta does not currently participate in a European Reference Network for rare diseases. Malta contributes to the following European registry: EUROCAT. Malta contributes to the EUROPLAN project.

Orphan drug committee and incentives

According to the Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products, “incentives for orphan medicinal products are not yet established in Malta and are still being considered. Incentives with regards to fees concerning pharmaceutical activities related to orphan medicinal products will be taken into consideration in the process⁷⁷.”

Orphan drug availability

According to the Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products, “no measures have been taken in Malta to exclusively target an increase in the availability of orphan medicinal products⁷⁸”.

Specialised social services

There are limited respite care services and there is an element of co-payment, as with all other residential long-term care services. Therapeutic recreational programmes are also available, and subsidies are available: these services are provided by a private foundation (The Eden Foundation). Support is also available to teachers to provide inclusive education at national level and also social security benefits for those with disabilities.

B.1.18.2 New initiatives and incentives in 2009

Hosted rare disease events

MYORES, the European Muscle Development Network, held their 2009 conference in Saint Julian (10-14 October 2009).

B.1.19 THE NETHERLANDS

B.1.19.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in the Netherlands accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10,000 individuals.

National plan for rare diseases and related actions

The Steering Committee on Orphan Drugs, along with the Dutch Genetic Alliance VSOP and the Forum Biotechnology and Genetics (FBG; www.forumbg.nl), are pushing for a national plan to be put on the political agenda, lobbying for the creation of centres of expertise and research programmes dedicated to rare diseases.

⁷⁶ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision) (pp17-18)*

⁷⁷ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision) (p17)*

⁷⁸ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision) (pp17-18)*

Currently, the health care system takes care of all diseases and funding for health care services (including those for rare diseases) is provided through government funding (prenatal screening, neonatal screening, social care, orphan drugs - intramural only) and health insurance (prenatal screening, diagnostic genetic services, treatment, orphan drugs, orphan drugs, rehabilitation).

The Dutch Organisation for Health Research and Development (ZonMw) and the Dutch Steering Committee Orphan Drugs are responsible for work package 7 in the EUROPLAN Project. The European Project for Rare Diseases National Plans Development (EUROPLAN) is a three-year project of the Programme of Community action in the field of Public Health (2003-08), involving at present representatives of the national health authorities of 21 EU MS. WP7 will develop the content of the EUROPLAN recommendations including methodological guidance on how to develop comprehensive and integrated strategies for guiding and structuring all relevant actions in the field of rare diseases

Centres of expertise

All Dutch stakeholders support the opinion that the care for patients suffering from rare diseases should be concentrated in a limited number of centres, in order to guarantee expert care and the possibilities for research. In order to stimulate the development of centres of expertise in the Netherlands the Steering Committee on Orphan Drugs is developing criteria for expertise centres together with different stakeholders (hospitals, doctors, patients, researchers). These criteria are in line with the criteria established by the Rare Disease Task Force's working group on Standards of Care. For now, the eight university medical centres in the Netherlands function as the main clinical reference centres for specific rare diseases, however, proper coordination for rare diseases on the whole is lacking, as well as an adequate funding structure. Other hospitals may also function as well-coordinated centres. The number of clinical reference centres for rare diseases varies considerably in the Netherlands, e.g. there are 16 haemophilia centres, 6 centres for cystic fibrosis, 2 for MPS, and one each for Gaucher disease and Fabry disease. University medical centres usually provide genetic testing and counselling.

Registries

There is no recent survey of patient registries in the Netherlands, but many patient registries exist for specific rare diseases, including registries maintained by patient organisations and at the main clinical reference centres. Since 2001, a national web-based facilitating registry has been developed: the Dutch Diagnosis Metabolic Diseases Registry. From 1 January 2007, an extended neonatal screening program was launched in the Netherlands, involving 17 disorders, and a registry of all patients referred with an abnormal neonatal screening result has been put into place at the RIVM (National Institute for Public Health and the Environment). The Netherlands contributes to European registries including TREAT-NMD, AIR, EURO CARE CF, EPCOT and EUROCAT.

Neonatal screening policy

On 1 January 2007, an extended neonatal screening program was launched in the Netherlands, for 17 rare disorders: phenylketonuria, hypothyroidism, congenital adrenal hyperplasia, biotinidase deficiency, galactosaemia, glutaric aciduria type I, HMG-CoA lyase deficiency, holocarboxylase synthase deficiency, homocystinuria, isovaleric acidemia, maple syrup urine disease, MCAD deficiency, 3-methylcrotonyl-CoA carboxylase deficiency, sickle cell disease, tyrosinemia type I, longchain hydroxyacyl-CoA dehydrogenase deficiency and very-long-chain acyl-CoA dehydrogenase deficiency.

National alliances of patient organisations and patient representation

VSOP (www.vsop.nl) regroups 60 member organisations and acts as the national alliance of rare disease patient organisations in the Netherlands, especially in the field of research, prevention and treatment. In addition to this, VSOP also represents more common genetic and congenital disorders and deals with societal issues in the field of genetics, prevention, ethics and research. Other umbrella organisations deal with other issues influencing the lives of people with rare disorders, such as the general organisation of health care (NPCF) and issues in the field of income, participation and care (CG-Raad).

A specific part of the Ministry of Health's budget (CIBG - Fonds PGO) subsidises all national patient organisations with a minimum of €30,000 (maximum €90,000) per year: this is intended to help organisations publish information and provide internet and help line services. Patient organisations can also apply for specific project funding, i.e. to organise conferences.

Patient organisations are represented in the Steering Committee on Orphan Drugs.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in the Netherlands, currently hosted by the VU University Medical Centre, Amsterdam and the Leiden University Medical Centre. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

The Steering Committee on Orphan Drugs functions as an information centre for rare diseases and orphan drugs: the committee produced a special information booklet on how to obtain orphan drugs in 2007. Their website www.orphandrugs.nl provides general information on rare diseases and orphan drugs. The Royal Dutch Association of Pharmacists (KNMP) has developed in collaboration with the Steering Committee on Orphan Drugs the website www.farmanco.knmp.nl/weesgeneesmiddelen which publishes practical information on European registered orphan medicinal products for pharmacists and patients.

The National Genetic Resource and Information Centre (Erfocentrum), founded by VSOP, has both a board of representatives of patient organisations and medical professionals and hosts the national helpline for information on genetic issues and rare diseases. The website www.erfocentrum.nl contains a database of rare diseases with information for both lay-persons and professionals (www.erfelijkheid.nl). In addition, public information is available on genetic, biomedical and pregnancy related issues⁷⁹.

VSOP also functions as a centre of expertise and advocacy for patients with a rare disease. Currently VSOP, in collaboration with disease-specific organisations, develops guidelines for general practitioners on rare diseases, works on the realisation of standards of care and centres of expertise and research.

General help lines are available, such as the ERFO line for information on hereditary diseases and pregnancy, which is now independent from VSOP after having been created under its auspices. Meldpunt (Information Desk) is another general health line for information concerning social services and health care insurance.

National rare disease events

On 29 February 2008 the first Rare Diseases day was organised in the Netherlands (www.zeldzameziektendag.nl). In Madurodam several hundreds of children and adults affected by rare diseases joined together for the event. Several speakers, including patients and their parents, discussed the importance of raising awareness about rare diseases. A petition to this effect was presented to members of the Dutch Parliament.

At the annual Week of the Chronically Ill (November 2008), the theme was 'living with medicines and medical devices, and a separate session paid attention to rare diseases.

Research activities and E-Rare partnership⁸⁰

Although there is no research programme dedicated to rare diseases in the Netherlands as yet, in order to provide a stimulus for translational research in the field of rare diseases in the Netherlands, the Dutch Organisation for Health Research and Development (ZonMw) and the Dutch Steering Committee Orphan Drugs participates in E-Rare, and participated in the 2nd Joint Transnational Call (2009).

The ZonMw has also provided and continues to provide funding through several research programmes for rare diseases research (e.g.) the Innovative Research Incentives Scheme, the Gene Therapy subsidy scheme and the programme on Expensive and Orphan Medicines. The Steering Committee on Orphan Drugs has funded and will continue to fund some rare disease projects (2001-2011; €50,000 per project per year).

An analysis has been carried out by a PhD student at the University of Utrecht of the 355 projects on rare diseases that applied for funding in the Netherlands during the period of January 2002 to April 2008. 25% of these proposed projects were selected for funding, accounting for an estimated total financing of €22.5 million for the whole period, or €3 million per year. The programme BioPartner FSG/STIGON which ran from 1998 – 2007 aimed to establish high-tech businesses and entrepreneurship in life sciences, including medicinal products for chronic and rare diseases. The total budget for the STIGON programme (including rare diseases) was about €9 million and was funded by several ministries and scientific institutions (no private funding was involved). Another programme specific to orphan drugs (STIGON-Weesgeneesmiddelen) involved two projects with a total budget of €500,000: the appointment of an orphan product developer and a PhD student to analyse factors in the success or failure in orphan drug development (see below).

⁷⁹ These sites provide further web based information www.biomedisch.nl; www.zwangernu.nl; www.zwangerwijzer.nl; www.slikeerstfoliumzuur.nl; www.prenatalescreening.nl

⁸⁰ This section has been written using the *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp53-62).

There are tax reductions for R&D in high-tech start-ups (named the “WBSO measure”) from which orphan drug companies can benefit. There are also several programmes from the Ministry of Economic Affairs to facilitate start-ups (Innovation Subsidy Collaboration projects (IS), Subsidy programme on exploiting knowledge and Technostarters) that orphan drug companies can benefit from.

Participation in European projects

The Netherlands participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, ENERCA EPI, EPNET, EUROHISTIONET, NEUROPED and PAAIR (main partner). The Netherlands participates in the following European research projects for rare diseases: ANTEPRION, ANTIMAL, BIGHEART, BIONMD, CARDIOGENET, CHEARTED, BIOMALPAR, BNE, CONTICANET, CURE-FXS, CRUMBS IN SIGHT, ELA2-CN, DIALOK, EDAR, EMVDA, EMINA, EUCLYD, EuPAPNet, EURO-CGD, EUMITOCOMBAT, EUNEFRON, EUROBONET, EURAMY, EUROCARE-CF, EUROAGENTEST, EUROGLYCANET, EUROPEAN LEUKEMIA NET, EUROSCA, EUROWILSON, EVI-GENORET, EURODS, EUROPADNET, EUROSTEC, HSCR, GENESKIN, GEN2PHEN, HDLOMICS, IMMUNOPRION, MLC-TEAM, NEMMYOP, NSEuroNet, NEUROISIS, NMD-CHIP, NOVSEC-TB, MITOCIRCLE, MITOTARGET, MMR-RELATED CANCER, MYASTAID, NEUROPRION, OLIGOCOLOR, PEROXISOMES, PNSEURONET, PRIBOMAL, PWS, TB-DRUG, TREAT-NMD, VACCINES4TB, VITAL, RD PLATFORM and REVERTANT-EB. The Netherlands contributes to the following European registries: TREAT-NMD, AIR, EUROCARE CF, EPCOT and EUROCAT. The Netherlands contributes to the EUROPLAN project.

Orphan drug committee and incentives^{81,82}

The Steering Committee on Orphan Drugs was established in 2001 by the Minister of Health: its mission is to encourage the development of orphan drugs and to improve the situation of patients with a rare disease, especially to strengthen the transfer of information on rare diseases. This committee is an independent organisation and the members are representatives of umbrella organisations for patients and for pharmaceutical companies, physicians, a pharmacist, a representative of the Dutch medicine evaluation board a representative of the Dutch health insurance board. The Steering Committee is involved in the EC projects E-Rare, Europlan and Polka. The action plan for this committee for 2008-2011 covers three priority areas: 1) improved access to health care and treatment through centres of expertise, 2) the stimulation of research and development of Orphan Drugs, 3) the creation of a sustainable reimbursement system. The budget of this committee is €450,000 per year.

In 2006 an orphan product developer was appointed within the Dutch Organisation for health Research (ZonMw) and development to stimulate Dutch academic researchers and pharmaceutical industries to develop orphan drugs. This project (as part of the STIGON-Weegeenesmiddelen programme) is paid for by the Ministry of Health over four years, after which it will be decided if this post should be handed to the Medicines Evaluation Board or an industry platform. In 2005 a PhD student was appointed to study the factors of success and failure in orphan drug development in collaboration with the ZonMw and orphan drug developers. Both persons worked closely with the Steering Committee on Orphan Drugs.

A waiver can be granted for the registration fee of a medicinal product if the medicinal product is already registered in one or several other EU member states and if the prevalence of the indicated disease is less than 1 in 200.000 inhabitants in the Netherlands.

Free advice is available from the Dutch Steering Committee on Orphan Drugs. In the case of orphan medicinal products for a rare disease for which no alternative treatments exist, there is no obligation for companies to show pharmaco-economic data. In individual cases this may also be the case for orphan medicinal products for a disease with a prevalence of less than 5:10,000 for which an alternative treatment does exist.

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.

⁸¹ This section has been written using *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp53-62)

⁸² 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)* (pp21-23)

Orphan drug availability^{83,84}

For the care of patients suffering from orphan diseases, special funding is available. For the use of orphan drugs in university hospitals, a new reimbursement method ("*beleidsregel weesgeneesmiddelen*") was introduced from 1 January 2006, to increase the use of orphan drugs for treating rare diseases. The costs of the orphan drugs in hospitals, in case they are accepted under this specific regulation, are totally refunded. For orphan drugs used outside the hospital (at home) there is a special reimbursement rule at the Medical Reimbursement System (GVS). In the Netherlands 38 Orphan Drugs out of the 50 with market authorisation are paid for (70%) by Health Care Insurance or policy rules. Reimbursement can be asked for at the Health Care Insurance Board in case of off-label use in less than 1:150,000 (i.e. less than 110 patients in the Netherlands. If a patient is chronically ill, they can request a personal budget (PGB) to obtain home care).

There is no specific policy for compassionate use for orphan drugs but there is a general policy for compassionate use of all drugs: off-label procedures are also the same for orphan and non-orphan drugs, and is accepted if scientific evidence attests of an added value of the treatment.

Specialised social services

Most respite care services are imbedded in the general health care system: these services include in-home respite, emergency respite, sitter-companion services, and therapeutic day care. A specialised nursing home for those with Huntington disease is run by the Health Insurance. Other therapeutic recreational services are provided by patient organisations, such as holiday homes for those with ataxia and neuromuscular diseases and camping car rental for Duchenne patients: patients may be asked to participate in the payment of such services. Social support, supported employment and support in travelling are available in order to help the integration of patients in daily life.

B.1.19.2 New initiatives and incentives in 2009**National plan for rare diseases and related actions**

The Dutch Organisation for Health Research and Development (ZonMw) and the Dutch Steering Committee Orphan Drugs continues to work on WP7 of the EUROPLAN project which will develop the content of the EUROPLAN recommendations including methodological guidance on how to develop comprehensive and integrated strategies for guiding and structuring all relevant actions in the field of rare diseases.

The National Alliance for Rare Diseases (VSOP) will organise in 2010 one of the national conferences to present the EUROPLAN recommendations and to discuss the transferability of the recommendations with local stakeholders

Registries

In April 2009, Dutch Orphan Disease Registry Consortium was established to create a web-based registry framework to collect information (such as incidence of the disease and outcome of treatment) on rare diseases to optimise patient care and advance drug development. This consortium will optimise the expertise of partners to develop guidelines for improving treatment and management. The project has a €1.5 million budget over a 3 year period. Data from the initial phase of the registry, targeting inborn errors of metabolism, will contribute to a sustainable plan of national and international implementation for other rare diseases. The registry framework is being established using the resources of the collaborative industrial and academic framework TI Pharma.

National alliances of patient organisations and patient representation

VSOP received about €1 million in funds from Fonds PGO in order to work on the themes of standards of care and centres of expertise and research from 2009 to 2012.

⁸³ This section has been written using *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp53-62)

⁸⁴ 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)* (pp21-23)

National rare disease events

In the Netherlands, the second Rare Disease Day 2009 was held on 8 April 2009. A large event took place in Wassenaar (The Hague) targeting all those (adults and children) suffering from a rare disease, and all stakeholders involved in care and treatment of patients with a rare disease. A symposium entitled "Equal Opportunities for Rare Diseases in Health Care and Research" was organised by VSOP with invited speakers from patient support groups, insurance companies, university medical centres, EURORDIS and the government. The symposium, and the Rare Diseases Day, closed with an open discussion between the public and a panel consisting of the invited speakers and Prof Martina Cornel representing Orphanet.

The Dutch Rare Disease Days (www.zeldzameziektendag.nl) are organised by a team of several organisations (Dutch Steering Committee Orphan Drugs, VSOP, ZZF, and KNMP). ZZF is the only National Fund specifically dedicated to rare disorders, collecting funds especially for research.

Hosted rare disease events

The 5th International Congress on Shwachman-Diamond Syndrome was held on 19-20 June 2009 in Amsterdam.

Research activities and E-Rare partnership

The research programme proposal 'Rare diseases and orphan drugs: from orphan status to cure' was presented to the Dutch Ministry of Health in spring 2007 will be granted funding from 2011. This is a five-year programme with a total budget of €13.5 million which aims to encourage pre-competitive translational research with the ultimate goal to develop treatments for rare diseases. The Netherlands Organisation for Scientific Research bequeathed €22.5 million to a consortium including 8 Dutch university medical centres and other research institutes and universities in order to establish a national biobanking infrastructure, the Biobanking and Biomolecular Resources Research Infrastructure Netherlands (BBMRI-NL), which will integrate clinical materials and data gathered over many years with the goal of improving access to human samples. Such samples are important to rare disease and orphan medicinal product research.

The Netherlands participated in the 2nd E-Rare Joint Transnational Call joint in 2009 with nine other partner countries. Many Dutch researchers were interested and applied for funding. €1.7 million was granted in funds for 14 Dutch research groups, involved in 9 of the 16 funded projects/consortia.

Orphan drug committee and incentives

As of 1 January 2009, the subsidy scheme Orphan Designation Dossier (ODD) is in action. This is an initiative of the Dutch Steering Committee Orphan Drugs and is executed by the Netherlands Organisation for Health Research and Development (ZonMw). This initiative will help stimulate the development of orphan drugs in the Netherlands by providing Dutch pharmaceutical Small and Medium-sized Enterprises (SMEs) a small subsidy for the costs of writing and submitting the ODD to the EMA. Analysis has shown that pharmaceutical SMEs are the engine behind orphan drug development. The scheme will run from January 2009 to the end of November 2011 with a total budget of €180,000. The scheme consists of two types of applicants – SME with ODD experience and SME without experience – and two types of subsidy – €7,200 and €3,600. Depending on their ODD experience, SMEs are allocated the large or small subsidy, provided their proposal meets all the formal criteria. A maximum of two ODD-support applications are permitted per SME per year.

B.1.20 POLAND

B.1.20.1 State of affairs before 2009

Definition of a rare disease

In Poland, there is no official definition for rare diseases; however the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals is widely used amongst stakeholders.

National plan for rare diseases and related actions

No national plan for rare diseases exists at the moment in Poland: measures are only in place for individual diseases (some of which are rare). There is no dedicated budget for rare diseases. However, at the first meeting of the newly-elected Commission of Systemic Diseases, a working group of Poland's paediatric scientific

committee (the Committee of Human Development) working within the framework of the independent government-funded research organisation the Polish Academy of Sciences, it was decided to focus on rare disease issues, including the possibility of developing a national rare disease programme for Poland. Rare diseases will be included in the Committee of Human Development working programme over a coming four-year period. The first action toward this goal is the appointment of an Orphanet Advisory Board to the Committee in cooperation with the Polish Paediatric Society.

In July 2008, the Polish Minister of Health established the Committee for Rare Diseases as an Advisory Board for rare diseases with multiple aims regarding various activities in the field. This group consists of fourteen people: the Vice-Minister of Health as leader, representatives of the Drug Registration Agency, HTA, national insurance company, patient organisations, National Forum on the Treatment of Orphan Diseases, pharmaceutical industry, research experts and other stake-holders. To date, at least two meetings have taken place in the Ministry of Health, during one of them the French National Plan and other European initiatives were presented.

Recently two working groups dedicated to rare diseases have been created at the Ministry of Health and the National Health Insurance. These working groups will play the role of advisory boards in exploring solutions for the problems associated with rare diseases in Poland. The first topics concerned financing enzyme replacement therapy for Polish patients.

In addition to this, the National Program to Combat Cancers is a measure which covers all cancers, including rare cancers

There is a list of chronic diseases which lists diseases for which some drugs are exceptionally reimbursed.

Centres of expertise

In Poland, the health care of patients with rare diseases is not organised in a specific framework and there are no official centres of expertise for rare diseases. Significant progress has been made as a result of the European Project of Centres of Excellence "PERFECT" *QLG1-CT-2002-90358*. The grant programme included problems associated with rare paediatric diseases in the field of genetics, metabolism, gastroenterology, cardiology, immunology and oncology.

Registries

Poland takes part in the European registries such as TREAT-NMD, EURO CARE CF and EUROCAT.

Neonatal screening policy

There is a national newborn screening program for phenylketonuria, congenital hypothyroidism and congenital deafness.

National alliances of patient organisations and patient representation

There is currently no national alliance for rare disease patient organisations in Poland. No national initiatives exist to support patient organisations as a whole, but smaller grants exist for projects such as the organisation of workshops and conferences.

Patients are represented on the Rare Diseases Team and have the right to vote.

Sources of information on rare diseases and national help lines

Since 2006 there is a dedicated Orphanet team in Poland, currently hosted by the Children's Memorial Health Institute, Warsaw. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no official information centre on rare diseases in Poland other than Orphanet and there is currently no national help line for rare diseases.

National rare disease events

The National Forum on the Treatment of Orphan Diseases⁸⁵ was created at the beginning of 2005 and grouped together associations that for many years have been seeking to ensure care and treatment are provided for

⁸⁵ <http://www.rzadkiechoroby.pl/> 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)* (p 18)

those suffering from orphan diseases. The members of the Forum include: *Stowarzyszenie Rodzin z Chorobą Gauchera* (Association of Families affected by Gaucher disease), *Stowarzyszenie Rodzin z Chorobą Fabry'ego* (Association of Families affected by Fabry disease), *Stowarzyszenie Chorych na Mukopolisacharydozę* (Association of Families affected by Mucopolysaccharidosis and related diseases), *Polskie Towarzystwo Chorób Nerwowo-Mięśniowych* (Polish Society of Neuro-Muscular Disorders) and *Fundacja Pomocy Rodzinom i Chorym na Mukowiscydozę MATIO* (Polish Cystic Fibrosis Foundation). As announced by the Ministry of Health on its website, on 13 July 2005 a meeting was organised by the Minister of Health with national non-government organisations representing patients. At that meeting, the Forum presented its demands regarding deficiencies in the operation of the National Health Fund from the viewpoint of patients suffering from orphan diseases. No further action has been reported.

Hosted rare disease events

Warsaw was the host of the first meeting of Eastern European Metabolic Academy (EEMA) held 28-29 November 2008. This meeting dealt with rare metabolic diseases.

Research activities and E-Rare partnership

There are no research programmes intentionally aimed at rare diseases in Poland. Poland is not currently a partner of the E-Rare project.

Participation in European projects

Poland participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, EPI, EPNET, ENERCA, EUOHISTIONET, PAAIR, Paediatric Hodgkin Lymphoma Network and RBDD. Poland also participates in the following European research projects EUROGLYCONET, ERNDIM, EUROCARE-CF, EUROAGENTEST, EUROPEAN LEUKEMIA NET, EUROWILSON, EUROSCA, EURADRENAL, EURO-GENE-SCAN, NEUPROCF, RD PLATFORM and SIOPEN-R-NET. Poland contributes to the following European registries: TREAT-NMD, EUROCARE CF and EUROCAT. Poland contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

According to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*, "Poland is contemplating a return to the concept of specialist drugs in the "Act on healthcare services financed from public funds". The draft of the Act, [which went before Parliament at the beginning of 2006], will introduce a specialist drugs category which will allow very expensive therapies (including treatments involving orphan drugs) to be covered by the reimbursement system.

"The National Health Plan (2004-2012) put in place by the "Act on general insurance in the National Health Fund" covers reparative and preventive medicine. It provides for access to the latest diagnostic and treatment techniques and is open-ended, i.e. it can be amended and supplemented. For that reason, it can be extended to include a programme encompassing patients suffering from rare diseases that takes account of the policy on orphan drugs⁸⁶."

Specialised social services

There are no social services designed specifically for patients for rare diseases, though respite care exists in general and educational centres can provide day care for children and education for patients: these are both privately and publically funded initiatives, provided on an application basis. Therapeutic recreational services such as camps are eligible for co-funding by the state social care (usually 30% patient co-payment). Patient organisations sometimes provide services which are financed from private funds. The state finances the integration of children with special needs, via integration classes in schools.

⁸⁶ 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)* (p 18)

B.1.20.2 New initiatives and incentives in 2009

National plan for rare diseases and related actions

Recently the working group dedicated to rare diseases was created at the National Health Insurance (decision of the Ministry of Health). The first task was to qualify patients as eligible for enzyme replacement therapy in the following inborn errors of metabolism: Gaucher disease, Pompe disease, MPS types I, II and VI.

Neonatal screening policy

Neonatal screening for cystic fibrosis was made available in 2009 across Poland.

National rare disease events

The Polish Cystic Fibrosis Foundation MATIO organised the 8th Polish Cystic Fibrosis week to coincide with Rare Disease Day 2009: conferences, workshops and awareness campaigns were organised to mark the event.

Hosted rare disease events

Warsaw was the host of the second meeting of Eastern European Metabolic Academy (EEMA) with a round-table discussion on various aspects of rare diseases, held on the 9-10 November 2009. Warsaw also hosted the Symposium on Standards of Care for Children with Cancer (13 May 2009).

B.1.21 PORTUGAL

B.1.21.1 State of affairs before 2009

Definition of a rare disease

Most stakeholders in Portugal accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

On 12 November, 2008, the Portuguese Minister of Health approved a national plan for rare diseases for Portugal. The plan adheres closely to the structure outlined during the European Conference on Rare Diseases, which took place in Lisbon in 2007. The "*Programa Nacional de Doenças Raras*", which has already undergone a period of public consultation, delineates two general and seven specific objectives and will be implemented within an initial timeframe running from 2008-2010, followed by a consolidation period stretching from 2010 to 2015.

The main objectives are the creation and improvement of national measures in order to satisfy the necessities of people with rare diseases and their families vis-à-vis medical services and care, and the improvement of the quality and equity of the provided health care measures to people with rare diseases. The objectives will be achieved by creating reference centres for rare diseases, improving the access of rare disease patients to adequate care, improving knowledge on rare diseases, promoting innovations in the treatment of rare diseases and accessibility to orphan drugs, and by assuring cooperation on national and international levels, including the countries from the EU and countries using Portuguese as their official language.

The specifics of the plan include in total 30 intervention strategies, 9 education and training strategies, and 8 strategies for data collection and information analysis. The plan also details 15 actions for evaluation. The Minister has chosen a coordinator and a national commission to oversee and put into action the various elements of the plan. This plan will cover all rare diseases: however, rare cancers are covered separately by a rare cancer plan. The budget for the kick-off year (2009) of the rare disease plan is €150,000, mostly dedicated to preparatory studies and the preparation of activities.

Centres of expertise

There are no official centres of expertise in Portugal at the moment. However, The National Plan for Rare Diseases will support the creation of officially recognised 'reference centres'.

Following recent legislation establishing norms for access to therapies for enzymatic diseases, the National Institute of Health has created a national network of treatment centres for these diseases: this programme cost €35 million in 2008. A list of enzymatic diseases benefiting from treatment free of charge in public hospitals is available.

Registries

The National Institute of Health is creating a national register for patients with Portuguese Familial Amyloidosis. Many hospitals have patient databases (especially Medical Genetics Services and Laboratories) but these databases are not networked. Portugal contributes to the TREAT-NMD, EUROCARE CF and EUROCAT European registries.

Neonatal screening policy

Neonatal screening for 25 diseases is available at one laboratory, at the National Institute of Health (Porto), with 10 corresponding treatment centres in main hospitals. Amongst the diseases screened are biotinidase deficiency, galactosaemia, maple-syrup urine disease, phenylketonuria and hypothyroidism.

National alliances of patient organisations and patient representation

FEDRA (*Federação Portuguesa de Doenças Raras*) is a national alliance of several rare disease patient organisations in Portugal.

Some Portuguese patient organisations receive financial support from the state, and there are many programmes sponsoring specific activities proposed by patient organisations. In 2008, the Ministry of Health launched calls for projects for rare disease patient organisations with a funding allocation of around €500,000. The Health Directorate has an organic 'civil society unit' that supports patient organisations and their projects.

FEDRA and Rarissimas (the National Association for Mental and Rare Disorders) participate in the committee for patients' and families' needs at the Directorate General of Health along with representatives of the Ministry of Health and the Ministry of Social Security. Patient organisations were involved in the public discussion of the rare disease plan and a project has been launched by the National Board for Rare Diseases (CNRD) to organise regular discussions with patient organisations.

Sources of information on rare diseases and national help lines

Since 2003 there is a dedicated Orphanet team in Portugal, currently hosted by the Institute of Molecular and Cell Biology (IBMC), Porto. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

No official information centre on rare diseases existed in Portugal before 2009: limited information on rare diseases is currently available on the health portal of the Portuguese Ministry of Health and extending this information is a priority for the upcoming national plan. Other information sources are Orphanet Portugal and the web sites of various rare diseases patient organisations. The patient organisation Rarissimas received funding from the Health Directorate in 2008 to prepare a rare disease help line which will soon be in place (an email address serves to answer queries for the moment) and which will be part of the Rare Disease Patient Solidarity (Rapsody) network⁸⁷. The Portuguese Haemophilia Association also provides some support by phone.

National rare disease events

FEDRA has been involved in the organisation of Rare Disease events in Portugal since 2008.

Hosted rare disease events

In 2007, the Fourth European Conference on Rare Diseases was held in Lisbon.

Research activities and E-Rare partnership

The public funding agency, Foundation for Science and Technology (FCT), runs several programmes to fund research on rare diseases, as well as the Ministry of Health itself and the private sector. Portugal joined the E-Rare project in 2009, for the 2nd Joint Transnational Call.

⁸⁷ http://www.rapsodyonline.eu/dev_rapsody/index/displaycenter/base/tOrganization/tOrganizationID/67

Participation in European projects

Portugal participates in the following European Reference Networks for rare diseases: Dyscerne, ENERCA NEUROPED, RBDD and TAG. Portugal participates in the following European research projects for rare diseases: CLINIGENE, EPOKS, EHDN (European Huntington Disease Network), EUROWILSON, EURAMY, EUROCARE CF, EUROAGENTEST, EVI-GENORET, LEISHMED, MMR-RELATED CANCER, NEUPROCF, PEROXISOMES, POLYALA, RHORCOD and SIOPEN-R-NET. Portugal contributes to the following European registries: TREAT-NMD, EUROCARE CF and EUROCAT. Portugal contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity.

Orphan drug availability

All Portuguese citizens are covered by the National Health Service, although they may have to participate towards the payment of prescription drugs. There are special programmes in place to facilitate access to growth hormone therapy and enzymatic therapy.

The data available on orphan drugs shows a variation in the use of orphan drugs in Portugal: according to an INFARMED report⁸⁸, between 2005 and 2006 there was a decrease of 7.6%, and between 2006 and 2008 there was an increase of 37.9% of usage of all orphan drugs available in Europe in Portugal.

Specialised social services

Respite care services exist, both in the public and private sector and patients pay for some services. Other respite facilities are run by patient organisations and some projects have been established with public support. There are some therapeutic recreational initiatives organised by hospitals with the support of public or private organisations, which are paid for through public and private funding; many programmes are organised by patient organisations. There are some projects to help the integration of patients in daily life, and the offer will hopefully improve under the national plan for rare diseases.

B.1.21.2 New initiatives and incentives in 2009

National plan for rare diseases and related actions

The national parliament approved a recommendation concerning the priority of access to health care for people with rare diseases in May 2009. A National Board for Rare Diseases (CNRD) was formed and its first meeting was held to prepare the plan (29 May 2009). A Coordinator for the National Plan and a National Commission were chosen by the Minister to oversee and put into action the various elements of the plan to run from 2008-2010 followed by a consolidation period stretching from 2010-2015. An action plan for 2009 and 2010 is being planned, which includes the autonomous regions of the Azores and Madeira. The main priority is the implementation of a national network of reference centres for rare diseases: the requirements for the designation of these centres are also currently under discussion.

With the funding of the Directorate General of Health, some projects concerning rare diseases were implemented in 2009.

Neonatal screening policy

Access to haemoglobinopathies screening, in Lisbon, is one of the aforementioned initiatives which received funding from the Directorate General of Health in 2009.

Sources of information on rare diseases and national help lines

With funding from the Directorate General of Health, a call centre and resources centre for rare diseases is scheduled to be implemented in 2009. Orphanet is referenced in the National Plan as the main source of information regarding activities related to rare diseases in Portugal.

⁸⁸ *Medicamentos órfãos utilizados*: INFARMED Report (2009) <http://www.acs.min-saude.pt/pns/acessibilidade-ao-medicamento/medicamentos-orfaos-utilizados/>

National rare disease events

FEDRA organised the second Rare Disease Day in Portugal on 28 February 2009 with the launch of an awareness campaign.

In Porto, 1-2 April 2009, a congress on Rare Disorders (*“Doenças raras: do indivíduo... à sociedade”*), was organised by the students of the Pharmacy Faculty of the University of Porto.

Hosted rare disease events

On 29-30 May 2009, an international workshop was held on Genomic Disorders, Disease-Associated Chromosome Rearrangements and Position Effect in Lisbon.

Research activities and E-Rare partnership

Portugal joined the E-Rare project in 2009 for the second transnational call in 2009: Portugal is represented by a team in one of the projects/consortia selected for funding, with a funding of around €200,000.

Education and training

The first Professional Master Course on Genetic Counselling was created, at ICBAS (Instituto de Ciências Biomédicas Abel Salazar), University of Porto, aiming at training the first generation of non-medical Genetic Counsellors, as these professionals are yet to be recognised as health professionals in Portugal.

Orphan drug availability

Data available from the first semester of 2009⁸⁹ showed an increase of 21% in the use of orphan drugs in Portugal, when compared with the same period in 2008.

B.1.22 ROMANIA **B.1.22.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in Romania accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

On 29 February 2008, the Romanian Ministry of Health and the country's National Alliance for Rare Diseases (RONARD) signed an accord to form a partnership in order to instate a national plan for rare diseases. A member from the ministry and from the alliance have been appointed to work together to review the national plan that was developed by rare disease stakeholders and presented to the government at the end of 2007, with the aim of creating an estimate of funding and resources required for each element of the plan. An expert team, including geneticists, paediatricians, endocrinologists, cardiologists, oncologists, informatics specialists, public policy experts and other specialists will be gathered to help evaluate the plan and develop a cost analysis for each item. The country's 2008 health budget was then to be readjusted to include funding for various elements of the rare disease plan. A working document has been developed with a timeline for implementing specific elements of the plan, which seeks to improve access to information; establish an adequate strategy for ensuring prevention, diagnosis, treatment and rehabilitation services; create a national registry; stimulate research; create rare disease training initiatives for professionals from various fields; and collaborate with various EU and international organisations.

A first action has been the creation of the National Committee of People with Rare Diseases, involving the Ministries of Health, Education, and Labour, as well as the National Medicine Agency, the Authority of People with Disabilities and the Child Welfare Authority. The activities of this committee include government

⁸⁹ *Medicamentos órfãos utilizados*: INFARMED Report (2009) <http://www.acs.min-saude.pt/pns/acessibilidade-ao-medicamento/medicamentos-orfaos-utilizados/>

decisions for coordination, guidance and control of services for rare disease patients, including social integration. A national registry is also being created.

Centres of expertise

There are no official centres of expertise in Romania at the moment; however this is a provision of the working document of the National Plan currently under consideration. The Romanian Prader Willi Association has been proposed as the future pilot national information and reference centre in collaboration with the Ministry of Health.

Registries

A national rare disease registry is one of initiatives proposed for inclusion in a national plan for rare diseases. Romania contributes to the EURO CARE CF European registry.

Neonatal screening policy

Currently neonatal screening is available for several diseases although screening for some diseases is not yet available nationwide. Physicians specialising in genetics only are allowed to provide genetic counselling.

National alliances of patient organisations and patient representation

RONARD (The Romanian National Alliance for Rare Diseases) is the national alliance for rare diseases founded by the Romanian Prader Willi Association which organises meetings and information services. Patient organisations also have the possibility of receiving accreditation as “organisations of public utility”, there is also a procedure in place to authorise the research capacity of a patient organisation. There are certain funding resources for patient organisations’ activities. Patient organisation representatives are able to act as ‘observers’ in different commissions: their representation is recognised but their opinion is not binding and there is usually no financial support for attending meetings.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in Romania, currently hosted by the Universitatea de Medicina si Farmacie, Iasi. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

The Romanian Prader Willi Association/RONARD acts as an information centre for Prader Willi and other rare genetic diseases, providing information on associations, centres, medical experts, encouraging the exchange of information and experiences between people affected by the same rare disease, and providing counselling and support groups as well as training. The Romanian Prader Willi Association/ RONARD also provides and funds an information line: this service is also subsidised by the Ministry of Labour. The site <http://bolirare.ro/> provides some information on rare and genetic diseases.

National rare disease events

Several events⁹⁰ were planned for the first Rare Disease Day on February 28th 2008. These included the following conferences and workshops aimed at raising rare disease awareness;

- 25 February 2008: Zalau, “Rare peoples and rare diseases”⁹¹;
- 18-22 February, 2008: Targu Mures, “A complex system for communication between those involved in the management of rare diseases” Workshop, University of Medicine and Pharmacy;
- 27 February 2008: Cluj Napoca, “Possibilities for diagnosis and treatment of rare diseases in Romania”;
- 28 February 2008: Iasi, “The First European Day for Rare Diseases and Orphanet”;
- 28 February 2008: Oradea, “The First European Day for Rare disease”;
- 29 February 2008: Timisoara, “Together for Rare Diseases”;
- 29 February 2008: Bucharest, Round table “Rare Diseases – a priority for health in Europe”, Ministry of Health.

⁹⁰ http://www.smromania.ro/ro/departament_evenimente/evenimente_recente/ziua_internationala_a_bolilor_rare/

⁹¹ <http://www.youtube.com/watch?v=ltLFSxXwymU&feature=related>

Research activities and E-Rare partnership

Funding is currently available from some sources in Romania. Romania is not currently a partner of the E-Rare project.

Participation in European projects

Romania participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, ENERCA and TAG. Romania contributes to the EUROPEAN LEUKEMIA NET project. Romania contributes to the following European registry: EUROCARE CF. Romania contributes to the EUROPLAN project.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

From 1 January 2007, date at which Romania became an EU Member State, all medicinal products were required to obtain new authorisations according to EU standards: this created significant delays in the importation of certain orphan drugs.

As a consequence of the creation of the National Plan for Rare Diseases, the Ministry of Public Health enlarged coverage of orphan drugs from July 2008 onwards in their health programme. Compassionate use is also sometimes practiced.

Specialised social services

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

B.1.22.2 New initiatives and incentives in 2009**National plans and related actions**

An official decision of the Romanian Government⁹² (25 March 2009) stipulated the necessity of various national health programmes in Romania, including a health programme for rare diseases to be funded by the state, covering the diagnosis of rare diseases, the medical treatment of rare diseases and the establishment of several registries linked to specific rare diseases, and rare diseases in general (see following section).

Registries

An official decision of the Romanian Government⁹³ of 25 March 2009 stipulates that National Registries should be established and maintained for cardio-vascular diseases (including congenital anomalies), cancer Registries, diabetes mellitus, haemophilia, thalassaemia, psychiatric diseases as well as a National Register for Rare Diseases.

National rare disease events

RONARD was involved in organising events and awareness campaigns for the second Rare Disease Day in Romania over a whole week (23-28 February 2009). The week opened with the launch of an awareness campaign with a performing arts show and distribution of brochures and other activities. A Rare Disease Day March was organised on 25 February 2009.

⁹² <http://www.emedic.ro/Legislatie/374.htm>

⁹³ <http://www.emedic.ro/Legislatie/374.htm>

In collaboration with the National Centre of Studies for Family Medicine, RONARD held a work shop entitled: "How to detect, treat and coordinate the care of patients with rare diseases". Events to mark the occasion were also organised by the organisation Multiple Sclerosis Romania.

Bucharest hosted the Neonatal Screening – A Chance to Life Conference (18-19 June 2009).

Hosted rare disease events

The Balkan Congress for Rare Diseases was held on 26-27 June 2009 in Cluj-Napoca.

B.1.23 SLOVAKIA

B.1.23.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Slovakia accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

No national plan for rare diseases currently exists in Slovakia, though the Ministry of Health has announced that rare diseases will be a focal point of its new policy. There has been discussion of establishing a Committee of Rare Diseases at the Ministry of Health, though this project has not advanced recently. There is no specific budget currently dedicated to rare diseases.

Centres of expertise

There are currently no official centres of expertise for rare diseases in Slovakia.

Registries

Slovakia contributes to the EUROCARE CF European registry.

Neonatal screening policy

Neonatal screening is available in Slovakia for phenylketonuria, cystic fibrosis, congenital adrenal hyperplasia and congenital hypothyroidism. In addition to this, newborns are screened nation wide for hearing impairments.

National alliances of patient organisations and patient representation

There is no national alliance of patient organisations at the moment in Slovakia, although patient organisations for certain rare diseases exist. There are no public funding schemes for patient organisations in Slovakia. There is no real platform for patients to voice their opinions: most complaints are dealt with on a case by case basis by the "Bureau for control of health care".

Sources of information on rare diseases and national help lines

Since 2006 there is a dedicated Orphanet team in Slovakia, the team was hosted before 2010 by the Institute of Molecular Physiology and Genetics in Bratislava. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no official information centre for rare diseases other than Orphanet in Slovakia. Information sources on rare diseases are mostly run by non-governmental organisations with a few projects supported by the state and its municipalities. There is currently no dedicated help line for rare diseases at the moment.

National rare disease events

The only regularly organised conference is Izakovic's Memorial Conference which is organised every year by the Society of Medical Genetics

Research activities and E-Rare partnership

Slovakia is not currently a partner of the E-Rare Project.

Participation in European projects

Slovakia participates in the following European Reference Network for rare diseases: Dyscerne. Slovakia participates in the following European research projects on rare diseases: ANTEPRION and NM4TB. Slovakia contributes to the following European registry: EUROCARE CF.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

Rare diseases patients are reimbursed for most medications, and the initiatives to improve access to treatment have come from patient organisations, with some governmental support. Patients may access unauthorised treatments through a special application via the Ministry of Health.

Specialised social services

Care services, both government-run and private, are available in Slovakia and partial or full reimbursement is available (depending on certain criteria). Therapeutic programmes such as spa stays are available and paid mainly through private health insurance.

B.1.23.2 New initiatives and incentives in 2009**National plans and other actions**

In Slovakia there have been no developments in 2009 regarding health care in the field of rare diseases, neither from the Government, nor from the Ministry of Health. Currently there is no defined strategy for the management of rare diseases: doctors therefore take their own initiatives in this field without advice from guidelines and cases are dealt with individually. Some doctors who take a special interest in a certain rare disease attempt to gather these patients and provide them with appropriate health care in collaboration with foreign institutes on the basis of personal contacts.

In 2009, owing to the economic crisis, the Ministry of Health froze projects concerning rare diseases and there no new calls for funding for the next year, where there were previously calls to obtain funding for projects concerning rare diseases, including rare disease research.

National rare disease events

Izakovic's Memorial Conference was organised by the Society of Medical Genetics in 2009.

B.1.24 SLOVENIA **B.1.24.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in Slovenia accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Slovenia and there is no dedicated budget for rare diseases and costs related to rare diseases are covered by the national health care insurance scheme. A new

Health Care Act is in preparation which foresees the establishment of reference centres for rare diseases across Slovenia.

Centres of expertise

There are no official centres of expertise in Slovenia, but the majority of patients with rare diseases in Slovenia are evaluated centrally at the University Medical Centre Ljubljana where there is an efficient system for the referral of genetic, endocrine, metabolic, and neurodegenerative disorders, amongst others. In addition to this, there is a Centre for Fabry disease in Slovenj Gradec. A new Health Care Act is in preparation which foresees the establishment of rare disease reference centres.

Registries

There is currently no national registry for rare diseases in Slovenia. Slovenia contributes to the EURO CARE CF European registry.

Neonatal screening policy

Neonatal screening is available for phenylketonuria and congenital hypothyroidism.

National alliances of patient organisations and patient representation

There is currently no national alliance of rare disease patient organisations in Slovenia. Patient organisations are financed through different sources: this may include funding from the government/public sector and the private sector (private sponsorships and donations). The Ministry of Health financially supports some programmes within patient organisations through calls for project proposals: the aims of these calls vary.

The role of patient organisations is recognised in other national plans, but as there is no national plan for rare diseases in place, this platform does not yet exist for representatives of rare disease patient organisations. Patient organisation representatives are usually consulted concerning legislative proposals and in some cases are included in the process of drafting legislation. Patient organisation representatives do not usually receive financial support in order to attend these meetings.

Sources of information on rare diseases and national help lines

Since 2006 there is a dedicated Orphanet team in Slovenia, currently hosted by the Division of Medical Genetics at the University Medical Centre Ljubljana. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no official information centre for rare diseases in Slovenia other than Orphanet, however information on rare diseases is available on some institutions' web sites, and web sites run by patient organisations. There is currently no information help line for rare diseases in Slovenia.

National rare disease events

The First Slovenian Medical Genetics Symposium was held in Ljubljana in September 2008: a session focusing on Rare Diseases (entitled "Rare Diseases in Slovenia") attracted international participation.

Research activities and E-Rare partnership

The Slovenian Research Agency is a government body which awards grants for research. Although not specifically aimed at rare diseases, in the past rare disease topics have been given research grants. Slovenia is not currently a partner of the E-Rare project.

Participation in European projects

Slovenia participates in the following European Reference Networks for rare diseases: Dyscerne, NEUROPED, TAG, and RBDD. Slovenia participates in the following European research projects on rare diseases: CONTICANET, EMSA-SG, MYELINET, PNSEURONET and SARS/FLU VACCINE. Slovenia contributes to the following European registry: EURO CARE CF. Slovenia contributes to the EUROPLAN project.

Orphan drug committee and incentives

In Slovenia, there are several measures concerning national incentives for orphan medicinal products according to the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*: "permission to use medicines labelled in any EU

language with stickers in Slovenian language; negotiation on drug prices; reduced fees for marketing authorisation procedure (if the centralised procedure was not followed)⁹⁴."

Orphan drug availability

In Slovenia, one of the criteria for including a drug among those covered by health insurance is an "ethical criteria" which applies in particular to severe and rare diseases: this has a positive influence on the accessibility of drugs for rare diseases patients.

Specialised social services

Some respite care services are available in Slovenia for patients with disabilities, and are provided by governmental and non-governmental organisations with either government or private financing. Some services are available in Slovenia for patients with disabilities. Therapeutic recreational programmes are available for patients with disabilities in Slovenia, and are provided by governmental and non-governmental organisations with government and private financing. Services are in place promoting the social integration of patients with disabilities in the workplace: most activities are provided through government institutions.

B.1.24.2 New initiatives and incentives in 2009

Slovenia has not reported any additional initiatives and incentives for 2009 in the field of Rare Diseases and our surveillance of literature and sources did not yield any data. Initial discussions are still currently taking place to explore the possibility of creating a national plan for rare diseases.

B.1.25 SPAIN

B.1.25.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Spain accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

In 1999, actions in the field of rare diseases were first taken by the *Instituto de Salud Carlos III* (ISCIII), as part of the Ministry of Health at that moment, with the creation of the first Information Centre for Rare Diseases (CISATER – SIERE, or *Sistema de información sobre enfermedades raras*) which was joined in its mission by the Research Institute for Rare Diseases (IIER) in November 2004. While these administrative and institutional changes were underway, a multidisciplinary and national coordination committee was appointed and issues concerning the definition of rare diseases and actions to be taken in areas such as research, health care and social support by the ISCIII, the Ministry of Health and other regional health authorities were agreed on under the leadership of CISATER. The first collaborative study on rare diseases patients' needs was then developed between IMSERSO (*Instituto de Mayores y Servicios Sociales* – Institute of the Elderly and Social Services) and CISATER. At the same time, a National Ethics Committee for rare diseases was set up in December 2004 with the participation of the IIER.

Before the launch of the National Strategy on Rare Diseases in 2009, some regional initiatives had already been put in place. The Regional Government of Andalusia (*Junta de Andalucía*) created a genetics plan, the *Plan de Genética de Andalucía 2006-2010*, which, in turn, led to the creation of the *Plan de atención a personas afectadas por ER 2008-2012*, a plan concerning care for people affected by rare diseases.

⁹⁴ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (p19)

In parallel to this, in 2008 the Spanish Senate launched an official declaration after reaching a general agreement by all political parties where a strong recommendation regarding rare diseases actions was addressed to the Government of Spain.

At the beginning of 2008, the Government began to work on a National Strategy on Rare Diseases creating two committees (the Institutional Committee and the Technical Committee) which developed the contents of the Strategy. The National Strategy was finally approved by the National Health System Inter-territorial Council (NHSIC) on 3 June 2009 (see section concerning 2009).

Moreover, in the area of social services, the year 2009 also saw the creation of the State Reference Centre for Rare Diseases Patients and their Families (Centro de Referencia Estatal de Atención a Personas con Enfermedades Raras y sus familias, CREER) by the General State Administration, the IMSERSO (see section concerning 2009).

Centres of expertise

In Spain, Royal Decree 1302/2006 of 10 November, which establishes the conditions regarding the procedure for the designation and accreditation of the Reference Centres, Services and Units (CSUR) of the Spanish NHS, refers to rare diseases by defining the characteristics that must be met by pathologies or groups of pathologies that are prevented, diagnosed or treated by means of techniques, technologies or procedures included in the Spanish National Health System's common services portfolio, in CSUR of the Spanish NHS: a) diseases that for their adequate care require preventive, diagnostic and therapeutic techniques, technologies and procedures of a *high level of expertise* requiring experience in their use, which can only be acquired and maintained through certain volumes of activity; b) Diseases that require *high technology* for their prevention, diagnosis or treatment and for which, in view of their cost-effectiveness and the available resources, the concentration of a minimum number of cases is required; c) *Rare diseases* which, because of their low prevalence, require a concentration of cases for their adequate care, which does not imply the ongoing care of the patient in the reference centre, service or unit, but rather that the latter can act as a support for diagnostic confirmation, the definition of therapeutic strategies and follow-up strategies and as an adviser for the clinical units that usually treat those patients.

The entire procedure for the designation of CSUR is formulated through the CSUR Designation Committee of the Spanish NHS, which was created in the aforementioned Royal Decree and which reports and submits proposals to the Interterritorial Council. The tasks of the Designation Committee are: to study the needs and propose the pathologies or the diagnostic or therapeutic techniques, technologies and procedures for which a CSUR needs to be designated; to propose the procedure for the designation and accreditation of a CSUR and to report on it; to assess the designation applications received and make designation proposals to the Interterritorial Council; to study and propose the renewal/revocation of the designation of CSUR; and to establish the procedure for the referral of users. Each of the different areas is being developed by groups of experts appointed by the Autonomous Communities, scientific societies and the actual Ministry of Health and Social Policy. Once the criteria has been agreed a period of CSUR application is opened, and the respective Autonomous Communities can present their proposals through the Designation Committee. Once they have been admitted for processing, the applications are sent to the Spanish NHS Quality Agency for the start of the audit and accreditation process. After the respective accreditation reports have been received, the said Committee studies them together with the other information on each file and submits its proposals for designation, or non-designation, to the Interterritorial Council. The Ministry of Health and Social Policy, at the suggestion of the Designation Committee and with the prior consent of the Interterritorial Council, decides on the designation of the CSUR for a maximum period of 5 years. Before that period has terminated the designation will have to be renewed, provided that, after a re-evaluation by the Spanish NHS Quality Agency.

Registries

The Spanish Network of Rare Diseases Research on Epidemiology (REpIER) was created in June 2008 and analysed the existing rare diseases registries in Spain as of 2005. It concluded that the identified registries did not fit the standard criteria for epidemiological surveillance except for those population based registries which were mainly focused on rare cancers. Most of the registries defined as rare diseases registries were hospital case series intended for clinical studies' development. In 2007 the ISCIII decided to start designing a rare diseases national registry. A Spanish patient's registry for rare diseases including several and different approaches and programmes has been developed and is online as of 2009. The Rare Diseases Research Institute (IIER), belonging to ISCIII, that since 2008 is part of the Ministry of Science and Innovation, is currently in charge of this registry.

In Spain, there are several population based cancer registries which officially reports to the International Agency of Research Cancer of the WHO. Since REPIER was put in place, a specific working group was set up for this particular group of rare diseases as well as for congenital malformations. Both groups are working in collaboration with European and international networks (including EUROCAT) and participate in several European projects.

Spain also contributes to the following European registries: EUROCAT, ERCUSYN, EUGINDAT-PIADATABASE, MOLDIAG-PACA, AIR, EURO CARE CF and TREAT-NMD.

Neonatal screening policy

The neonatal screening programme offer differs greatly among Spanish regions⁹⁵. National neonatal screening is in place for phenylketonuria and hypothyroidism.

In 2007 the Public Health Commission of the Interterritorial Council of the Spanish NHS (CISNS) carried out a study on the situation of newborn screening programmes in Spain, the *Informe sobre la situación de los programas de cribado neonatal en España*⁹⁶. The aim of the study was to strengthen and promote the early identification and treatment of affected persons, thereby avoiding neurological damage and reducing morbidity, mortality and possible disabilities associated with certain diseases through timely interventions. Accordingly, the new recommendations of child health programmes stress the importance of the early detection of diseases and at-risk groups, as well as the supervision of the growth and overall development of the child, which enables the identification by paediatricians and other health professionals of warning signs and of the early detection of developmental disorders, which can be part of the symptoms associated with several rare diseases.

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 180 members is recognised as an umbrella organisation for the 3 million people with rare diseases in Spain and their families. Several services to patients have been developed, funded by public and private, national and regional funds, published on their website www.enfermedades-raras.org. FEDER has been very active in advocating for an Action Plan in different National Conferences (2005, 2006), as well as participating in the Technical Committee of the Ministry of Health and Social Policy for the development of the National Strategy for Rare Diseases. Apart from this, FEDER is active at European level, present on the EURORDIS board and participating in many European projects at national level. FEDER is a member of the Spanish Committee of Disabled (CERMI) and the Spanish Patients' Forum and is usually represented at regional level at the Health Councils. Support for patient organisations is provided by private and public (Labour Ministry and Ministry of Health) funds and organisations for patients with disabilities are also supported by the IMSERSO (Ministry of Health and Social Policy).

Sources of information on rare diseases and national help lines

Since 2002, there is a dedicated Orphanet team in Spain, currently hosted by CIBERER (Centre for Biomedical Network Research on Rare Diseases). This team is in charge of collecting data on rare diseases related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. The Orphanet portal is available in Spanish.

The Rare Diseases Research Institute (IIER) developed a public information system named "*Sistema de información sobre enfermedades raras en español – SIERE*" (Information System on Rare Diseases in Spanish) in 2002. There are also plans for updating this system to include epidemiological information by disease.

Other sources of information were developed by rare diseases research networks such as REPIER, INERGEN, GIN; ORGEN, REDEMETH, REC-GEN, etc. They are in different stages of development and some have been recently closed or their information is being transferred to the national registry website.

FEDER maintains a website with information on rare diseases and certain documentation and runs a specialised helpline, the Information and Support Service (SIO) which has received more than 18'000 consultations since 2000, when it was established with the support of the former Social Affairs Ministry. The

⁹⁵ "Report on the neonatal screening programmes situation in Spain" elaborated by the *Comisión de Salud Pública del Consejo Interterritorial del SNS (2007)* (Committee for Public Health of the Interterritorial Council of the National Health System) (2007)

⁹⁶ "Report on the neonatal screening programmes situation in Spain" elaborated by the *Comisión de Salud Pública del Consejo Interterritorial del SNS (2007)* (Committee for Public Health of the Interterritorial Council of the National Health System) (2007)

help line provides information on rare diseases, patient management of the disease, experts and consultations, obtaining a diagnosis, access to medicinal products, clinical trials, genetic tests, rehabilitation, publications, guidelines for creating a patient organisation, and information on financial support and respite care. Social, legal, psychological support as well as training is provided to individual patients, associations, professionals (and others) by specialised staff. FEDER's help line also provides information to callers from Spanish speaking countries. It also acts as a contact point for experience exchange amongst patients with the same pathology/pathology group. The help line belongs to the European Help Lines Network, led by Eurordis.

CIBERER also runs a website with information regarding its main lines of research.

Guidelines

Since 2000, *IMSERSO* (the main Spanish Institution in charge of providing social support for disability patients and families) has also been collaborating with FEDER in order to develop other guides for rare diseases families, i.e. Amyotrophic Lateral Sclerosis, Achondroplasia, Familial Spastic Paraparesis and Aniridia, amongst others.

*GuíaSalud*⁹⁷ is a programme which is supported by the Ministry of Health and Social Policy through the NHS Quality Agency. Since its first steps in mid-2002 until now, it has been immersed in framework changes within the quality of the NHS Plan. The measures were described in the Quality Plan of 2007, which implicated important changes to objectives, introducing into the work portfolio the development of products, based on scientific evidence, to assist health professionals in decision-making. Several guidelines for specific rare diseases have been developed by GuíaSalud, i.e. related to congenital anomalies or skin care in epidermolysis bullosa.

There is also a Health Technology Assessment Agencies network that develops reports concerning specific rare diseases since 2006 (i.e. ataxias, inborn errors of metabolism or genetic tests).

CIBERER has developed a programme aimed at facilitating information to all those interested through guides and brochures on specific illnesses and/or through scientific lectures meant for patients. CIBERER has produced 59 clinical guides on rare diseases in 2007 and 75 in 2008 intended for nurses, general practitioners and clinical specialists. This research centre also organises therapeutic conferences, workshops and seminars in cooperation with other bodies such as patients' associations. CIBERER is committed to ensuring excellence amongst their scientific laboratories. Most of them are already accredited and some others are in the process of obtaining the best level of standard quality through external validation processes.

National rare disease events

Since 2007 the CIBERER holds an annual scientific meeting where the principal investigators and pre-doctoral/postdoctoral researchers present their recent results in the field of the biology, pathophysiology, clinical research and therapies, and epidemiology in the field of rare diseases. FEDER has organised various National Conferences on rare diseases and Regional Conferences and many other rare diseases specific patients association 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.

Hosted rare disease events

Every year since 2000, the Royal College of Pharmacists in Seville has organised the International Congress on Orphan Drugs and Rare Diseases, discussing topics in the field of rare diseases.

The International Conference on Rare Diseases and Orphan Drugs 2006 was held in Madrid (25 October), as a 1-day-meeting back-to-back with the EPPOSI Meeting in Madrid (26-27 October 2006). ICORD 2006 was an organisational meeting aimed at identifying important areas for future work and further organisation of upcoming ICORD conferences.

Research activities and E-Rare partnership⁹⁸

In Spain, research related to rare diseases is gathered in the "*Plan Nacional de Investigación Científica*" (National Plan for Scientific Research), "*Desarrollo e Innovación Tecnológica*" (Development and Technological Innovation) (2008 – 2011), and specifically within the "*Acción Estratégica en Salud*" (Strategic Action on Health), in which rare diseases constitute one of the most important research subjects. In September 2007, the

⁹⁷ <http://www.guiasalud.es/home.asp>

⁹⁸ This section was written using updated information originally from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (p19)

outlines of the National R&D&I Programme were presented. According to the Ministry of Education and Science, the General State Administration will increase its investment at a rate of 16% per year starting in 2008 and up to a total expenditure of 2.2% of GDP in 2011, in line with European Union recommendations. This estimate includes the business sector, which will finance 55% of the total investment.

The most relevant government initiative for research on rare diseases was the creation of the Biomedical Research Network on Rare Diseases (CIBERER, which depended at its creation on the Ministry of Health) in November 2006. This network acts as a public consortium of 30 institutions; the network has more than 700 professionals integrating 61 research groups and is mainly funded by the Spanish Ministry of Science and Innovation through the Carlos III Health Institute. The aims of CIBERER are: to improve the resources available for researching rare diseases and rare disease treatments, to promote the integration between basic and clinical biomedical research groups in order to aid collaboration between the laboratory with the clinical setting, to develop cooperative investigational projects that allow for the exploration of new scientific hypotheses and technological developments, to demonstrate the value of rare disease research, and to establish collaborative efforts with the pharmaceutical and biotechnological industry.

The following institutions give support for academic / industrial research on rare diseases:

- Fund for Health Research (FIS) (which belongs to the Institute of Health Carlos III) funds single and multi-centre research projects as well as technology assessment projects since 2001. Thus, for example 12 Cooperative Health Thematic Health Networks (RETICS) were created, which involved research groups and centres belonging to the National Health System with a budget amounting to €20 million for three years.
- CIBERER (which belongs to The Institute of Health Carlos III) was given funding amounting to €6.2 million in 2007, €8 million in 2008 and €7.7 million in 2009 for research activities (basic, clinical, epidemiological and translational) in the field of rare diseases.
- *Instituto de Investigación de Enfermedades Raras* – IIER (National Research Institute for Rare Diseases), within the Institute of Health Carlos III (ISCIII) was founded in November 2003 to promote basic, clinical and epidemiological research on rare diseases.
- *Federación Española de Enfermedades Raras* – FEDER (Spanish Federation of Rare Diseases) is a federation which includes most Spanish patient organisations for rare diseases. FEDER also provides funding for research on rare genetic diseases in the scope of the national R&D plan.
- Two different calls for proposals of projects addressed to study the potential of new orphan drugs have been funded by the Ministry of Health and Social Policies (MSPS) and managed by the FIS (ISCIII).

Since the National Strategy on Rare Diseases began, rare diseases have been considered as a priority research area of the Fund for Health Research (FIS) and the Strategic Action in Health (AES) for 2008-2009. Rare diseases are also taken into account in the area of "additional performances" contemplating the strengthening of both basic research and clinical trials or the development of orphan drugs.

Spain represented by the Institute of Health Carlos III (ISCIII), is a partner of the E-Rare. Spain has participated in the two calls for proposals managed by the Fund for Health Research (FIS), the Public Health Agency for Health Research, which is part of the ISCIII. Spain participated in the 2007 and 2009 E-Rare transnational calls with a total of €3.25 million of initial funding committed to the project Spain. Spanish teams participate in 6 of the 13 funded projects/consortia selected following the 1st Joint Transnational Call.

Participation in European projects

Spain participates in the following European Reference Networks for rare diseases: Dyscerne, EPI, EPNET, ENERCA (main partner), EUROHISTIONET, NEUROPED, Paediatric Hodgkin Lymphoma Network, PAAIR and RBDD. Spain participates in the following European research projects for rare diseases: ANTEPRION, ANTIMAL, BNE, CLINIGENE, CHD-PLATFORM, CONTICANGET, CAV-4-MPS, CureFXS, EMSA-SG EUGINDAT, EuroRETT, ENRAH, EUGINDAT, EUMITOCOMBAT, EUROBONET, EUROAGENTEST, EUROAN LEUKEMIA NET, EVI-GENORET, EUROSCA, EPINOSTICS, EUROBFNS, EuroGeBeta, GEN2PHEN, GENESKIN, HSCR, HMA-IRON, LEISHMED, LEISHDRUG, MALARIA AGE EXPOSURE, MCSCS, MOLDIAG-PACA, NANOTRYP, NEUROKCNQPATHIES, MLC-TEAM, PNSEURONET, TRYPOBASE, RISCA, RAPSODI, RD PLATFORM, RevertantEB, SIOPEN-R-NET, SERO-TB, TAMAHUD, TREAT-NMD, and WHIMPath,. Spain contributes to the following European registries: EUROCAT, ERCUSYN, EUGINDAT-PIADATABASE, MOLDIAG-PACA, AIR, EURO CARE CF and TREAT-NMD. Spain also participates in the EUROPLAN project.

Orphan drug committee and incentives

The Spanish Agency of Medicines and Medical Devices (AEMPS) is the National Authority responsible for evaluating medicines before approval as well as for conducting a continuous supervision post authorisation of its benefits and risks in order to update the approved conditions of use of any medicine. In the case of orphan drugs designated at the European level, this evaluation process is undertaken by all national European agencies under coordination of the EMA, i.e. 'centralised procedure'.

There are specific scientific advice procedures in place at the AEMPS to give guidance and advice to any potential orphan medicinal product development. These procedures can be applied within the context of a centralised advice coordinated by the EMA or on a purely national basis.

Since 2007, there is an annual call for public financing of clinical trials of medicines with no commercial interest. In this call, medicines for rare diseases (either designated as orphan medicines or not) are one of the priorities, together with paediatrics, antibiotics and studies of major interest for the National Health System). In the scope of this call, proposals for studies concerning medicines for the treatment of rare diseases have an outstanding rate of success in obtaining full public financing.

In Spain, the 29/2006 Act on "Guarantees and Rational Use of Medicines and Medical Devices" states in Article 2, referring to supplying and dispensation guarantees of orphan drugs, that: "the Government, in order to ensure the supplying of medicines, will be able to adopt special actions in relation with their manufacture, importation, distribution and dispensation. In the case of "orphan drugs," (pursuant to the Regulation (EC) number 141/2000 "medicines without any commercial interest") the Government could adopt, besides the above mentioned, other actions related to the economic and fiscal policy of the so-called medicines".

Orphan drug availability

Access to orphan medicines is extensive in Spain, with all designated orphan medicines authorised at the European level, also authorised by the Spanish authorities and included in National Health System coverage.

Until 2009 almost all authorised orphan medicines are marketed in Spain (87% of the drugs with European authorisation) and for the rest, the pharmaceutical companies have not yet started commercialisation in Spain.

All orphan medicines are fully reimbursed by the National Health System. Nevertheless, in some Autonomous Communities (Regional Governments), there are protocols and systems to follow the access of patients to the treatment under the National Health System coverage.

An authorisation procedure for access to non-authorised medicines is in place. The AEMPS authorises either individual access for specific patients (compassionate use) or access to groups of patients through a certain protocol (temporary authorisation of use). The procedure for granting this access has recently been improved (Royal Decree 1015/2009) in order to make it faster, through entirely telematic communication with the hospitals at the same time that it has been reinforced the follow up of safety information by the AEMPS and the information systems.

In Spain, when marketing authorisation is granted either by the EMA or AEMPS, the Ministry of Health initiates a procedure to decide on reimbursement of this new product on the national reimbursement list. If a reimbursement status is approved, the pricing is decided simultaneously. Up till now all orphan drugs approved by the EMA are reimbursed in Spain in one of these categories: 1) for use only in hospitals (hospital Use: H) or 2) in a non-hospital environment, but prescribed only by a specialist doctor (hospital diagnostic: DH).

Specialised social services

Respite care is provided for rare disease patients considered as living in a situation of dependency. These services can take the form of nursing homes, day care centres, home care, remote assistance, or as a residential stay such as those offered for free at the Burgos' National Reference Centre for Rare Diseases. These services are either public or private and co-payment is often required. Patients suffering from a disability are eligible for government allowances for resort and spa stays with 20% to 50% of the total cost covered (this includes travel and stay as well as insurance costs).

B.1.25.2 New initiatives and incentives in 2009

Definition of a rare disease

The Spanish Strategy on Rare Diseases approved on 2009 accepts the European Orphan Drug Regulation definition of a prevalence of no more than 5 cases per 10,000 inhabitants.

National plans and related actions

National initiatives: The Rare Diseases Strategy was approved by the Interterritorial Council of the Spanish NHS on 3 June 2009⁹⁹. It is set within the framework of the Quality Plan of the Spanish National Health System (NHS) which includes, amongst its other objectives, improving care for people with rare diseases and their families. The elements defined in the Spanish strategy allow for the fulfilment of the recommendations established by the European Council Recommendation on an Action in the Field of Rare Diseases. Through this initiative the Spanish Government aims to formulate a feasible and adequate response to the needs of people affected by rare diseases, and the combined efforts of all those involved was fundamental to the achievement of that objective. The Spanish NHS Rare Diseases Strategy represents a consensus between the Ministry of Health and Social Policy, the Ministry of Science and Innovation, Autonomous Communities, patient organisations, scientific societies and experts. A rigorous approach to any rare disease calls for a set of actions that establish evidence-based, agreed criteria regarding the guidelines to be followed in any one of the strategy lines set out herein, in order to enhance the effectiveness and quality of the treatment of these pathologies in all the health services of the Spanish health system.

Two Committees were set up: a Technical Committee made up of 15 scientific societies and 3 patient organisations and an Institutional Committee made up of the representatives appointed by the Health Departments of the Autonomous Communities. One of its main tasks was to assess the suitability and feasibility of the proposed objectives, since they, the Autonomous Communities and their Health Services, will be in charge of actually organising and providing the healthcare.

The Strategy is structured into three parts. The first part, General aspects, includes the justification, the purposes of the Strategy (its mission, principles, the values it inspires), the definition of rare diseases and their situation in Spain. In addition it covers their historical development and epidemiological situation. Finally, it sets out the strategy development methodology. The second part, Development of strategy lines, sets out the objectives and recommendations. The participants of the Strategy decided, by consensus, to establish the following strategy lines: Information on rare diseases, Prevention and early detection, Healthcare, Therapies, Integrated health and social care, Research and Training.

The strategy lines are broken down into 13 general and 37 specific objectives, with their respective technical recommendations and monitoring and evaluation indicators. This will contribute to an improvement in the quality and outcomes of the services and healthcare provided in the field of rare diseases. In short, this document aims, on the basis of available information/evidence, to establish a set of objectives and recommendations to be achieved which, in a realistic manner and according to the available resources and the areas of competence of the Autonomous Communities, will help improve the quality of interventions and outcomes in the field of rare diseases. The third part, Monitoring and Evaluation, sets out the process that makes it possible to monitor the proposed actions. Evaluation will take place in two years.

Given the decentralised health administration (management) of the Autonomous Communities (regional governments), the Strategy will act as a framework and a set of recommendations for the different regions, who will in turn be in charge of implementation. Funds are allocated through a call for proposals opened to the Autonomous Communities in order to facilitate the implementation of the Strategy. The strategy for rare diseases as well as any other related measures or actions aimed at rare diseases are included in the Spanish National Health Budget. The Ministry of Health and Social Policy uses the *Funds for the Implementation of Health Strategies* in particular: these funds are used by the Autonomous Communities to implement the new Strategy for Rare Diseases of the National Health System.

Regional initiatives: The Extremadura Autonomous Community is developing its regional rare disease plan based on general recommendations from Europe and the Spanish National Strategy (Extremadura Rare Diseases Integral Plan 2009-2014). The Health Department of the Autonomous Government of Catalonia (*Generalitat de Catalunya*) recently approved an Order for the creation of an Advisory Commission on

⁹⁹ <http://www.msc.es/organizacion/sns/planCalidadSNS/docs/enfermedadesRaras.pdf>
http://ec.europa.eu/health/ph_threats/non_com/docs/rare_strategy_spain_en.pdf

minority diseases, with the aim of enhancing the implementation of specific health policies aimed at these pathologies, some of which are already included in Catalonia's different existing master plans (on integrated health and social care, mental health, oncology, etc.). And the Regional Government of Andalusia (*Junta de Andalucía*) continues with the aforementioned *Plan de Genética de Andalucía 2006-2010*, which, in turn, led to the creation of the *Plan de atención a personas afectadas por ER 2008-2012*, a plan regarding care for people affected by rare diseases.

Centres of expertise

Based on the strategy for the designation of centres, services and units of expertise developed by the Ministry of Health through the aforementioned Royal Decree 1302/2006 (10 November 2006) which defined a designation procedure of centres of reference for single diseases or groups of diseases, referring specifically to both high technology and rare diseases centres of reference, some Centres of Reference for rare diseases have already been designated. Up to now, the Interterritorial Council and the Ministry of Health and Social Policy have agreed to designate 90 CSUR for some pathologies or procedures, including some related to rare diseases. The process continues with other specialisation areas in order to define some more pathologies and procedures, rare diseases included which should be assisted or carried out in CSUR of NHS.

A centre for rare diseases in Burgos, "State Reference Centre of Health and Social Care for People with Rare Diseases and their Families" (CREER) was inaugurated on 30 September 2009 by the Spanish Minister of Health and Social Policy (MSPS). This is a centre of expertise with the following missions, amongst others: coordination, research, innovation, professional training, dissemination of information and awareness raising and support to other Spanish organisations. CREER can accommodate up to 60 people distributed in 12 family flats and additional day care places with the aim of providing integral care following the recommendations of the EU. CREER will also play an important role anticipating respite programmes for the families, promoting the mutual knowledge and exchange of experiences between patients and families and providing information training concerning welfare policy, as well as social and health care. All areas are coordinated to feed into one another: new knowledge is applied to improve care and quality of life of people with rare diseases and their families.

Neonatal screening policy

The offer of neonatal screening varies from region to region in Spain. There are 6 Autonomous Communities that have extended the newborn screening programme by Tandem Mass Spectrometry.

A working group with representatives from the Ministry of Health and Social Policy, Regional health services and scientific associations, is currently reviewing scientific evidence and will produce a report and recommendations about neonatal screening for the National Health System in 2011.

Also, several Spanish Technology Health Assessment Agencies have been developing report criteria for the cost-effectiveness of a neonatal screening programme using Tandem Mass Spectrometry. It is expected that new European initiatives could provide some guidelines regarding this issue¹⁰².

National alliances of patient organisations and patient organisations

FEDER continues participating actively in the implementation and evaluation of the National Strategy on Rare Diseases.

FEDER is developing several specific agreements with CREER in order to improve the collaboration and the empowerment of FEDER patient organisation.

Sources of information on rare diseases and national help lines

CREER is working with FEDER and the IIER on a new system to improve the coordination of different competences for providing several types of information on rare diseases. The System of Information for Patients (FEDER Help line) is thus also improved.

CIBERER supports the translation into Spanish of the Orphanet website content and contributes to the site with national data. The Spanish Rare Diseases Registry (ISCIII) has just signed an agreement with Orphanet in order to use the same rare diseases classification system.

¹⁰² Cf section A.2.2a.4.1

Education and training

Several short courses have been organised in 2009 in addition to the creation of the First University Master organised by the Pablo Olavide University, Seville (Autonomous Community of Andalusia), in collaboration with the CIBERER and the FEDER Foundation. The University of Zaragoza (Autonomous Community of Aragón) is developing a course on rare diseases for pre-graduate medical students and a similar course is being planned for Madrid universities along with a course on occupational therapeutics for pupils and the applicability to the field of rare diseases.

CREER is also involved in the study of socio-educational needs of children affected by some types of rare diseases.

National rare disease events

The official launch of Spanish Rare Disease Strategy took place on 20 October 2009 under the auspices of the Spanish Ministry of Health and Social Policy. The official launch included the presentation of the experiences and initiatives related to the elaboration, implementation and evaluation of other Member States on rare diseases plans, such as Italy, Portugal and France, and also the Council Recommendation on an action in the field of rare diseases.

In 2009, FEDER, as member of the Council of National Alliances of Eurordis, led the organisation of Rare Disease Day events in Spain, along with its member organisations across the country. Events included demonstrations and official ceremonies, such as the official launch of the NHS's Rare Disease Strategy. Many institutions also organised activities aimed at raising awareness of this social and health issue. For this occasion, CIBERER (Biomedical Network Research Centre for Rare Diseases) and the Isabel Gemio Foundation presented the evolution of rare disease research in Spain at a meeting entitled 'International Rare Disease Day: To Research is To Advance' (26 February 2009).

In October 2009 CIBERER's annual meeting was held in San Lorenzo del Escorial, Madrid. The National Rare Diseases Meeting ("*Encuentro Nacional de Enfermedades Raras*") was held in Totana (27-29 November 2009).

Hosted rare disease events

On 19-21 February 2009 the participants of the IV International Congress on Orphan Drugs and Rare Diseases approved the "Seville Declaration" a document consisting of 17 different recommendations of actions for both regional and national level government to undertake in order to improve the quality of life of rare disease families and patients.

The International Meeting on Familial Lipodystrophies was held on 3-4 April in Santiago de Compostela. The 4th Molecular Imaging Meeting was held in Barcelona (27-30 May 2009). The 8th Hereditary Hemorrhagic Telangiectasia International Scientific Conference was held in Santander (27-31 May 2009). The 10th European Symposium on the Prevention of Congenital Anomalies organised by Eurocat was held on the 10th June 2009 in Bilbao. The European Science Foundation held a conference in Biomedicine entitled "Rare Diseases II: Hearing and Loss" on 22-27 November 2009 in Saint Feliu de Guixols. A conference was held on the "Applications of cell and gene therapy for the treatment of genetic instability disorders" in Madrid (12-13 November 2009).

The Eurordis Round Table of Companies "Eurordis Strategy 2010-2015 and partnership with ERTC members" was held in Catalonia (19 June 2009).

Research activities and E-Rare partnership

Spain participated in the 2nd E-Rare Joint Transnational Call, and Spain is represented in 6 of the 16 consortia/projects selected for funding, with a total funding of around 580,000€.

In 2009 a €12 million budget in R&D&I and more than 700 researchers were made available as resources for translational research into rare diseases.

CIBERER was provided with funding amounting to €7.7 million in 2009 for research activities (basic, clinical, epidemiological and translational) in the field of rare diseases.

In 2009 the funds from the 'Marató de TV3' (telethon) organised in Catalonia by one of the region's main TV channels will be dedicated to rare diseases research. Other calls for project proposals or fellowships devoted to rare diseases were launched by charities, bank foundations and pharmaceutical company foundations.

Orphan drug availability

In 2009, 5 new orphan drugs were included in the national reimbursement list. Moreover, a new law which improves the regulation of compassionate use (particularly for orphan drugs) and foreign medications legally distributed in other countries but not authorised in Spain came into force in 2009.

B.1.26 SWEDEN **B.1.26.1 State of affairs before 2009¹⁰³****Definition of a rare disease**

The Swedish Medical Products Agency (MPA) adheres to the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals in the EU. However, the information database of the Swedish National Board of Health and Welfare defines rare diseases as "disorders or injuries resulting in extensive handicaps and affecting no more than 100 individuals in one million inhabitants".

National plan for rare diseases and related actions

There is currently no national plan in Sweden for rare diseases and there are no earmarked funds for rare diseases as rare diseases are included within the general health system budget. *Riksförbundet för Sällsynta Diagnoser*, the National Organisation for Rare Diseases, held a hearing in mid-November 2008, during which the Director of the Health Care Division at the Ministry of Health and Social Affairs, presented plans by the Ministry to investigate the situation of rare disorders in Sweden.

Centres of expertise

Sweden's health care system is decentralised and run at county level (there are 20 counties in Sweden). The National Board of Health and Welfare, based on an agreement with the Federation of County Councils in 1990, has issued a catalogue of providers of specialist care, intended to provide a recommendations on reference points for local administrators. Examples of national centres of expertise in place are a Rett syndrome centre, four cystic fibrosis centres, a porphyria centre and a centre for children with congenital malformations and syndromes.

Registers

There is a National Patient Register (NPR) funded by the National Board of Health and Welfare, where all in-patient and some out-patient visits (including day-surgery and psychiatric) from both private and public caregivers are included. Primary care is not yet covered in the NPR. This registry is a quantity register, not a quality register, and is mainly used for statistics.

There is no official list of all Swedish patient registries. In many instances, individual departments, county councils and regions have created quality registries to enable them to monitor their own activities. These local quality registries have yet to be inventoried centrally.

In order to improve quality a system of about 70 National Quality Registries has been established in the Swedish health and medical services in the last few decades (<http://www.kvalitetsregister.se/>), supported by the Swedish Association of Local Authorities and Regions (SALAR). All National Quality Registries contain individual-based data concerning problems and diagnosis, treatment interventions and outcomes. However, these registries are mainly general and do not solely concern rare diseases, although patients with rare diseases may be in the registries, for example the Swedish Dementia Registry. SALAR encourages managers of registries to apply for funding to become a National Quality Register in order to increase quality of health care on a national level as well as the accessibility of the registry.

Sweden contributes to the EURO CARE CF and AIR European registries.

¹⁰³This section was 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)* (p20)

Neonatal screening policy

A newborn screening programme is in place for phenylketonuria, hypothyroidism, congenital adrenal hyperplasia, biotinidase deficiency and galactosaemia in Sweden.

National alliances of patient organisations and patient representation

Riksförbundet för Sällsynta Diagnoser (The Swedish National Organisation for Rare Diseases) is the national alliance of rare disease patient organisations. The alliance aims to create a holistic view on the common problems of rare diagnoses, to support the small handicap groups, to ease the particular difficulties of patients with rare diagnoses, and to promote and protect human rights. *Riksförbundet för Sällsynta Diagnoser* also provides funds to support the empowerment of patient organisations.

Patient organisations for rare diseases are mainly sponsored by private sponsors, but also through public sponsoring for specific projects. No national initiatives exist to support nationwide patient organisations as the Swedish healthcare system places the accent on decentralisation and organisation at municipal and county level. There is no specific platform for the representation and consultation of patient organisations in policy issues for rare diseases at the moment in Sweden.

Sources of information on rare diseases and national help lines

Since 2006 there is a dedicated Orphanet team in Sweden, currently hosted by Karolinska Institutet. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

Since 1996, the Swedish Information Centre for Rare Diseases (*Smågrupps Centrum*) at the Sahlgrenska Academy at the University of Gothenburg provides resources on rare diseases at a national level. It is financed by the National Board of Health and Welfare. Anyone may contact the centre, which is open to all age groups from children to adults. The Swedish National Board of Health and Welfare also maintains a freely-accessible rare disease database, currently providing expert validated information about 247 rare diseases. The material is also published (in PDF and paper versions) in English and 70 information texts are now available in translation. The Swedish Information Centre for Rare Diseases also has a telephone number for information on rare diseases which also acts as a helpline and source of information for patients, families and professionals.

Ågrenska, a national competence for rare diseases, serves as an important information point for patients and families and provides information (including information on available social services) on their website¹⁰⁵. In cooperation with The Swedish National Organisation for Rare Diseases it has formed the National Competence Centre for Rare Diseases. The main objective of the centre is to gather, develop and spread knowledge on rare diseases and their consequences. Ågrenska also participates in maintaining the Nordic web resource www.rarelink.eu, which is run by governments in the Nordic countries. In some cases Ågrenska can provide additional information by telephone.

Riksförbundet för Sällsynta Diagnoser has an online database with information on 60 rare diseases in Swedish.

National rare disease events

Riksförbundet för Sällsynta Diagnoser took the initiative to mark Rare Disease Day on 29 February 2008, and organised a national rare disease conference in Stockholm inviting patient organisations, politicians, representatives from the authorities, industry and academia.

Hosted rare diseases events

The secretariat of ICORD (International Conference for Rare Diseases and Orphan Drugs) in Sweden participated in organising an international conference on rare diseases in Washington DC in May 2008.

Research activities and E-Rare partnership¹⁰⁶

According to the *Inventary of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*: "the Swedish Research Council is a government agency under the Ministry of Education and Science. The scientific council for medicine evaluates and prioritises research in medicine, pharmacy, odontology and care sciences and, on behalf of the Swedish

¹⁰⁵ <http://www.agrenska.se/>

¹⁰⁶ Written using information from the *Inventary of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (pp20-21).

Research Council, decides on project grants in these fields. Project funding is based on quality criteria (bottom-up procedure) and not subject to prioritisation based on research areas, with a few exceptions. The Swedish Research Council for Medicine has an annual budget of around €47 million. It sponsors mainly individual research projects and funding is in the response mode. Project grants usually cover 10-20% of total project costs. Junior research positions are also funded. The Swedish Research Council for Medicine also makes decisions to provide financing of principal investigators in areas of research where directed support is of strategic value.¹⁰⁷ Rare diseases are thus funded through a yearly call for proposals for project grants: however, there is no dedicated budget for rare diseases, instead rare diseases applications compete with other applications on the basis of the quality of the proposal and not subject to prioritisation of research areas, with a few exceptions. Project grants and salaries for principal investigators can thus be awarded in areas that are related to rare diseases (€1.1 million in 2005). Because research projects are only partly funded by the SRC, the total amount of funding for research in rare diseases in Sweden is greater than what is funded by the Research Council.

The Swedish Cancer Society is a non-profit organisation which contributes to the funding of cancer research (including rare diseases), giving information about cancer and supporting activities which aim to improve cancer treatment and care. Research projects are funded following the same policy as that of the Swedish Research Council. *“The Swedish Cancer Society is the major source for cancer research in Sweden and provides support for high quality research projects [for] all types of cancer as well as to various types of academic research positions. Based on the current project catalogue, it is estimated that the support to clinical research into rare cancer types, fulfilling the orphan drug criteria, amounts to 27 million SEK in 2004 (approximately €3 million). This support varies [...] slightly from year to year¹⁰⁹.”*

It is not possible to dissociate the support to research into the disease itself from that oriented towards orphan drug development as these research efforts are often mixed but probably very little is used to directly support drug development.

Sweden is not currently a partner of the E-Rare project.

Participation in European projects

Sweden participates in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, ENERCA EPI, EPNET, EUROHISTIONET, Paediatric Hodgkin Lymphoma Network and PAAIR. Sweden participates in the following European research projects for rare diseases: ANTEPRION, BIOMALPAR, BNE, CHD PLATFORM, CUREHLH, CLINIGENE, EMVDA, EUMITOCOMBAT, EURAPS, EUCLYD, EUROSD, EUROBONET, EUROAGENTEST, EUROPEAN LEUKEMIA NET, EVI-GENORET, EMSA-SG, EUROCRAN, EURADRENAL, EURAMY, EURO-GENE-SCAN, GENESKIN, HDLMOICS, INHERITANCE, NMD-CHIP, LYMPHANGIOGENOMICS, MANASP, MOLDIAG-PACA, NEUPROCF, NEOTIM NEUROPRION, NEWTBDRUGS, PRIBOMAL, PWS, TRYPOBASE, TB-DRUG OLIGOCOLOR, TREAT-NMD, RD PLATFORM and VITAL. Sweden contributes to the following European registries: AIR, EUROCAT and EURO CARE CF. Sweden is a partner of the EUROPLAN project.

Orphan drug committee and incentives^{110, 111}

The Medical Products Agency (MPA¹¹²) is responsible for the regulation and surveillance of the development, manufacturing and marketing of drugs and other medicinal products, including orphan drugs in Sweden. The MPA can apply a fee waiver for clinical trial applications and scientific advice for researchers/applicants/companies lacking support from industry. Concerning the provision of free of charge IMP by the sponsor in clinical trials, 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.

In its “letter of regulation” for 2008 to the MPA, the Ministry of Health and Social Affairs, commissioned the MPA (in collaboration with the Board of Health and Welfare) to propose measures that could contribute to the development and rational use of orphan drugs in Sweden, according to Article 9 of the

¹⁰⁷ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision) (pp20-21).*

¹⁰⁹ *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision) (p21).*

¹¹⁰ Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp 59-62).*

¹¹¹ 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) (pp20-21).*

¹¹² www.mpa.se

Orphan Regulation (EC) 141/2000. In the report, several measures were proposed: to form a national strategy for rare diseases, to use national quality registers for the follow-up of orphan drugs in clinical practice, to adjust financing of orphan drugs to facilitate early introduction of (and access to) orphan drugs, to institute national centres for rare diseases for efficient use of orphan drugs, to stimulate research and development of orphan drugs in Sweden and to explore areas of potential collaboration within the EU using the Swedish presidency in 2009 as a platform.

Orphan drug availability¹¹³

In November 2008, 40 orphan drugs were available in Sweden. There is no legislation in Sweden governing compassionate use or off-label use of orphan drugs. For orphan drugs not yet available in Sweden, the MPA can approve “named patient prescription” of a certain drug for a certain patient on a yearly basis: this procedure also applies for non-orphan drugs. Reimbursement decisions are taken by the Dental and Pharmaceutical Benefits Board (DPBB), a government agency commissioned to make decisions on state subsidies for dental and pharmaceutical products. If a positive decision on reimbursement has been taken by the DPBB, orphan drugs are fully reimbursed by social insurance in Sweden (there are no conditions specific to orphan drugs) and are available through hospital and community pharmacies when prescribed by a specialist physician or a general practitioner. Solidarity funding between Swedish county councils is available for three diseases, two of which are rare diseases (Gaucher’s disease and haemophilias): the basis for the solidarity funding of these very rare diseases is to compensate for costs due to the uneven distribution of these patients between the different counties in Sweden. Concerning drugs used in hospitals (orphan or non-orphan) the decision on availability for the patients as well as the payment is decided at the local hospital/county level since in-hospital drug costs are not included in the reimbursement system.

Specialised social services

Ågrenska offers families, adults and children affected by rare diseases the possibility to benefit from educational and holistic activities adapted to their needs as well as individual home visits, assistance and educational courses. These programmes run throughout the year and guidance is also provided to best orientate patients regarding the available social services.

The Mo Gård Group coordinates measures for patients with communication disabilities, some of which are linked to rare diseases.

In addition local government institutions provide fully reimbursed activities, such as respite care services, therapeutic recreational programmes and services aimed at the integration of patients in daily life. These activities are not aimed specifically at rare diseases patients.

B.1.26.2 New initiatives and incentives in 2009

National plans for rare diseases and related actions

An investigation focusing on the organisation of resources (health care and information) for rare diseases in Sweden has been initiated by the National Health and Welfare Board and is supported by the Ministry of Health: this investigation is ongoing and a report will be produced in 2010.

National alliances of patient organisations and patient representation

New parliamentary bills have been passed by the Swedish parliament to support patient organisations and their activities. One supports a conference for *Riksförbundet för Sällsynta Diagnoser* members and non-members, held on 14 November 2009. Another supports further development of a communication platform on the website www.sallsyntadiagnoser.se where a diagnosis database for members will be available for those concerned to reach both formal and non-formal contacts and get into contact directly via a web community and a web forum.

Sources of information on rare diseases and national help lines

The National Health and Welfare Board have updated their printed information sheets concerning Rare Diseases. The results form the 2009 Swedish EU Presidential Conference on “Assessing Drug Effectiveness”

¹¹³ Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 59-62)

have been published in a special booklet (www.lakemedelsverket.se). The Ågrenska Academy has been inaugurated, which provides live cast lectures and conferences via the web page and an education centre (The National Competence Centre for Rare Diseases). In addition to this, a new information sheet concerning orphan drugs has been published by LIF (the research-based pharmaceutical industry in Sweden) (www.lif.se).

National rare disease events

Rare Disease Day will be marked in 2012 (every fourth year). During 2009's annual summer conference for politicians there was participation and lobbying from the National Organisation for Rare Diseases.

On 26 May 2009, LIF organised a seminar on the subject of rare diseases and orphan drugs with presentations and participation from the government, authorities, academia and industry.

On 14 November 2009 *Riksförbundet för Sällsynta Diagnoser* held a national conference for members and stakeholders.

Hosted rare disease events

On 1 July 2009, Sweden took over the Presidency of the European Union (EU). Maintaining the momentum initiated by France and sustained by the Czech Republic, during which the adoption of the Council Recommendation on an Action in the Field of Rare Diseases was achieved in June of this year, the Swedish presidency organised a conference of experts. On 28-29 July 2009, the conference "Assessing Drug Effectiveness – Common Opportunities and Challenges for Europe" gathered stakeholders from throughout Europe to discuss how to develop cooperation across Europe for the collection and sharing of data on drug effectiveness and safety following marketing authorisation. Speakers included Thomas Lönngren, Executive Director of the EMA, along with representatives from government, industry, research, and patient organisations. A workshop specific to orphan drugs, an area for which cooperation is considered critical as most individual countries have too few patients and resources to sustain a comprehensive follow-up scheme, brought together a panel of experts. The conference moved forward the process of post-marketing assessment harmonisation via the decision to follow a pilot project "for structured follow-up for initial testing on an orphan drug" for which several candidate products were proposed by the workshop panellists. A meeting during the autumn of 2009 brought together stakeholders interested in participating in the pilot project.

The secretariat of ICORD in Sweden participated in the organisation of an international conference on rare diseases in Rome in April 2009 and will take part in the arrangements of the upcoming conferences in Argentina (2010) and (Japan 2011).

Stockholm hosted the 2009 Porphyrins and Porphyrias conference (14-18 June 2009).

Education and training

Riksförbundet för Sällsynta Diagnoser organised a university course on Diagnoses and Identity where health care professionals and members of the authorities are active participants. The course will be held again in 2010. Another course entitled "Empowerment of the carrier of a rare disease", has been organised twice in 2009. The course structure will be promoted to commercial and public institutions.

Orphan drug availability

According to the MPA 46 orphan drugs were sold in Sweden during 2009. These drugs are Afinitor, Aldurazyme, Atriance, Busilvex, Carbaglu, Cystadane, Diacomit, Duodopa, Elaprase, Evoltra, Exjade, Fabrazyme, Firazyr, Glivec, Gliolan, Increlex, Inovelon, Litak, Lysodren, Mozobil, Myozyme, Naglazyme, Nexavar, Nplate, Orfadin, Pedeia, Prialt, Replagal, Revatio, Revlimid, Savene, Soliris, Somavert, Sprycel, Tassigna, Thalodimide Celgene, Thelin, Torisel, Tracleer, Ventavis, Vidaza, Volibris, Wilzin, Xagrid, Yondelis and Zavesca. The PDBB has decided to reimburse 28 of these 46 drugs. When a drug is not subsidised, the individual counties decide whether a patient should get access to a treatment. This means that orphan drug availability may vary in different parts of the country.

B.1.27 UNITED KINGDOM

B.1.27.1 State of affairs before 2009

Definition of a rare disease

There is no official definition of a rare disease in the UK. The definition, used by the National Commissioning Group (NCG, which supersedes the National Specialist Commissioning Advisory Group) for national commissioning and designation purposes in England is no more than 1 person per 50,000 or lower, or no more than 1'000 patients in the UK, which covers 35 conditions (in 2009), diagnoses or procedures (mostly concerning genetic diseases, especially in children). The definition for specialist commissioning is the presence of conditions requiring a planning population of 1 million or more, as explained in the following section. Similar arrangements apply in the devolved administrations of Scotland, Wales and Northern Ireland.

National plan for rare diseases and related services

There is currently no national plan for rare diseases in the UK.

The basic concept in the National Health Service is not that of 'rare diseases' but rather that of 'specialised services'. There are three tiers for the planning and management of health services – local, specialist commissioning and national commissioning. 'Specialist commissioning' applies to any service with a planning population of 1 million or more, such as rare diseases. Services are selected into national commissioning by ministerial decision¹¹⁴. This involves an assessment of the population's needs and deciding what to prioritise taking into account a wide range of factors. A comprehensive list of services likely to need specialist commissioning has been developed (the Specialised Services National Definition Set). The demand for services always exceeds the ability of the NHS to pay for these services.

The majority of services are commissioned by Primary Care Trusts (PCTs) in partnership with general practice. A large proportion of the money is spent on services for conditions affecting large numbers of people. Services for rarer or more unusual conditions, known as "specialised services" are subject to different commissioning arrangements. Specialised services are those with low patient numbers but which need a critical mass of patients to maintain quality and make treatment centres cost-effective; a catchment population of more than 1 million is needed. As these services are high-cost and low volume, under arrangements which were strengthened by the Carter Review in 2006, PCTs group together to commission such services through 10 specialised commissioning groups (SCGs). Each SCG covers a population of approximately 3-7 million people. The National Specialised Commissioning Group (NSCG), co-ordinates specialised commissioning.

Services for certain very rare conditions (generally less than 400 people nationally) are commissioned by the NCG. The NCG is a standing committee of the NSCG. A list of specialised services¹¹⁵ (see section on "National plan for rare diseases and related services") is available for use in determining whether services should be commissioned locally or by the specialist commissioning group, but there is no official list of rare diseases: this applies to England. Different but equivalent arrangements exist in Scotland, Wales and Northern Ireland.

There has been criticism that the lack of a co-ordinated approach to services for rare conditions engenders late, missed or incorrect diagnoses – often with severe health consequences. A range of wait targets and measures are applied across the NHS: the target of particular importance to patients with rare diseases is the 'wait' target (the maximum wait from first contact with a doctor to initiation of definitive treatment). This implies a very strict approach to establishing a definitive diagnosis quickly as this wait is viewed from the patient's perspective.

Different arrangements exist in Scotland, Wales and Northern Ireland. Funds for care of patients with rare diseases are included in the current expenditure within the general Department of Health budget, although the national commissioning group has its own budget, as do each of the 10 specialist commissioning groups in England whose budgets are pooled from constituent PCTs in each region: there are budgets for the equivalent structures in Scotland, Wales and Northern Ireland.

¹¹⁴ List and criteria are available at www.ncg.nhs.uk

¹¹⁵ List and criteria of specialised services, developed by the Department of Health and now held by the National Specialised Services Team, are available at www.ncg.nhs.uk

Centres of expertise

The NCG funds designated centres for the diagnosis of procedures relating to particular conditions. In line with the remit of the NCG, designated centres provide services for conditions generally affecting less than 400 and no more than 1000 people nationally. Specialist centres themselves can apply for national commissioning of a particular service, subject to the agreed eligibility criteria.

Arrangements are in place enabling patients in Scotland, Wales and Northern Ireland to access designated centres although funding is provided by the relevant body in each country. Regional specialist services also exist for genetic diseases but these are funded separately. There is an annual call for applications for national commissioning and designation. Research and epidemiology are not funded under this system.

Genetic services are commissioned regionally by the SCGs. Genetic testing and counselling is thus available regionally and for some conditions in specialist centres, often linked to an area of research. Genetic counselling is an officially recognised profession and training courses are available.

Registries

The British Paediatric Surveillance Unit (BPSU) was established in 1986 to allow paediatricians to contribute to the epidemiological surveillance and further study of rare disorders affecting children. The BPSU published its latest Scientific Annual Report¹¹⁶ in 2008. This study typically includes 12 rare childhood disorders (or rare complications of common diseases) “of such low incidence or prevalence as to require cases to be ascertained nationally in order to generate sufficient numbers for study”. The 2008 report spotlights childhood scleroderma, congenital adrenal hyperplasia, progressive intellectual and neurological deterioration in childhood, and vitamin K deficiency bleeding, amongst other conditions. The report also includes a progress report of the international network of paediatric surveillance units. Following the establishment of the BPSU, other countries have developed similar methodologies, including Australia, Cyprus, Germany, Greece, Latvia, the Netherlands, New Zealand, Portugal, and Switzerland. Argentina, Italy and Poland have also expressed interest in developing units. International-level action over the past two years, according to the report, includes the surveillance of 70 different rare conditions covering a child population of over 50 million and involving over 10,000 clinicians.

The United Kingdom contributes to the following European registries: EUROCAT, TREAT-NMD, AIR, EUROCARE-CF, EUHASS, EUROPAC, European Prader-Willi database and EUROWILSON.

Neonatal screening policy

Neonatal screening¹¹⁷ is available for phenylketonuria, congenital hypothyroidism, cryptochidism, sickle cell diseases, haemoglobinopathies, cystic fibrosis, congenital cataract, congenital heart disease, developmental dislocation of the hip, newborn hearing loss and medium-chainacyl-CoA dehydrogenase deficiency.

National alliances of patient organisations and patient representation

The major alliances representing rare disease patient organisations in the UK are Rare Disease UK, the Specialised Health Care Alliance (SHCA) and the Genetic Interest Group¹¹⁸ (GIG). Rare Disease UK was established in November 2008 as a joint initiative between the GIG and others in response to the unmet health care needs of families who currently struggle to get access to integrated care and support from the NHS. Rare Disease UK is an alliance of patients, clinicians, industry, academics and researchers campaigning for a strategic plan for rare diseases in the UK.

Established in 2003, the SHCA is a broad coalition of patient groups supported by a smaller number of corporate members campaigning on behalf of people with conditions which require specialised medical care. These conditions tend to be rarer and both complex and expensive to treat.

GIG is a national alliance of over 130 patient organisations which support children, families and individuals affected by genetic disorders. As around 80% of rare diseases have a genetic origin many of GIG’s members have a strong interest in rare diseases.

Amongst the sources of funding available for patient organisations, the government makes funding available to patient organisations through a system known as a Section 64 grant. Many patient organisations have also obtained funding from the National Lottery which is obliged by law to give a percentage of its profits to charitable organisations: activities such as capacity building, networking, dissemination of information, educational events, exchange of best practices, capacity building to improve patients’ integration in social

¹¹⁶ http://www.bpsu.inopsu.com/publications/annual_reports/BPSU%202008%20Annual%20Report.pdf

¹¹⁷ An official list of screening policies is available <http://www.screening.nhs.uk/policydb.php>

¹¹⁸ <http://www.gig.org.uk/>

environments and outreach to very isolated patients are all eligible for funding by these schemes. Grants are available to support patients' organisations: for example in 2008, the NCG accorded funding to two patient support groups in order to finance clinics in the UK for Alström Syndrome and Ataxia-telangiectasia. This is a novel structure where the clinic is partnered by patient groups, hospitals and the NHS.

Patient organisations are officially recognised thanks to a strong government policy for public and patient involvement (PPI). Hospitals and health services are required to consult their patients about changes to the service and there are continuous surveys a patient experience and patient satisfaction in NHS hospitals. Patient opinion is not binding. In most cases patients' representatives are eligible for reimbursement of expenses.

Sources of information on rare diseases and national help lines

Since 2004 there is a dedicated Orphanet team in the United Kingdom, hosted by the University of Manchester. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in the United Kingdom and in Ireland for entry into the Orphanet database.

Information, advice and support are generally provided by patient organisations dealing with particular rare diseases. Some information is provided by the NHS websites www.nsc.nhs.uk and www.ncg.nhs.uk.

Contact-a-Family is a key resource for rare diseases. It runs a help line and an online service putting patients in contact with other patients with the same disease (rare or non-rare) and support groups. Other larger patient organisations, both large and small are instrumental in providing information and support. Many run help lines providing general and technical information, provide written information and psychological support: these are funded through various means including donations, fundraising, pharmaceutical companies and grants for the government and other organisations. Many hospitals, especially in the nationally commissioned services also run help lines: these are funded using general health services funds.

Guidelines

In 2008, Nowgen, the UK-based genetics knowledge park, received funding from the UK Williams Syndrome Foundation to develop clinical guidelines and care tools for the patients of the Syndrome. The American Academy of Paediatrics' recommendations for the Syndrome will be reviewed by an expert panel. A range of other guidelines for rare and very rare diseases are posted on the NCG website (www.ncg.nhs.uk) or published in professional journals.

National rare disease events

The UK based charity 'Jeans for Genes' holds an annual awareness day to raise funds for genetic disorders¹¹⁹. The GIG has coordinated UK action for the Rare Disease Day.

Research activities and E-Rare partnership

Rare diseases research has been supported in the UK up till now although no special funding mechanism is as of yet in place. Government funding is mostly available through the research councils (i.e. the Medical Research Council) and the National Institute for Health Research (NIHR). There are several major funding charities, particularly for cancer and heart diseases, and a number of rare diseases charities fund research (such as the Muscular Dystrophy Campaign, the Cystic Fibrosis Trust, the Dystrophic Epidermolysis Association etc). Many products for rare diseases have been put through trials in the UK by major pharmaceutical companies (i.e. enzyme replacement therapies, drugs for pulmonary hypertension, etc).

The UK is not currently a partner of the E-Rare project.

Participation in European projects

The United Kingdom participates in the following European Reference Networks for rare diseases: Dyscerne (main partner), ECORN CF, EPI, EPNET, ENERCA, EUROHISTIONET, NEUROPED, Paediatric Hodgkin Lymphoma network, PAAIR and RBDD. The United Kingdom participates in the following European research projects for rare diseases: AAVEYE, ANTEPRION, ANTIMAL, BIG HEART, BIOMALPAR, BNE, CARDIOGENET, CHD PLATFORM, CHEARTED, CRUMBS IN SIGHT, CILMALVAC, CLINIGENE, CONTICANET, CSI-LTB, EMSA-SG, EUROCRAN, EMVDA, EURADRENAL, ENRAH, EPOKS, EUMITOCOMBAT, EURAMY, EUREGENE, EUROBONET, EURO CARE CF, EUROAGENTEST, EUROGLYCANET, EURO IRON1, EUROSCA, EUROTRAPS, EUCILIA, EURO-LAMINOPATHIES,

¹¹⁹ <http://www.jeansforgenes.com/about>

EUNEFRON, EUROPADNET, EUROWILSON, ENCE-PLAN, EVI-GENORET, ESDN, GEN2PHEN, GENESKIN, INHERITANCE, HUMALMAB, LEISHDNAVAX, PWS, MITOTARGET, MPCM, MALARIA AGE EXPOSURE, MITOCIRCLE, MM-TB, MOLDIAG-PACA, MPCM, MYELINET, MYORES, NEOTIM, NEUPROCF, NEUROKCNQPATHIES, NEUROPRION, NEUROSIS, PSYCHCNVS, NEWTBDRUGS, PNSEURONET, PULMOTNESION, PWS, RATSTREAM, SPASTICMODELS, RD PLATFORM, STEM-HD, TAMAHUD, TREAT-NMD, VITAL and THERAPEUSKIN, Biology of cilia formation and intraflagellar transport project, and Relationship of BBS proteins in Wnt pathways project. The United Kingdom contributes to the following European registries: EUROCAT, TREAT-NMD, AIR, EUROCARE-CF, EUHASS, EUROPAC, the European Prader-Willi database and EUROWILSON. The United Kingdom contributes to the EUROPLAN project.

Orphan drug committee and incentives¹²⁰

The promotion of the development of orphan drugs in the UK takes place at a European, and not national, level: orphan drugs obtain Marketing Authorisation through the centralised procedure at the EMA.

Orphan drug availability^{121,122}

The NHS provides all medicines almost free of charge to all patients: there is a small co-payment ('prescription charge') for out-of-hospital drugs. However the elderly, children and those on low income (and other groups) are exempt from this charge. There is no prescription charge in Scotland and Wales.

Orphan drugs obtain Marketing Authorisation through the centralised procedure at EMA. The body responsible for regulatory approval in the UK is the Medicines and Healthcare products Regulatory Agency (MHRA): accessibility to medicinal products is generally determined by the National Institute for Clinical Excellence (NICE).

Licensed drugs are paid for by the NHS in the UK. Decisions are taken by relevant funding bodies at PCT level, not nationally, in the light of available funds. The NCG funds certain orphan drugs at national level; however, it is possible for those not funded to be funded locally by PCTs. This has led to criticism that access to drugs can be a "postcode lottery" i.e. access varies widely depending on where an individual lives. Drugs used in services commissioned nationally by the NCG are available uniformly throughout England on the basis of agreed principals.

Orphan drugs, like other drugs, are distributed through hospital pharmacies and specialist centres. Home delivery is available for various products, for example enzyme replacement therapies.

Patients with rare diseases can receive unlicensed drugs; in such cases the doctor applies to the MHRA to import it on an individual named patient basis.

The publication *Social Value Judgements: Principles for the Development of NICE Guidance* issued a second edition in July 2008, updating the principles guiding National Institute for Health and Clinical Excellence (NICE¹²³) policy in the UK. The guidance mentions rare conditions in chapter 4, stating that evaluation of products for rare conditions should be the same as for any treatment. However, treatments for "ultra-orphan" disorders (defined by the NHS as conditions or diseases that occur in less than 1 in 50,000 of the population) are to be evaluated by "other mechanisms" that the Department of Health has developed. The document also states that the "rule of rescue" is to be weighed against "the needs of present and future patients of the NHS who are anonymous and who do not necessarily have people to argue their case on their behalf".

The 2008 audit produced by the Rarer Cancers Forum¹²⁴, revealed that the system of approving medicines for rare cancers in England is arbitrary, resulting in wide variations in patient access to treatment between different regions of the country. Guidelines for many rare cancers do not exist. This puts the decision in the hands of individual primary care trusts (the agencies responsible for managing healthcare funding locally in England) which often do not have access to information and must rely on an "exceptional case" decision-making process. For rare cancers, the audit found that of 5,000 patients obliged to demonstrate 'exceptionality' in the period studied, 1,300 had their requests rejected. Some 3000 patients apply each year for "exceptional funding" for high-priced treatments, often to be used off-licence, and primarily for very

¹²⁰ Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 62-66)

¹²¹ Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 62-66)

¹²² 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).

¹²³ <http://www.nice.org.uk/>

¹²⁴ <http://www.rarercancers.org.uk/index.html>

advanced cancers. The most requested products include sunitinib (Sutent), erlotinib (Tarceva), cetuximab (Erbix) and bortezomib (Velcade) – all of which have orphan designations in Europe or the USA. There is no nation-wide guidance on how to consistently reach exceptional-funding decisions, and this has resulted in an inequity throughout the land, with some primary care trusts approving all exceptional-funding applications and others systematically refusing identical requests. The report makes several recommendations to alleviate the current situation.

Specialised social services

Respite care services are available in most parts of the UK and are provided by the NHS and charitable organisations. Patient groups also organise holiday camps for children and adolescents. Reimbursement varies: all NHS services are free but charities may ask for a small co-payment in some cases. The provision of recreational programmes is patchy but it is difficult to obtain full information: schemes are usually run by individual patient organisations or by local authority social service departments. A small co-payment is usually expected. Services to integrate patients in daily life are the responsibility of local authority social services departments which are government financed.

B.1.27.2 New initiatives and incentives in 2009

National plan for rare diseases

After successfully campaigning for the UK government to adopt the Council of the European Union's Recommendation on an action in the field of rare diseases (adopted on 9 June 2009), Rare Disease UK (RDUK) is now campaigning for the adoption of a plan for rare diseases. RDUK has been meeting with government officials and key people within the National Health Services in all four home nations to highlight the need for planning for rare diseases. RDUK has also established 5 working groups comprising of expert stakeholders looking into various aspects of planning for rare diseases in the UK in order to aid the establishment of a plan.

The Government has said that it is scoping to see how the Recommendation's actions can be imbedded into the political systems across the UK. An All Party Parliamentary Group (APPG) for Rare Diseases, chaired by Anne Milton MP, has been established to act as forum in Parliament for patient groups, clinicians, officials, academics and industry to profile the needs of the rare disease community with parliamentarians.

National rare disease events

For the second Rare Diseases Day, Rare Diseases UK in collaboration with the Genetic Interest Group, hosted three events, at the Welsh Assembly, the Scottish Parliament and the House of Commons, in order to raise awareness about rare diseases, specifically amongst policy makers.

A large number of events in the field of rare diseases take place every year in the United Kingdom, organised by patient groups and leading clinicians. Amongst the events held in 2009 and announced in *OrphaNews Europe* were: the BPSU's annual conference (London, 3 March 2009), the Genomics Disorders 2009 meeting (Cambridge, 9-11 March 2009), the British Paediatric Neurology Association's Rare Disorders Symposium (Harrogate, 29 September 2009).

Hosted rare disease events

The 7th International Progressive Supranuclear Palsy Medical Workshop was held in London (7 July 2009). The Cornelia de Lange Syndrome World Conference was held in Brighton (23 July 2009). The International patient Organisation for Primary Immunodeficiencies held their First Global leaders Meeting in London (30 October – 1 November 2009). The monthly meetings of the EMA's COMP are held in London.

Sources of information on rare diseases and national help lines

In 2009 the National Genetics Reference Laboratories in the UK launched an innovative free online diagnostic technology forum destined for professionals in the field of genetic testing. Professionals internationally can share in-house assessments of diagnostic technologies ranging from diagnostic kits and sequencing platforms to analysis software. LabSight is a non-profit tool in response to a lack of reliable comparative reporting on new technologies. The forum will serve as an online resource for documentation, and will also list upcoming events and calls for collaborations. With rare disease research and diagnostics particularly vulnerable to limited budgets and resources, LabSight offers a money-saving tool helping professionals find the best technology for their diagnostic laboratories.

Orphan drug accessibility

The United Kingdom's National Institute for Health and Clinical Excellence (NICE) has launched a consultation process for a new scheme that would permit patients with rare or uncommon disorders to access innovative treatments that have not yet been subject to appraisal by NICE. The NICE "Innovation Pass" will make selected innovative medicines available on the National Health Service for a time-limited period prior to receiving a NICE appraisal. Funding will be drawn from a new ring-fenced £25 million (€27.6 million) budget. The Innovative Pass allows patients earlier access to innovative medicinal products while simultaneously facilitating the gathering of further evidence to "support a subsequent NICE appraisal". The consultation is open until 8 February 2010, seeking views from the NHS, industry and other stakeholders.

B.2 OTHER EUROPEAN COUNTRIES**B.2.1 CROATIA** **B.2.1.1 State of affairs before 2009****Definition of a rare disease**

Stakeholders in Croatia accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

There is no official strategy of plan in Croatia regarding rare diseases. In 2008, the Croatian Society for Rare Diseases¹²⁵ was established as part of Croatian Medical Association. The Society is preparing a proposal to be presented to governmental authorities (including the parliament and the Ministry of Health and Social Welfare of Republic of Croatia) for the development of a national plan for rare diseases but at this stage it is not clear how long this process will take and some significant development can be expected. There is no earmarked budget for rare diseases in the national health care budget, but special funding is available however for orphan drugs and there is a "List of Especially Expensive Drugs".

Centres of expertise

There are currently three Referral Centres for rare diseases acknowledged by the Croatian Ministry of Health and Social Welfare: the Referral Centre for Birth Defects (Children's University Hospital Zagreb, Decision UP/I-510.01/02-01/18, No 534-05-01/8-03-10), the Referral Centre for Rare Diseases and Metabolic Disorders (Department of Internal Medicine, Clinical Hospital Centre Zagreb; Decision UP/I-510-01/08-01/11, No 534-07-1-2/6-08-12), and the Referral Centre for the Metabolic Diseases in Children (Department of Paediatrics, Clinical Hospital Centre Zagreb, Decision UP –I-510-01/95-01/0005, No534-02-10-99-0003). These centres of expertise foster a multidisciplinary approach to rare disease patient care adhering to high medical standards. There are some other centres dealing with particular diseases, for instance the Referral Centre for Hemophilia.

Registries

Currently, there is no national registry for rare diseases in Croatia. However, many patients are registered through the mentioned referral centres and patient organisations (phenylketonuria, Prader-Willi syndrome, , etc.) or international on-line registries. The registry for birth defects (part of the Eurocat project) covers four regions of Croatia (17% of annual births) and this initiative should soon be extended. Croatia also contributes to the European registry EURO CARE CF.

¹²⁵ <http://www.idizajn.hr/hlz/linkovi.html>

Neonatal screening policy

Neonatal screening is centralised in Croatia and is an obligatory part of health care. Neonatal screening is provided for phenylketonuria and hypothyroidism. In addition, in 2003 national screening for hearing impairment was implemented and covers the whole of the country.

Genetic testing

Genetic testing is covered by the Croatian Institute for Health Insurance: when a certain test is not available in Croatia, a second medical opinion is needed before a sample can be sent abroad.

National alliances of patient organisations and patient representation

Since its registration as a non-profit humanitarian organisation in April 2007, the Croatian Society of Patients with Rare Diseases¹²⁶ has been working on developing relations with the stakeholders who have an impact on the lives of rare diseases patients. The Society is a coalition of patient groups and NGOs. The Society cooperates with the Ministry of Health and Social Welfare, the Croatian Institute for Health Insurance and other national health institutions, national and European-level civil society organisations, and medical professionals who work with rare disease patients. The Society works to raise general awareness concerning rare diseases and lobbies political stakeholders. Thanks to the initiatives of the CSPRD, the Croatian President declared 2008 the Year of Rare Diseases and offered assistance for future actions.

Patient organisation activities are supported by the government and other non-governmental bodies: this financial support is intended for capacity building, networking activities, dissemination of information and information sharing and events

Representatives of patient organisations are also invited to participate in the meetings of the Croatian Society for Rare Diseases when policy issues (and other issues of interest are discussed). Financial support is available for patients to attend these meetings. Most patient organisations' boards usually include a medical professional involved with patients in consultations, policy making etc.

Sources of information on rare diseases and national help lines

Since 2006, there is a dedicated Orphanet team in Croatia, currently hosted by the Zagreb University School of Medicine. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is currently no official information centre on rare diseases in Croatia apart from Orphanet. However, information on rare diseases is provided by the Croatian Society for Rare Diseases and by institutions hosting the mentioned referral centres. There are also certain public information sources on rare diseases, including help lines and websites run by patient organisations and non-governmental organisations. The site run by the Croatian Society of Patients with Rare Diseases (<http://www.rijetke-bolesti.hr/>) includes information on certain diseases and groups of diseases. The Croatian Society for Rare Diseases is developing a website which will contain comprehensive information for professionals and patients (<http://www.idizajn.hr/hlz/linkovi.html>). Help lines run by patient organisations provide general information for rare diseases diagnostic and management.

National rare disease events

Every year since 2008 the national "Rare Disease Day" serves to raise awareness on rare diseases. In Croatia, there are regular professional meetings dedicated to rare diseases organised by the Croatian Society for Human Genetics, Croatian Society for Rare Diseases, the Section for Metabolic Diseases of the Croatian Paediatric Society and different professional and patient organisations.

Research activities and E-Rare partnership

There are around 40 projects funded by the Ministry of Science, Education and Sports for the investigation of genetic diseases and various other groups of rare diseases. Some pharmaceutical companies involved in the management of rare diseases support investigations of specific rare diseases. Croatia is currently not an E-Rare partner and has not yet participated in these calls.

¹²⁶ <http://www.rijetke-bolesti.hr/>

Participation in European projects

Croatia participates in the following European Reference Network for rare diseases: TAG. Croatia participates in the following European research projects on rare diseases: EUROGLYCANET and EUROPEAN LEUKEMIA NET. Croatia contributes to the following European registries: EUROCARE CF and EUROCAT. Croatia contributes to the EUROPLAN project.

Orphan drug committee and incentives

In Croatia there is no orphan drug committee, although the Croatian Health Insurance Institute has a drug committee which controls drug use and makes any drug available if approved after individual request by selected national experts.

Orphan drug availability

In Croatia, treatment for rare diseases was originally covered using the hospitals' budget and hospitals were reluctant to begin a therapy presenting such a heavy financial burden. After a long negotiation between patients' organisations and professionals involved in the treatment of rare diseases with authorities, the Ministry of Health established in 2006 a "List of Especially Expensive Drugs" (Legislative Decree Class: 025-04/06-01/91, No: 338-01-01-06-1, Zagreb, 9. March 2006.) and the treatment of rare diseases is now covered from specially allocated funds from general health system budget. Orphan drugs are thus now approved by the Croatian Institute for Health Insurance: all available orphan drugs are reimbursed by the Croatian health insurance fund ("expensive drug fund") for rare diseases. Compassionate use is possible from the time of diagnosis to the approval for the use of the drug. The importation of relatively cheap drugs is sometimes problematic, because there is no obligation for companies to provide the drug.

Specialised social services

There are possibilities for different types of social and respite care services in some parts of the country, although not specifically for rare disease patients, but for those affected with chronic disorders in general: these services are fully reimbursed by national health care. Therapeutic recreational programmes such as summer camps are organised by patient organisations (e.g. children's camps for those affected by rare forms of solid tumours and lymphomas): this is fully reimbursed by the patient organisation. Social and/or financial support for families and patients with disabilities is regulated by a number of legislative decisions/regulations. Fostering of employment for the integration of handicapped individuals in daily life is partly financed by the government. Recently the National Strategy for Equal Possibilities for Handicapped Individuals 2007-2015 (Class 562.01./07-01/02, No 5030108-07-1, June 2007) was introduced in order to regulate the area of services aimed at the integration of patients with handicaps in daily life.

B.2.1.2 New initiatives and incentives in 2009**Definition of a rare disease**

The European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 inhabitants was officially adopted at the joint meeting of the Croatian Society for Human Genetics and Croatian Society for Rare Diseases that took place on 15 May 2009.

National plan for rare diseases and related actions

There were repeated initiatives by the Croatian Society for Rare Diseases and by the Croatian Society of Patients with Rare Diseases to establish a committee for rare diseases of the Ministry of Health and Social Welfare with the intention of developing a national plan for rare diseases.

Neonatal screening policy

Preliminary activities to extend the newborn screening program by tandem mass spectrometry are underway.

National rare disease events

The CSPRD organised events for the 2009 Rare Disease Day: members of the Society were invited to a meeting with the President of the Republic of Croatia, Stjepan Mesić, to raise awareness about the lack of available treatments and social services for those with rare diseases.

Hosted rare disease events

The 8th Balkan Meeting on Human Genetics which this year had as a topic 'Rare diseases – public policy, research, diagnosis and management' was held in Cavtat (14-17 May 2009).

Orphan drug availability

Thanks to a programme based on the Decision of the Croatian Institute for Health Insurance (latest Decision, *Narodne novine*, 46/09, 11 May 2009) the following drugs are now available for the treatment of rare diseases in Croatia: imiglucerase, laronidase, galsulfase, pegademase, activated concentrate of the prothrombin factor complex, coagulation factor VIII, oktokog alfa, recombinant factor VIII, factor IX, concentrate of factor VIII with von Willebrand factor, activated recombinant factor VII A, somatrophin, temozolomid, sunitinib, irinotecan, imatinib mesilate, bortezomib, erlotinib, interferon beta 1a, interferon beta 1 b, aglasidase alfa, aglucosidase alfa, gemcitabin, paklitaxel, rituximab, transtuzumab, irinotecan, peginterferon alfa-2a.

A tender for drugs for rare diseases was introduced in 2009. This resulted in introduction of only one drug for the treatment of a certain disease, for example for Fabry disease this is aglasidase alfa, whilst aglasidase beta was put on the hospital budget. This caused problems for patients treated with aglasidase beta, as hospital management has asked treating physicians to change the treatment to aglasidase alfa.

B.2.2 NORWAY **B.2.2.1 State of Affairs before 2009****Definition of a rare disease**

In Norway a medical disorder is considered rare when there are fewer than 100 known cases per million inhabitants. In Norway this corresponds to fewer than 500 known cases. Some medical disorders with a higher prevalence may also be considered rare if only a small number of people have been diagnosed.

National plan for rare disorders and related actions

Services for people with rare disorders and their family have been area of priority in the government's plans of actions for the disabled (1990-1993 and 1994-1997). In the following years these action plans have been implemented, followed up and developed to meet current needs.

As users of long-term, coordinated health care and/or social services, patients are entitled to an Individual Plan, which is a personal overall plan for service provisions. Particularly relevant to rare disorders patients, and not conditional on any particular diagnosis or age, this plan will contain an outline of the objectives, resources and the services the patient requires. Despite the various mechanisms in place in Norway for rare disease patients, a study reveals that more specialist knowledge is needed, along with an "integrated approach" to health care.

Centres of expertise

In Norway there are 16 different state-financed Resource Centres for people with rare and little-known disorders, providing services for more than 16'000 people with more than 300 different rare disorders which lead to disability. In order for a service to be established for a rare disease, the condition must furthermore meet the criteria of being "congenital and complex/compound, and there must be a need for multidisciplinary and cross-institutional services". These centres also facilitate the development and dissemination of expertise, and they provide forms of support unmet by standard services.

The centres are administered under the Regional Health Authorities (RHF). The grants to the resource centres are earmarked through the state budget.

There are several departments of medical genetics in Norway. Genetic counselling is free and genetic testing is available on demand for certain requests.

Registries

Each national resource centre has its own registry: they report to their respective Regional Health authority, as well as to the Directorate of Health. Public Health Registries also exist (such as the medical birth registry, cause

of death registry, patient registry and social security registry). Norway contributes to the EURADRENAL and EUROCARE European registries.

Neonatal screening policy

Neonatal screening for phenylketonuria and hypothyroidism is in place. A report from 2008 suggests an expansion of neonatal screening to cover 23 different conditions.

National alliances of patient organisations and patient representation

There is currently no alliance of rare disease patient organisations in Norway, but the Norwegian Federation of Organisations of Disabled People (FFO) is recognised as the co-ordinating body for organisations of disabled people, including many rare disease patient organisations. The government contributes financially to many patients organisations. There must be 250 members in an organisation to qualify for government co-funding. Organisations with less than 250 members may merge with others in order to qualify for government financial support.

Sources of information on rare disorders and national help lines

Since 2006 the national coordinator for Orphanet in Norway is located at the Norwegian Directorate of Health and is in charge of collecting data on rare disease related services for entry into the Orphanet database.

The National Resource Centres develop and revise professionally reviewed information about the different syndromes for which they provide services¹²⁷. This information is published on their websites and in paper copies, often available on site at the Centres from staff dedicated to informing patients and family members. Since 1999, the Norwegian Directorate of Health services a free help-line for rare disorders. The Directorate's website also offers publications concerning rare diseases available to the public. Norway is also part of Rarelink (www.rarelink.eu), a Nordic website which contains a compilation of links relating to information on rare disorders, published by organisations commissioned by the governments of Sweden, Finland, Denmark and Norway.

National rare disease events

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

Research activities and E-Rare partnership

Norway is not currently a partner of the E-Rare project.

Participation in European projects

Norway participates in the following European Reference Networks for rare diseases: Dyscerne, Paediatric Hodgkin Lymphoma Network, EPI, EPNET RBDD. Norway participates in the following European research projects: CHEARTED, ECFR, EUROCRAN, EURAPS, EURADRENAL, EUROBONET, HUE-MAN, MYELINET, NEUROXSYS, NEUROKCNQPATHIES, SIOPEN-R-NET and VITAL. Norway contributes to the following European registries: EURADRENAL, EUROCAT and EUROCARE-CF.

Orphan drug committee and incentives

No specific activity reported.

Orphan drug availability

Norway has an extensive reimbursement system for pricing and reimbursement, and orphan drugs follow these overall principals.¹²⁸

Specialised social services

Rare Disease Resource Centres, such as Frambu¹²⁹, offer residential courses for patients, families and professionals, with lectures, group discussions, consultations and joint activities: these courses are free of

¹²⁷ Accessible on these sites amongst others <http://www.sjeldnediagnoser.no/> and <http://www.frambu.no/>

¹²⁸ More general information available in the PPRI report *Pharmaceutical Pricing and Reimbursement Information: Pharma Profiles Norway (October 2008)* http://ppri.oebig.at/Downloads/Results/Norway_PPRI_2008.pdf

charge for patients and their families. Frambu also offers summer camps for four groups of around 50 children and adolescents each year, offering a chance to meet others in the same situation and build a network of friends and contacts. The Resource Centres for Rare Diseases provide these types of social services, which are meant to supplement generally available programmes.

B.2.2.2 New initiatives and incentives in 2009

National plan for rare diseases and related actions

There is ongoing political and practical activity in the field of rare disorders in Norway. The grants to the Resource Centres for Rare Diseases are earmarked through the state budget.

In 2008, the regional health authorities initiated a revision of the current cross-regional, national, and trans-national resource functions (including the resource centres for rare disorders). The aim of this process was to identify in a five year perspective which centres of excellence/ resource centres are needed and where in the specialist health services they should be placed. The report refers to the ongoing process in the EU to develop national action plans (supported by the EUROPLAN project), and suggests a complete review of the system and services directed to patients with rare disorders. This also includes the distribution of allocated resources. One of the main goals is to facilitate the expansion of the services to even more rare disorders.

National alliances of patient organisations and patient representation

The Directorate of Health started a project in 2009 to bring together smaller organisations in order to qualify for financial support which has been completed.

Sources of information on rare diseases and national help lines

The Directorate of Health continues to provide a free help line and resource centres will continue to develop and disseminate the information they produce. Rarelink continues as a Nordic cooperative rare disease information project.

Guidelines

There is a continuous evaluation of the need for best practice guidelines. Currently there are initiatives to evaluate the services to people with Velocardiofacial syndrome and Ehler Danlos syndrome.

Education and training

The Resource Centres are active in competence building on many levels, and they play a central role in education and training on rare disorders. The Directorate of Health wishes to continue a project to raise awareness about the field of rare disorders in different educational sectors and levels.

B.2.3 SWITZERLAND

B.2.3.1 State of affairs before 2009

Definition of a rare disease

The Therapeutic Products Act (TPA) adopted the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals and this applies for the simplified authorisation of orphan drugs. Stakeholders in Switzerland accept the European Orphan Drug Regulation definition of a prevalence of no more than 5 in 10'000 individuals.

¹²⁹ <http://www.frambu.no/>

National plan for rare diseases and related actions

There is currently no national concerted plan for rare diseases in Switzerland. One of the difficulties in establishing national initiatives and incentives in Switzerland is that, in addition to Federal policy, there are 26 cantons each promoting their own public health policies. Since 1919, the CDS (Swiss Conference of Cantonal Health Directors) provides political coordination, and promotes inter-cantonal cooperation, in the field of health care. Since 2006 the Swiss legislation provides for a simplified authorisation of orphan drugs. In 2007, the law on Human Genetic Testing (LHGT) became effective, thus regulating the quality of genetic analyses and aiming to avoid discrimination, mainly of patients with rare diseases, and misuse. The CDS also supports the publication of a manual for the employees of the information and counselling centres for prenatal testing and coordinates the offer of highly specialised medicine in Switzerland, including rare disease patients. The only specific project for rare diseases supported by the CDS is Orphanet Switzerland.

Centres of expertise

Several specialised care centres have been established as centres of reference by reputation, usually in University Hospitals.

Registries

Switzerland contributes to the following European registries: AIR, CAPS, REAT-NMD, EURO CARE-CF and EUROCAT. Switzerland participates in the following European rare disease research projects: CSI-LTB and NM4TB.

Neonatal screening policy

A newborn screening programme covering all of Switzerland is in place and includes screening for phenylketonuria, congenital hypothyroidism, galactosaemia, congenital adrenal hypoplasia, biotinidase deficiency, and medium-chain acyl-CoA dehydrogenase (MCAD) deficiency.

Genetic testing

More than 60 public and private laboratories provide genetic testing, although not all tests are reimbursed although efforts are being made to increase the number of tests eligible for reimbursement. Genetic counselling is usually provided by doctors specialised in medical genetics or by referring doctors. The medical genetics specialisation exists for laboratory directors (FAMH) and medical doctors.

National alliances of patient organisations

Before 2009, the only body that represented patients with rare diseases was Telethon Switzerland.

Sources of information on rare diseases and national help lines

Since 2001 there is a dedicated Orphanet team in Switzerland, currently hosted by the Medical Genetics Department of the University Medical Centre of Geneva. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is no help line available for rare diseases. The CDS supports the establishment of cantonal information and counselling centres for prenatal testing and the LHGT requires non directive genetic counselling before and after genetic testing. However, the existence of four national languages complicates the organisation of collective national projects. The only funds specifically earmarked for rare disease and orphan drug research are the funds collected via the Swiss Telethon. Orphanet Switzerland is currently the only rare disease project supported financially by the CDS.

National rare disease events

Fund raising events are organised by Telethon Switzerland.

Hosted rare disease events

No specific activity reported.

Participation in European projects

Switzerland participates in the following European Reference Networks for rare diseases: Dyscerne, ENERCA, EPI, EPNET, PAAIR and RBDD. Switzerland participates in the following European research projects for rare diseases: AAVEYE, ANTIMAL, AUTOROME, BIOMALPAR, CLINIGENE, CSI-LTB, CSI-LTB, EMVDA, EURADRENAL,

EURO-LAMINOPATHIES, EUGINDAT, EURAPS, EUREGENE, EUROBONET, EUROAGENTEST, EUROGLYCANET, EUROPEAN LEUKEMIA NET, EVI-GENORET, GENESKIN, GEN2PHEN, HDLOMICS, HUMALAB, IMMUNOPRION, LEISHMED, LYMPHANGIOGENOMICS, MYELINET, MILD-TB, MPCM, MYORES, NEUROPRION, NANOTRYP, NOVSEC-TB, NM4TB, PEMPHIGUS, PULMOTENSION, TRYPOBASE, THERAPEUSKIN, and SIOPEN-R-NET. Switzerland contributes to the following European registries: AIR, TREAT-NMD, EUROCARE-CF and EUROCAT.

Research activities and E-Rare partnership

Although there is no specific national budget for rare disease research, the Telethon Suisse raises funds specifically for rare diseases, and research into rare diseases. Moreover, many projects on rare diseases are supported by the Swiss National Science Foundation and a few public foundations (i.e. the Gebert R uf Foundation). Orphanet Switzerland is the only specific project for rare diseases supported by the Swiss Conference of the Cantonal Ministers of Public Health. Switzerland is not currently a member of the E-Rare project.

Orphan drug committee and incentives

Companies acquiring orphan drug designation for their products are allowed tax exemption for certain administrative taxes but are not however allowed market exclusivity.

Orphan drug availability

The Swiss Orphan Drug Regulation was introduced in 2006: this regulation stipulates that orphan drug status applies to products treating diseases affecting no more than 1 in 2000 persons. The availability of orphan drugs has been improved since 2006 thanks to the simplified authorisation procedures and the recognition of the orphan drug status for any drug for which this status has been granted in a country with a comparable drugs authority.

Specialised social services

No specific activity reported.

B.2.3.2 New initiatives and incentives in 2009

Neonatal screening policy

The implementation of neonatal screening for cystic fibrosis has been initiated by the Swiss Cystic Fibrosis Task Force.

National alliances of patient organisations

The first steps have been made to create a national alliance of rare disease patient organisations in Switzerland. In late March 2009, representatives from some 38 German and French-speaking patient organisations met to create a plan for establishing a national patient alliance for rare diseases. Organised by Orphanet Switzerland in tandem with the patient group Enfance et Maladies Orphelines (AEMO), participants considered the structure and experiences of the national rare disease alliances in Germany and France. While Switzerland recognises human genetics as a specialised branch of medicine, and care for rare disorders is available in five university hospitals, the country has no designated specialised centres for rare diseases and its insurance policy does not cover many costs linked to rare disease care, such as travel, technical equipment, and care obtained outside of the country. There is no help line available for rare disorders. Funds specifically earmarked for rare disease and orphan drug research are the funds collected via the Swiss Telethon and grants from the Swiss National Science Foundation as well as from the Gebert R uf Foundation which has specific calls for Rare Diseases. With a system of governance diffused over 26 independent cantons, each responsible for its own health, welfare, law, and education, and four official languages, organising a centralised project such as a patient alliance in Switzerland is not without its challenges. Despite this, participants recognised the need for a united front in order to obtain resources for rare diseases, and voted virtually unanimously in favour of creating a national alliance. The first topics the alliance will address are national level health issues such as health insurance, genetic testing, and orphan medicinal products. A working group was formed to work on a charter, by-laws, and a strategy for the alliance.

The first meeting of the working group for the Swiss Alliance of Rare Diseases was organised by Orphanet Switzerland and AEMO in July 2009. The needs and the objectives of such an Alliance were discussed.

Certain tasks were planned in order to officially create the Alliance (named ProRaris) in February 2010 on the 3rd Rare Disease Day.

National rare disease events

The first Rare Diseases Information Day in Switzerland was held on 17 November 2009 at the University Hospital of Geneva and was organised by Orphanet Switzerland. The programme covered a wide range of topics, from an introduction to the field of rare diseases and a presentation of the Orphanet database to the topics of access to diagnosis, access to treatment, centres of expertise, registries and the creation of national alliance for rare disease patient organisations in Switzerland.

Hosted rare disease events

The 14th International World Muscle Conference was held in Geneva (9-12 September 2009).

B.2.4 TURKEY

B.2.4.1 State of affairs before 2009

Definition of a rare disease

Stakeholders in Turkey accept the European Orphan Drug Regulation definition of no more than 5 in 10'000 individuals, although there is no official definition. The Ministry of Health accepts pricing of human medicinal products to be considered under the 'orphan' approach when such a product is indicated for the treatment of diseases for which the aetiology is not clearly defined and those which affect no more than 1 in 100'000 individuals¹³⁰.

National plan for rare diseases and related actions

There is currently no national plan for rare diseases in Turkey: rare diseases are currently funded within the general health system budget¹³¹. The MOH has recently started collaboration with Orphanet-Turkey in specific projects for the establishment of a National Plan for Rare Diseases. The recognition of a national plan is mandatory for assigning priority actions for rare diseases. EU regulations 141/2000 and 847/200 have not yet been adopted in Turkey. Under the "National Health Transformation Programme" the Ministry of Health has suggested developments in medicinal product use, medical and social care, surveillance and other relevant actions¹³².

Centres of expertise

Though no centres of expertise for rare diseases currently exist, Turkey is planning to establish national networks for the prevention, surveillance, diagnosis and treatment of rare diseases. Projects to establish national centres of reference for rare diseases are expected to start by 2011. These centres will be part of the overall planning of healthcare in the country. The Ministry of Health and the different regional healthcare authorities will have to coordinate their approach and harmonise regional network activities.

¹³⁰ Notification regarding the Pricing of Medicinal Products for Human Use

(<http://www.iegm.gov.tr/Default.aspx?sayfa=regulations&lang=en&thelawtype=14&thelawId=225>)

¹³¹ Notification regarding the Pricing of Medicinal Products for Human Use

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¹³² Turkey Health Transformation Program

(<http://www.saglik.gov.tr/EN/BelgeGoster.aspx?17A16AE30572D313AAF6AA849816B2EF1DACD7356F6C2568>)

<http://www.orpha.net/actor/EuropaNews/2009/doc/TurkHealthPolicy.pdf>

Registries

In order to identify the rare diseases currently prevalent in Turkey, there is a significant need to complete a comprehensive epidemiological survey at national level: this is currently being developed by stakeholders. Turkey participates in the European registries TREAT-NMD and EURO CARE CF.

Neonatal screening policy

No specific activity reported.

National alliances of patient organisations and patient representations

There is currently no national alliance of rare disease patient organisations in Turkey. Some private foundations (such as the Foundation for Metabolic Disorders – METVAK) are active in counselling, creating public awareness and networking for patients and families.

Sources of information on rare diseases and national help lines

There is no official, rare disease specific information centre on rare diseases in Turkey other than Orphanet. Since 2006 there is a dedicated Orphanet team for Turkey currently hosted by the Istanbul University Experimental Medical Research Institute Department of Genetics. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database.

There is currently no official help line for rare diseases in Turkey.

National rare disease events

Some rare diseases have an annual designated day (e.g. phenylketonuria day) to raise awareness of the diseases.

Research activities and E-Rare partnership

TUBITAK (The Scientific and Technological Research Council of Turkey) supports past research on rare diseases in Turkey. Turkey, represented by TUBITAK, is also currently a member of the E-Rare project and has participated in the first two Joint Transnational Calls. In the 1st Joint Transnational Call, Turkey was represented in 2 of the 13 consortia/projects selected for funding.

Participation in European projects

Turkey participates in the following European Reference Networks for rare diseases: Dyscerne, TAG and RBDD. Turkey participates in the following European research projects on rare diseases: CRANIRARE, ELA2-CN, EMINA, EURO-CGD, NEUTRONET and PodoNet. Turkey contributes to the following European registries: TREAT-NMD and EURO CARE CF. Turkey contributes to the EUROPLAN project.

Orphan drug committee and incentives

In Turkey, licencing applications for all human medicinal products are submitted, by accredited licence holders, to the Ministry of Health Directorate General of Pharmaceuticals and Pharmacy, in line with the “Regulation on Licensing for Medicinal Products for Human Use”.

Data exclusivity is applied in terms to original products for which no generic registration application has been submitted in Turkey since 1 January 2005 among the original products which have been registered for the first time in one of the countries within the Customs Union Area after 1 January 2001, and original products which shall be registered for the first time in one of the countries within the Customs Union Area after 1 January 2005. The data exclusivity period consists of 6 years to commence as of the first registration date of these products in the Customs Union Area. With regard to those products which benefit from patent protection in Turkey, the implementation of the data exclusivity period of 6 years is limited to this patent period.¹³³

Orphan drug availability

At present, the Turkish Ministry of Health (MOH) has not yet developed a national policy with reference to “rare diseases” and “orphan drugs”, as commonly defined inside the European Union (EU). Therefore, patients suffering from known rare diseases in Turkey access treatment with nationally licenced or non-licenced human medicinal products that have been granted marketing authorisation by the EMA under “orphan designation”

¹³³ Regulation on Licensing of Medicinal Products for Human Use
(<http://www.iegm.gov.tr/Default.aspx?sayfa=regulations&lang=en&thelawtype=14&thelawId=226>)

and/or indicated for the treatment of specific rare diseases. Nearly 20 of the orphan medicinal products authorised in the EU are also licenced for the treatment of patients diagnosed with rare diseases in Turkey. Other EU orphan medicinal products which are not licenced in Turkey can be provided for patient access in Turkey through individual prescription approvals via pre-licencing medicinal product approval procedures.

Specialised social services

Some therapeutic recreational programmes and services aimed at the integration of patients in daily life are provided by patient organisations and private foundations with the aid of private donations.

B.2.4.2 New initiatives and incentives in 2009

National rare disease events

The 4th National Dysmorphology Days were held in Istanbul (24-25 April 2009).

Hosted rare disease events

In July 2009, a workshop was held in Ankara, Turkey, for the Technical Assistance and Information Exchange Instrument (TAIEX) of the Institution Building unit of Directorate-General Enlargement of the European Commission. Its aim is to provide to the new Member States, acceding countries, candidate countries, and the administrations of the Western Balkans, short-term technical assistance in line with the overall policy objectives of the European Commission, and in the field of approximation, application and enforcement of EU legislation. Assistance is also provided to those countries included in the EU's European Neighbourhood Policy, as well as Russia. The workshop had two main objectives. The first sought to gain knowledge on ways to establish an Internet website for Orphanet Turkey in the country's national language, through which all users - patients and the various professionals - are able to access information on rare diseases. The second objective was to gather an advisory board on a regulatory platform, which will collaborate with Orphanet Turkey on issues regarding data provided to Orphanet within the country, and form a consortium of experts within the Turkish Ministry of Health, who shall follow-up with data collection and maintain quality control of current/emerging rare diseases within the country. The best way to position Orphanet in the country was discussed extensively. Consensus centred on an official endorsement of the activity by the ministry of health and a formal contract between the Orphanet team in Istanbul and the ministry, an approach very similar to the arrangement in France, where Orphanet was first established twelve years ago. The participants expressed a strong wish for an action plan in the field of rare diseases and orphan drugs. A national workshop to continue discussions was planned for October 2009.

The European Society for Phenylketonuria held their annual conference in Antalya (30 October – 1 November 2009).

Research activities and E-Rare partnership

In the 2nd Joint Transnational Call E-Rare, Turkey was represented in 4 of the 16 consortia/projects selected for funding, with a total of around €300,000 funding.

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ANNEX 3 : LIST OF EUROPEAN RESEARCH PROJECTS

The following annex is a list of European research projects on rare diseases, previously or currently funded by the European Commission (Directorate General for Health, Directorate General for Research – Framework Programmes 5, 6 and 7 for research, technological development and demonstration activities) and the ERA-Net for research on rare diseases (E-Rare).

A recapitulative table gives the total number of projects by country and by funding programme with indication of the number of projects for which the country is a coordinating and/or participating partner.

Projects are presented by funding programme in alphabetical order by project name. The coordinating country is given, as is a list of the countries participating in the project. The diseases concerned by the project are also listed.

This information was collected from the following websites: Directorate General Health and Consumersⁱ, E-Rareⁱⁱ, CORDISⁱⁱⁱ (FP5, FP6, FP7 projects).

ⁱ http://ec.europa.eu/health/rare_diseases/european_reference_networks/erf/index_en.htm

ⁱⁱ <http://www.e-rare.eu/>

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

Number of projects by country

Countries	DG SANCO		ERARE		FP5		FP6		FP7	
	Participating	Coordination	Participating	Coordination	Participating	Coordination	Participating	Coordination	Participating	Coordination
AT	4	1	3	0	3	2	15	3	4	1
BE	8	0	0	0	3	0	28	4	7	2
BG	1	0	0	0	0	0	1	0	0	0
CY	3	0	0	0	0	0	2	0	1	0
CZ	7	0	0	0	1	0	13	0	3	0
DE	9	2	23	5	3	1	54	14	26	7
DK	6	0	0	0	3	0	21	6	3	0
EE	1	0	0	0	0	0	2	0	1	0
ES	9	1	12	1	2	0	26	3	8	1
FI	3	0	0	0	1	0	16	1	1	0
FR	9	4	24	9	4	0	44	13	22	9
GB	10	1	1	0	3	1	48	5	22	4
GR	5	0	2	1	0	0	10	0	1	0
HU	3	0	0	0	1	0	10	1	1	0
IE	4	0	0	0	0	0	11	0	2	0
IT	9	1	19	6	3	0	44	8	20	5
LT	2	0	0	0	0	0	1	0	0	0
LV	2	0	0	0	0	0	0	0	0	0
NL	7	1	9	1	0	0	34	6	15	2
PL	8	0	0	0	1	0	7	0	3	0
PT	5	0	1	0	2	0	10	0	2	0
RO	4	0	0	0	0	0	1	0	0	0
SE	7	0	0	0	3	1	29	3	12	1
SI	4	0	0	0	1	0	3	0	1	0
SK	1	0	0	0	0	0	2	0	0	0
CH	6	0	0	0	2	0	29	2	9	0
HR	0	0	0	0	0	0	2	0	0	0
IL	2	0	3	0	2	0	14	0	5	0
NO	6	0	0	0	2	0	8	0	4	1
RS	2	0	0	0	0	0	2	0	2	0
TR	3	0	5	0	0	0	4	0	1	0
others	18	0	5	0	2	0	44	0	23	1
TOTAL	168	11	107	23	42	5	535	69	199	34

DG Health and Consumers

Network acronym / title	Participating countries	Coordinating country	Concerned diseases
Dyscerne: a European network of centres of expertise for dysmorphology	BE, BG, CH, CY, CZ, DE, DK, ES, FI, FR, GB, GR, IE, IL, IT, LV, MK, NL, NO, PL, PT, RO, SE, SI, SK, TR	GB	Rare developmental defect during embryogenesis
ECORN-CF - European centres of reference network for cystic fibrosis	BE, CZ, DE, GB, GR, LT, NL, PL, RO, SE	DE	Cystic fibrosis
ENERCA: European network for rare and congenital anaemias	BE, CH, CY, DE, ES, FR, GB, GR, IT, NL, PL, PT, RO, RS, SE	ES	Rare constitutional anemia
EPI: European Porphyrin Initiative	BE, CH, CZ, DE, DK, FI, ES, FR, GB, HU, IE, IL, IT, NL, NO, PL, SE	FR	Porphyria
EPNET: European network on centre of reference on porphyria	BE, CH, CZ, DE, FI, ES, FR, GB, HU, IE, IT, NL, NO, PL, SE	FR	Porphyria
EURO HISTIO NET: study group on histiocytosis	AT, ES, FR, GB, IT	FR	Langerhans cell histiocytosis
European network of paediatric Hodgkin's lymphoma - European-wide organisation of quality controlled treatment	AT, CZ, DE, DK, ES, FR, GB, IE, NO, PL, SE	DE	Hodgkin lymphoma
NEUROPED: European network of reference for rare paediatric neurological diseases	AT, BE, CZ, DE, DK, ES, FR, GB, IT, NL, NO, PT, SI	AT	Alternating hemiplegia of childhood Childhood-onset epilepsy syndrome Congenital hypothalamic hamartoma syndrome Infantile epilepsy syndrome Narcolepsy without cataplexy Narcolepsy-cataplexy Neonatal epilepsy syndrome Sturge-Weber syndrome
PAAIR: Patient's Association and Alpha-1 International Registry network	AT, BE, CH, CZ, DE, DK, EE, ES, GB, IT, LT, LV, NL, PL, SE	NL	Alpha-1 antitrypsin deficiency
RBDD: Rare Bleeding Disorders Database network	BE, BR, CH, CN, CO, DE, DK, EG, ES, FR, GB, GR, HU, IN, IQ, IR, IT, KW, NO, NZ, OM, PA, PE, PL, PT, RU, RS, SI, TH, TR, US, VE, VN	IT	Combined deficiency of factor V and factor VIII Congenital factor II deficiency Congenital factor V deficiency Congenital factor VII deficiency Congenital factor X deficiency Congenital factor XI deficiency Congenital factor XIII deficiency Congenital fibrinogen deficiency Congenital vitamin K-dependent coagulation factors deficiency
TAG: TogetherAgainstGenodermatoses - improving health care and social support for patients and family affected by severe genodermatoses	CY, FR, GR, IT, PT, RO, SI, TR	FR	Familial palmoplantar keratoderma Genetic ichthyosis Hereditary epidermolysis bullosa Neurofibromatosis type 1 Xeroderma pigmentosum

E-RARE

Network acronym / title	Participating countries	Coordinating country	Concerned diseases
CAV-4-MPS: understanding and treating neurodegeneration caused by mucopolysaccharidoses	DE, ES, FR	ES	Mucopolysaccharidosis
CRANIRARE: an integrated clinical and scientific approach for craniofacial malformations	DE, FR, TK	DE	Cranial malformation
CUREFXS: targeting Rho-signalling, a new therapeutic avenue in fragile-X syndrome	DE, ES, FR, IT, NL	ES	Fragile X syndrome
ELA2-CN: congenital neutropenia with ELA-2 mutations (ELA2-CN), identification of (epi)genetic co-factors and molecular pathways underlying clinical heterogeneity	DE, IL, NL, TR	DE	Autosomal dominant severe congenital neutropenia Neutropenia cyclic
EMINA: European multidisciplinary initiative on neuroacanthocytosis	AT, DE, FR, NL, TR	DE	Neuroacanthocytosis
EPINOSTICS: "autoimmune liver diseases" epitope peptide mapping - The entry to novel and innovative diagnostic and therapeutic applications	DE, ES, FR, IS, IT, GR, UK	DE	Chronic autoimmune hepatitis
ERMION: European research project on Medelian inherited optic neuropathy	DE, FR, IT	FR	Genetic optic neuropathy
EUPAPNET: European pulmonary alveolar proteinosis network: molecular determinants of causes, variability and outcome	DE, IT, NL	IT	Pulmonary alveolar proteinosis
EUROBNFS: Benign Familial Neonatal Seizures (BNFS) as a disease model for human idiopathic epilepsies: expansion of genotype-phenotype correlations and insights into novel disease mechanisms	DE, ES, FR, IT	IT	Benign familial neonatal seizures
EURO-CGD: genetics and pathogenesis of chronic granulomatous disease and development of new gene transfer therapeutic approaches		IT	Chronic granulomatous disease
EUROGEBETA: European network on genetics, pathophysiology and translational research into rare pancreatic beta-cell insufficiency diseases	ES, FR, IL, IT	FR	Rare pancreatic beta cell insufficiency diseases
EURORETT: European network on Rett syndrome	DE, ES, FR, IS, IT	FR	Rett syndrome
EUROSPA: European & Mediterranean network on spastic paraplegias	DE, FR, IS, IT	FR	Familial spastic paraplegia
GETHERTHAL: improvements of vector technology and safety for the gene therapy of thalassemia	DE, FR, GR	GR	Alpha-thalassemia Beta-thalassemia

HAE III: genetics, pathophysiology, and therapy of hereditary angioedema type III	DE, FR, IT	DE	Hereditary angioedema type 3
HMA-IRON: towards improved diagnosis and treatment of rare inherited microcytic hypochromic anemias related to iron metabolism	DE, ES, FR, IT	FR	Sideroblastic anemia Microcytic anemia with liver iron overload
HSCR: International Hirschsprung disease consortium	ES, FR, IT, HK, NL, US	FR	Hirschsprung disease
KINDLERNET: International Kindler syndrome network	DE, FR, IT	DE	Kindler syndrome
MLC-TEAM: megalencephalic leukoencephalopathy with subcortical cysts: from molecular basis to search for therapy	ES, NL	ES	Megalencephaly - cystic leukodystrophy
MTMPATHIES: myotubularinopathies: common molecular mechanism and tissue specificity	FR, IT	FR	X-linked centronuclear myopathy
NEMMYOP: functional characterisation of the nemaline myopathy in a murine model with the nebulin mutation: moving from basic understanding towards therapeutic interventions	DE, FR, NL	FR	Nemaline myopathy
NEUTRONET: inherited inhibition of inborn immunity: an integrated molecular genetic approach to discover novel human gene defects	AT, DE, FR, TR	DE	Rare genetic immune disease
NSEURONET: European network on Noonan syndrome and related disorders	DE, FR, IT, NL	IT	Noonan syndrome and Noonan-related syndrome
OSTEOPETR: new genes and therapeutic approaches to osteopetrosis	DE, FR, IT	IT	Osteopetrosis
PODONET: consortium for clinical, genetic and experimental research into hereditary diseases of the podocyte	DE, FR, IT, TK	DE	Familial idiopathic steroid-resistant nephrotic syndrome Sporadic idiopathic steroid-resistant nephrotic syndrome
REVERTANTEB: identification of revertant mosaicism in epidermolysis bullosa and subsequently using the revertant keratinocytes in a pre-clinical mouse model suitable to test revertant cell therapy	DE, ES, NL	NL	Hereditary epidermolysis bullosa
RISCA : Prospective study of individuals at risk for spinocerebellar ataxia type 1, type 2, type 3 and type 6 (SCA1, SC2, SCA3, SCA6)	DE, ES, FR, IT	DE	spinocerebellar ataxia type 1 spinocerebellar ataxia type 2 spinocerebellar ataxia type 3 spinocerebellar ataxia type 6
RHORCOD: comprehensive analysis of rod-cone photoreceptor degeneration associated with Rhodopsin gene mutations	AT, DE, FR, IL, IT, PT	FR	Congenital stationary night blindness Retinitis pigmentosa
WHIMPATH: understanding the WHIM syndrome and search for new therapies: molecular analysis of CXCR4 in leukocyte trafficking and activation	ES, FR, IT	IT	WHIM syndrome

DG Research FP5

Network acronym / title	Participating countries	Coordinating country	Concerned diseases
EMSA-SG: the European Multiple System Atrophy study group	AT, CN, DE, DK, ES, FR, GB, IL, IT, PT, SE, SI, US	AT	Multiple system atrophy
ESDN: European Skeletal Dysplasia Network	BE, CH, DE, FI, FR, GB	GB	Rare bone disease
EUROCRAN: European collaboration on craniofacial anomalies - Eurocleft clinical network	DK, GB, NO, SE	SE	Facial cleft
SIOPEN-R-NET: International society of paediatric oncology European neuroblastoma research network	AT, BE, CH, CZ, DK, ES, FR, HU, IL, IT, NO, PL, PT, SE	AT	Neuroblastoma
WHIPPLE'S DISEASE: European network on Tropheryma whipplei infection	AT, BE, DE, FR, IT	DE	Whipple disease

DG Research FP6

Network acronym / title	Participating countries	Coordinating country	Concerned diseases
ANTEPRION: development of a pre-clinical blood test for prion diseases	DE, ES, FR, GB, IL, NL, SE, SK	NL	Transmissible spongiform encephalopathies
ANTIMAL: development of new drugs for the treatment of malaria	BE, BF, CH, DE, ES, FR, GA, GB, IT, KE, NL, UA, ZA, ZW	GB	Malaria
AUTOROME: from immune responses in rare autoimmune diseases to novel therapeutic intervention strategies-a personalized medicine approach	CH, DE, FR, IE, IL, NL	DE	Stiff-man syndrome Systemic autoimmune disease Vasculitis
BIOMALPAR: biology and pathology of the malaria parasite	CH, CM, DE, FR, GB, GR, IN, IT, ML, NG, NL, SD, SE, UG	FR	Malaria
BNE: BrainNet Europe II: European brain tissue bank - Network for clinical neuroscience and basic research	AT, DE, ES, FI, FR, GB, GR, HU, IT, NL, SE	DE	Rare neurologic disease
CILMALVAC: The tetrahymena system as an innovative approach to malaria antigene expression	DE, DK, GB	DE	Malaria
CLINIGENE: European network for the advancement of clinical gene transfer and therapy	AT, CH, CZ, DE, ES, FI, FR, GB, IL, IT, PT, SE, US	FR	-
CONTICANET: Connective Tissue Cancers Network	BE, DE, ES, FR, GB, IE, IT, NL, SI	FR	Soft tissue sarcomas
CSI-LTB: the role of chromosome stability in persistence, latency and reactivation of mycobacterium tuberculosis	CH, GB, IN, IT	CH	Tuberculosis
EMVDA: the European malaria vaccine development association	CH, DE, DK, GB, NL, SE, TZ	DK	Malaria
ENRAH: European Network for Research on Alternating Hemiplegia in Childhood	AT, BE, CZ, DE, ES, FR, GB, IT, NL	AT	Alternating hemiplegia of childhood
EUGINDAT: European genomics initiative on disorders of plasma membrane amino acid transporters	CH, DE, ES, FI, IL, IT	ES	Amino acid transport disease
			Alpers syndrome Kearns-Sayre syndrome

EUMITOCOMBAT: rational treatment strategies combating mitochondrial oxidative phosphorylation (OXPHOS) disorders	CZ, DE, ES, FI, FR, GB, IT, NL, SE	NL	Leber hereditary optic neuropathy (LHON) Leigh syndrome MELAS syndrome MERRF syndrome Myoneurogastrointestinal encephalopathy syndrome (MNGIE) NARP/MILS syndrome Pearson syndrome Progressive external ophthalmoplegia (CPEO)
EURAMY: systemic amyloidoses in Europe	BE, DE, FR, GB, IT, NL, PT, SE	SE	Amyloidosis
EURAPS: autoimmune polyendocrine syndrome type I - a rare disorder of childhood as a model for autoimmunity	AU, CH, CN, DE, EE, FI, GB, IE, IT, NO, SE	SE	Autoimmune polyendocrinopathy type 1
EUREGENE: European renal genome project	BE, CH, DE, DK, FI, FR, GB, IT	DE	Rare renal disease
EURHAVAC: European network for harmonisation of malaria vaccine development	-	DK	Malaria
EUROBONET: European bone tumors network	BE, CH, DE, DK, ES, FI, GB, HU, IT, NL, NO, SE	NL	Rare bone tumor
EUROCARE CF: European coordination action for research in cystic fibrosis	BE, CZ, DE, FR, GB, IL, IT, NL, PL, PT, SE	GB	Cystic fibrosis
EUROGENTEST: Network for test development, harmonization, validation and standardization	BE, CH, CZ, DE, EC, ES, FI, FR, GB, HU, IE, IT, ME, NL, PL, PT, RS, SE	BE	-
EUROGLYCANET: European network on Congenital Disorders of Glycosylation	BE, BG, CH, CZ, DE, DK, ES, FR, GB, GR, HR, IL, IT, NL, PL, PT	BE	CDG syndrome
EURO-IRON1: abnormal iron distribution in humans	AT, DE, FR, GB, IL, IT	FR	rare hemochromatosis
EUROPEAN LEUKEMIA NET: Strengthen and develop scientific and technological excellence in research and therapy of leukemia	AT, BE, BY, CH, CY, CZ, DE, DK, ES, FI, FR, GB, GR, HR, HU, IE, IL, IT, LT, ME, NL, NO, PL, RO, RS, RU, SE, TR	DE	Acute lymphoblastic leukemia Acute myeloid leukemia Chronic B-cell lymphocytic leukemia Chronic myeloproliferative disease Myelodysplastic syndromes
EUROSCA: European integrated project on spinocerebellar ataxias	BE, DE, ES, FR, GB, HU, IT, NL, PL	DE	Autosomal dominant cerebellar ataxia
EUROWILSON: European network on Wilson disease	AT, DE, FR, GB, HU, IT, NL, PL	GB	Wilson disease
EVI-GENORET: functional genomics of the retina in health and disease	BE, CH, DE, ES, FR, GB, GR, IE, IT, NL, PT, SE	FR	Genetic retinal dystrophy
FASTEST-TB: Development and clinical evaluation of fast tests for tuberculosis diagnosis	BE, DE, IN, MX, NG, TR	DE	Tuberculosis
GENESKIN: European network on rare genetic skin diseases	AT, BE, CH, DE, ES, FR, GB, HU, IE, IT, NL, SE	IT	genetic skin diseases
HDLOMICS: functional genomics of inborn errors and therapeutic interventions in high density lipoprotein (HDL) metabolism	CH, DE, DK, GR, NL, SE	DE	HDL metabolism disorder
HUE-MAN: Towards the development of an effective enzyme replacement therapy for human alpha-mannosidosis	BE, CZ, DE, DK, FR, NO	DE	Alpha-mannosidosis
HUMALMAB: human monoclonal antibodies as tools for malaria research and therapy	CH, DK, GB, TZ	DK	Malaria
IMMUNOPRION: strains, species and immunology in prion diseases	BE, CH, FR, GB, NL	FR	Transmissible spongiform encephalopathies
LEISHMED: Monitoring risk factors of spreading of Leishmaniasis around the Mediterranean Basin	BE, CH, CY, CZ, DE, DK, ES, FR, GB, GR, IL, IT, JO, MA, PT, TN, TR	BE	Leishmaniasis
LYMPHANGIOGENOMICS: genome-wide discovery and functional analysis of novel genes in lymphangiogenesis	AT, BE, CH, DE, FI, FR, SE	FI	Lymphedema
MALARIA AGE EXPOSURE: age of exposure and immunity to malaria in infants	AU, ES, GB, IN, IT	ES	Malaria
MANASP: Development of novel management strategies for invasive aspergillosis	DE, FR, IE, IT, SE	DE	Allergic bronchopulmonary aspergillosis Aspergillosis
MILD-TB: immunogenicity of Mycobacterium tuberculosis lipids in the non-replicating status of latency	CH, CI, FR, IT	IT	Tuberculosis

MITOCIRCLE: mitochondrial diseases: from bedside to genome to bedside	FR, GB, IT, NL	NL	Mitochondrial disease
MMR-RELATED CANCER: prevention, diagnosis and molecular characterisation of mismatch repair defect-related hereditary cancers of the digestive system	DK, FI, NL, PT	NL	Rare digestive tumor
MM-TB: molecular markers of M. tuberculosis early interactions with host phagocytes	FR, GB, IT	IT	Tuberculosis
MOLDIAG-PACA: Novel molecular diagnostic tools for the prevention and diagnosis of pancreatic cancer	DE, EE, ES, GB, IE, IT, SE	DE	Familial pancreatic carcinoma
MPCM: pathogenic role of micro-vesiculation in cerebral malaria	AU, CA, CH, FR, GB, MW	FR	Malaria
MYASTAID: European network on myasthenia	BE, DE, DK, FR, GR, IL, NL	FR	Myasthenia gravis
MYORES: European Muscle Development Network	AU, CH, CZ, DE, ES, FR, GB, IL, IT, US	FR	Neuromuscular disease
NEOTIM: innate and adaptive immunity in clinical and experimental mycobacterial infection in neonates and infants	BE, DE, FR, GB, IT, SE	SE	Tuberculosis
NEUPROCF: new diagnostic and prognostic biomarkers in cystic fibrosis	DE, FR, GB, PL, PT, SE	FR	Cystic fibrosis
NEUROKCNQPATHIES: cell biology of rare monogenic neurological KCNQ disorders	DE, DK, ES, GB, IT, NO	ES	Benign familial neonatal seizures Episodic ataxia type 1 Familial paroxysmal ataxia Nonsyndromic genetic deafness
NEUROPRION: European network dedicated to research on prion diseases	AT, BE, CH, DE, DK, ES, FR, FI, GB, GR, IE, IL, IT, NL, NO, SE	FR	Transmissible spongiform encephalopathies
NEWTBDRUGS: New Drugs for Persistent Tuberculosis	DE, GB, SE	DE	Tuberculosis
NM4TB: new medicines for tuberculosis	CH, DE, DK, FR, GB, HU, IT, RU, SE, SK, ZA	CH	Tuberculosis
PEROXISOMES: Integrated project to decipher the biological function of peroxisomes in health and disease	AT, BE, DE, FI, FR, IT, NL, PT, SE	AT	Peroxisomal disease
PNSEURONET: European network on Paraneoplastic Neurological Syndromes	AT, CZ, DE, ES, FR, GB, IT, NL, NO, SI	IT	Paraneoplastic neurologic syndromes
PRIBOMAL: pre-clinical studies towards an affordable, safe and efficacious two component paediatric malaria vaccine	DE, DK, NL, SE	NL	Malaria
PROTHETS: prognosis and therapeutic targets in the "Ewing" family of tumors	AT, DE, ES, FI, FR, IT, RU	IT	Ewing sarcoma Neuroepithelioma Medulloblastoma
PULMOTENSION: Functional genomics and therapy of lung vascular remodelling	AT, BE, CH, DE, DK, FI, FR, GB, GR, IE, IT	DE	Rare pulmonary hypertension
PWS: Prader-Willi Syndrome: a model linking gene expression, obesity and mental health	AT, BE, DE, FR, GB, IL, NL, SE	GB	Prader-Willi syndrome
RATSTREAM: European project on the characterisation of transgenic rat models for neurodegenerative and psychiatric diseases: Automated home cage analyses, live imaging and treatment	BE, CH, DE, FR, NL	DE	Genetic Parkinson disease Huntington disease Spinocerebellar ataxia type 17
SARS/FLU VACCINE: development of a combined Influenza/SARS vaccine	AT, CZ, DE, SI	AT	Severe acute respiratory syndrome
SCRIN-SILICO: finding promising drug candidates against tuberculosis with multidisciplinary protocol based non-conventional search	CZ, DE, HU, IT	HU	Tuberculosis
SERO-TB: development of a specific serological kit for the diagnosis of TB	DK, ES, ET, TR	DK	Tuberculosis
SPASTICMODELS: genetic models of chronic neuronal degeneration causing hereditary spastic paraplegia	DE, DK, GB, IT	IT	Familial spastic paraplegia
STEM-HD: embryonic stem cells for therapy and exploration of mechanisms in Huntington disease	BE, FR, GB, IL, IT	FR	Huntington disease
TAMAHUD: identification of early disease markers, novel pharmacologically tractable targets and small molecule phenotypic modulators in Huntington's Disease'	DE, ES, GB, IT	IT	Huntington disease
TB TREATMENT MARKER: establishing a TB treatment efficacy marker	DK, GW	DK	Tuberculosis
TB-DRUG OLIGOCOLOR: development of a molecular platform for the simultaneous detection of Mycobacterium tuberculosis resistance to rifampicin and fluoroquinolones	AR, BE, CO, NL, SE	BE	Tuberculosis
THERAPEUSKIN: European network on gene therapy of hereditary epidermolysis bullosa	CH, DE, FR, GB	FR	Hereditary epidermolysis bullosa
TREAT-NMD: Accelerating Treatments for Neuromuscular Diseases	BE, CH, DE, ES, FI, FR, GB, HU, IT, NL, SE	GB	Neuromuscular disease
VACCINES4TB: genome- and HLA- wide scanning and validation of cytotoxic CD8 T cell responses against Mycobacterium tuberculosis	DE, DK, NL	DK	Tuberculosis
VITAL: development of optimised recombinant idiotypic vaccines for subset-specific immunotherapy of B cell lymphomas	GB, IT, NL, NO, SE	IT	B-cell non-Hodgkin lymphoma

DG Research FP7

Network acronym / title	Participating countries	Coordinating country	Concerned diseases
AAVEYE: gene therapy for inherited severe photoreceptor diseases	CH, EE, GB, IT	IT	Optic neuropathy Leber congenital amaurosis Retinitis pigmentosa
BIG-HEART: bench-to-beside integrated approach to familial hypertrophic cardiomyopathy: to the heart of the disease	DE, GB, IT, NL	GB	Familial hypertrophic cardiomyopathy
BIO-NMD: identifying and validating pre-clinical biomarkers for diagnostics and therapeutics of neuromuscular disorders	DE, FR, IT, NL, SE, US	FR	Bethlem myopathy Congenital muscular dystrophy, Ullrich type Muscular dystrophy, Duchenne type
CARDIOGENET: definition of a genetic network involved in congenital heart disease	DE, FR, GB, IT, NL	IT	Congenital heart malformation

CHD PLATFORM: Establishment of a European parent- and patient-oriented information and communication platform on Congenital Heart Defects	DE, ES, GB, NO, SE	DE	Congenital heart malformation
CHEARTED: gene-environment interactions in heart development	AU, BE, DE, FR, GB, NL, NO	NL	Congenital heart malformation
CRUMBS IN SIGHT: restoring Mueller glia cell photoreceptor interactions with Crumbs	DE, FR, GB, NL	NL	Congenital Leber amaurosis Retinitis pigmentosa
CUREHLH: European initiative to improve knowledge, treatment and survival of haemophagocytic syndromes in children	DE, FR, IT, SE	DE	Hemophagocytic syndrome
ENCE CF-LAM-LTX: European networks of centres of expertise for CF (Cystic Fibrosis), LAM (Lymphangioleiomyomatosis), and LTX (Lung Transplantation)	AT, CZ, DE, FR, GB	DE	Cystic fibrosis Lymphangioleiomyomatosis
EPOKS: European patient organizations and knowledge society in the field of rare diseases	FR, GB, IE, PT	FR	-
EUCILIA: Pathophysiology of rare diseases due to ciliary dysfunction: nephronophthisis, oral-facial-digital type 1 and bardet-biedl syndromes	DE, GB, IT	IT	Nephronophthisis-associated ciliopathy Oral-facial-digital syndrome type 1 Retinal ciliopathy due to mutation in Bardet-Biedl gene
EUCLYD: A European consortium for Lysosomal disorders	DE, IT, NL, SE	IT	Lysosomal disease
EUNEFRON: the European network for the study of orphan nephropathies	BE, CH, DE, DK, FR, GB, IT, NL	BE	Rare renal disease
EURADRENAL: pathophysiology and natural course of autoimmune adrenal failure in Europe	CH, DE, GB, IT, NO, PL, SE	NO	Autoimmune polyendocrinopathy type 1 Autoimmune polyendocrinopathy type 2 Addison disease
EURIPFNET: European IPF network: natural course, pathomechanisms and novel treatment options in idiopathic pulmonary fibrosis	AT, DE, FR, GB, IT	DE	Idiopathic pulmonary fibrosis (UIP)
EURODSD : European collaborative study on disorders of sex development	DE, FR, GB, IT, NL, SE	DE	Disorder of sex development of endocrine origin Malformative disorder of sex development
EURO-GENE-SCAN: European genetic disease diagnostics	DE, GB, PL, SE	SE	Rare genetic disease
EURO-PADNET: the pathophysiology and natural course of patients with Primary Antibody Deficiencies (PAD)	CZ, DE, FR, GB, IT, NL, SE	GB	Primary Antibody Deficiencies
EUROTRAPS: European network on TRAPS syndrome	AT, DE, FR, GB, IL, IT	FR	Familial mediterranean fever Hyperimmunoglobulinemia D with recurrent fever TRAPS syndrome
GEN2PHEN: genotype-to-phenotype databases: A holistic solution	BE, CH, DE, ES, FI, FR, GB, GR, IN, IS, NL, PT, SE, ZA	GB	Rare genetic disease
INHERITANCE: Integrated HEart Research In TRAnslational genetics of dilated Cardiomyopathies in Europe	DE, DK, ES, FR, IT, NL, SE	IT	Dilated cardiomyopathy
LEISHDNAVAX: development of a DNA vaccine for visceral leishmaniasis	DE, GB, IL, IN, TN	GB	Leishmaniasis
LEISHDRUG: targeting the Leishmania kinome for the development of novel anti-parasitic strategies	DE, ES, FR, IL, IT, KR, TN, UY	FR	Leishmaniasis
MITOTARGET: mitochondrial dysfunction in neurodegenerative diseases: towards new therapeutics	BE, DE, FR, GB, NL	FR	Amyotrophic lateral sclerosis Familial spastic paraplegia Huntington disease
MYELINET: Myelin orphan diseases in health	AT, BE, CH, CY, DE, DK, ES, FR, GB, IL, IT, NO, PL, RS, SI, TR	AT	Leukodystrophy
NANOTRYP: exploiting nanobodies in development of new diagnostic tools and treatment methods for trypanosomiasis	BE, CH, ES, KE, MZ	BE	American trypanosomiasis African trypanosomiasis
NEUROSIS: efficacy and safety of inhaled budesonide in very preterm infants at risk for bronchopulmonary dysplasia	CZ, DE, FR, GB, IL, IT, NL	DE	Bronchopulmonary dysplasia
NMD-CHIP: development of targeted DNA-chips for high throughput diagnosis of neuromuscular disorders	BE, DE, FR, HU, IT, NL, SE	FR	Neuromuscular disease
NOVELPID: the genetic dissection of herpes simplex encephalitis (HSE) in children	-	FR	Herpetic encephalitis
NOVSEC-TB: novel secretion systems of Mycobacterium tuberculosis and their role in host-pathogen interaction	CH,FR, IE, IT, NL, ZA	FR	Tuberculosis
PEMPHIGUS: from autoimmunity to disease	CH, DE, FR, IT	DE	Paraneoplastic pemphigus Pemphigus vulgaris
PSYCHCNVS: copy number variations conferring risk of psychiatric disorders in children	GE, GB, IS, MK, RS, RU, UA	IS	Rare pediatric psychiatric disease
RAPSODI: pre-clinical studies of a PSA-based human vaccine candidate targeting visceral, cutaneous and mucocutaneous leishmaniasis and development of the associated procedures for further clinical trials	ES, FR, IN, TN, PE	FR	Leishmaniasis
TRYPOBASE: nucleobase derivatives as drugs against trypanosomal diseases	CH, ES, IN, SE, UY	ES	American trypanosomiasis African trypanosomiasis

ANNEX 4: SAMPLE EUROPLAN QUESTIONNAIRE



Questionnaire to collect information on activities dedicated to rare diseases in EU Countries

The European Project for Rare Diseases National Plans Development (EUROPLAN) is a three-year project part of the Programme of Community action in the field of Public Health (2003 - 2008), which began in April 2008.

The main goal of the EUROPLAN project is to develop recommendations on how to define a plan/strategy¹ for rare diseases (RDs). Focusing on the already available Member States experiences on RDs, EUROPLAN will contribute to share information, models and data on effective strategies to address RDs.

We are therefore kindly asking you, as EUROPLAN Partner, to collaborate in the retrieval of information by providing key data regarding actions on RDs in your Country. To reduce your workload, we are focusing this request of information on the following areas:

- National plans/strategies¹/measures/actions for RDs and related organization
- Funding of actions regarding RDs
- Definition, inventorying and provision of information and support of RDs
- Research on RDs
- RD Patient empowerment
- Programmes to facilitate provision of medicines to RD patients
- Specialised social services

Indeed, information on RDs in other areas also relevant for the definition of comprehensive actions in this field is already available as the result of other surveys and will be exploited as far as possible in the preparation of the project deliverables.

Information in the areas, which are in the scope of this questionnaire, may be available on the web; however, this information may be incomplete and need validation, and much more information may be published in national languages, which we cannot retrieve and analyze. Therefore, we kindly ask you to provide in English all information relevant to the questionnaire, and especially the one available in your national language only. You may refer to information published in English in the web; in this case we presume you have validated its contents.

Wherever possible please collect information from official sources and quote the supporting documents. In case that the requested information is not easily available to you, we kindly ask

¹ A **plan/strategy** for rare diseases is intended as a comprehensive and integrated programme aimed at guiding and structuring all relevant measures/actions in the field of rare diseases

you to contact the specific experts in your countries who have the information, in order to facilitate the flow of information and avoid language barriers.

We attach also a sample questionnaire filled with information collected from Italy, to exemplify the type of information and level of detail which should be communicated.

It is important that contact details of persons competent for specific areas are provided, especially in case of complex actions which may require lengthy descriptions or *ad hoc* inquiries. This information will be kept in our files for our direct use, should we deem necessary to have some explanations or interviews. These contact details will not be distributed to other parties.

Please send the filled in questionnaire within 16 June 2009 to: euoplan@iss.it

Please do not hesitate to contact L.Vittozzi or F. Capozzoli at euoplan@iss.it for any further clarification or information.

We thank you in advance for your cooperation and look forward to receiving your feedback at your earliest convenience.

Yours sincerely

Fiorentino Capozzoli and Luciano Vittozzi
EUROPLAN Project Coordination Team

	Areas and questions	Answers and additional inputs (please provide a short and factual description quoting the source of your information, e.g.: documents, websites, names of key informants etc.)
1	Country and respondent identification:	
	Plans/strategies¹/measures/actions regarding RD	<u>Information on the plans from Bulgaria, France, Portugal and Romania are in our hands and it is not necessary to add it.</u>
2	Please provide information on national and/or regional plans/strategies ¹ /measures/actions, whose implementation is mandatory, addressing different aspects of RDs (such as research, orphan drugs, medical and /or social care, surveillance or others). Please provide information also on measures in preparation, including their contents, determinants and objectives as well as reference to key documents, if existing.	
3	Please provide information on any other (non-binding) national and/or regional measures/actions aimed to improve the management of RDs and RD patients.	
4	Please provide information on any measures/actions which are not aimed specifically at RDs, but are applied to support priority actions addressing RDs, e.g.: diagnosis of RDs, treatment of and assistance to RD patients.	
5	Please clarify whether plans/strategies ¹ /measures /actions available in your country are intended “horizontally” for “all” RDs or are targeted to specific RDs	

	Areas and questions	Answers and additional inputs (please provide a short and factual description quoting the source of your information, e.g.: documents, websites, names of key informants etc.)
6	Please provide contact details of national authorities and Institutions dealing with RDs a) Ministerial Office(s) and contact person(s) under whose competence RDs fall b) National Centre/Body, if present, dealing with RDs and main expert dealing with RDs	
	Funding of actions (excluding research) regarding rare diseases	
7	How funds for plans/strategies ⁱ /measures/actions regarding rare diseases are allocated? a) As current expenditures ⁱⁱ within the general health system budget b) As funds dedicated exclusively to rare diseases? c) As current expenditures within the general health system budget plus ad hoc funding on the basis of RDs projects?	
8	In the case that plans/strategies ⁱ /measures/actions regarding RDs are funded from current funding, is it possible to identify the budget dedicated to RDs? (yes/no)	
	Definition, inventorying and provision of information and support on RDs	
9	Official definition of RDs used in your Country (if different from the EU one where RDs not more than 5/10.000 EU population)	

	Areas and questions	Answers and additional inputs (please provide a short and factual description quoting the source of your information, e.g.: documents, websites, names of key informants etc.)
10	<p>Availability of an official list of RDs Please clarify the purpose of the list (such as reimbursement, surveillance, provision of social support etc.)</p> <p>Please specify who develops it (such as government, regional authorities etc.)</p>	
11	<p>Availability of website-based information (Yes/No)</p> <p>Please clarify whether the service is intended for all RDs, or for specific groups of RD. In addition, please specify whether they are run by the government, by patients association or by other non-governmental bodies.</p>	
12	<p><u>Help Lines</u>^{III}</p> <p>a) Do national/local help lines for all rare diseases (or for main groups) exist in your country?</p> <p>b) Is the service provided and funded by patient organisations? National/local governmental institutions? private companies? other?</p> <p>c) what kind of service is provided (psychological support? Provision of general information to patients? Provision of technical information?</p>	
	Research on RDs	
13	<p>Availability of research programmes for RDs (Yes/No)</p> <p>Please describe the mechanisms and the sources (governmental bodies, charities, private foundations, pharmaceutical companies) for funding research programmes encompassing RDs</p>	

	Areas and questions	Answers and additional inputs (please provide a short and factual description quoting the source of your information, e.g.: documents, websites, names of key informants etc.)
	Empowerment of patients organisations	
14	<p><u>Support to the activities of patient organisations</u> Do activities aimed at empowering patient organisations receive in your country:</p> <p>a) official recognition in legal or policy documents?</p> <p>b) are there public funding schemes to support activities aiming at, e.g.:</p> <ul style="list-style-type: none"> • Capacity building – including counselling, training and education of patients, families and/or caretakers, in the legislative, research, social and healthcare fields; • Networking activities and events; • Dissemination of information and information sharing, such as events to exchange best practices among associations, scientific information, etc.; • Capacity building to improve patients' integration in social environments (school, work, etc.); • Outreach to very isolate patients 	

	Areas and questions	Answers and additional inputs (please provide a short and factual description quoting the source of your information, e.g.: documents, websites, names of key informants etc.)
15	<p><u>Representation and consultation of patient organisations</u></p> <p>Are there mechanisms in place for the involvement of patients? If yes, are there areas in which (a) patients are consulted? (b) negotiations with patients take place? (c) the opinion of patients is binding? If possible and applicable, please indicate also:</p> <ul style="list-style-type: none"> • The type of body where patients are represented • If such representation is officially recognised • Do patient representatives receive financial support for the attendance of the meetings 	
	Programmes to facilitate provision of medicines to RD patients (including so-called compassionate use programmes^{iv})	
16	<p>Please provide short information on programmes to facilitate provision of medicines to RD patients, if existing, specific for or applied to RDs, including its legal base.</p> <p>Is there any orphan drug or drug used for the treatment of RDs accessible thanks to such programme in your country (in case, please list the drugs)</p>	
	Specialised social services	

	Areas and questions	Answers and additional inputs (please provide a short and factual description quoting the source of your information, e.g.: documents, websites, names of key informants etc.)
17	<u>Respite Care Services^v</u> a) Do patient in your country have access to Respite Care Services? b) When service is provided, is it fully reimbursed, or does the patient/family have to pay part or all of it? c) Is service provided by patient organisations? National or local governmental institutions? private company? other?	
18	<u>Therapeutic Recreational Programmes^{vi}</u> a) Do patients in your country have access to Therapeutic Recreational Programmes? b) When service is provided, is it fully reimbursed, or does the patient/family have to pay part or all of it? c) Is service provided by a patient organisation? National or local governmental institutions? private companies? other?	
19	<u>Services aimed at the integration of patients in daily life^{vii}</u> a) Do such services exist in your country? Which ones? b) How are they financed? By government institutions and budget? By private initiative or patient associations?	

Please send the filled questionnaire to: europlan@iss.it

Thank you for your collaboration

ⁱ A **plan/strategy** for rare diseases is intended as a comprehensive and integrated programme aimed at guiding and structuring all relevant measures/actions in the field of rare diseases

ii **Current expenditures:** Current expenditure is expenditure on goods and services consumed within the current year, which needs to be made recurrently to sustain the services

iii **A help line** refers to any service where the primary mission is to provide information and technical or psychological support via telephone, email, post or on-site visits. A help line service can range from a ad hoc mobile phone number at a patient association, to a more advanced professional service with paid staff, a data management system (anonymous calls or recorded) and a yearly statistical report. Help line working hours can vary from a 24/24 7/7 to a few hours per week

iv The Commission Communication indicates as “**so-called compassionate use**” the provision of medicines to rare diseases patients before approval and/or reimbursement of new drugs. This is an option, which exists at the level of Member States, to accelerate or facilitate the availability of promising medicinal products to RD patients, when this is justifiable.

v **Respite care** is provided on a temporary basis for people who normally live at home, so that their carers can have a break from care giving. One of the important purposes of respite is to give family members time and temporary relief from the stress they may experience while providing extra care for a family member living with a rare disease. Respite care is provided to give the person living with the RD time and place to perform recreational and meaningful activities away from their parents/other caregivers.

There are several different approaches/ services to offering respite care:

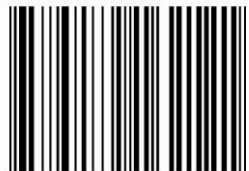
- a) Centre based respite care: requires that the individual come to a day centre, respite group home with assisted living facilities or a nursing home institution.
- b) Residential based respite: the person living with a rare disease goes away to be looked after by someone else/a “respite care family”.
- c) Domiciliary care: Some services allow a caregiver to come to the family’s home and take over for a certain period so the care giver(s) can have some time off

vi **Therapeutic Recreational Programmes.** Any formally or informally organised recreation activity (summer camp, ad hoc trip) which has been setup with the needs of children or young adults with rare diseases in mind. Activities are centred on fun, leisure and entertainment. They may include regular or ad hoc activities, at offsite summer camp or at the association’s site

vii **Examples of such social services:**

- Educational support for patients, relatives and caretakers;
- Individual support at school at different schooling levels, for both pupils with rare diseases and teachers;
- Promotional activities aimed to foster higher education for people with rare diseases;
- Supporting mechanisms to enter and stay in work life for people with disabilities

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