



Rare drugs **isolated** Patient  
 Looking after families  
**Reaching out to rare disease patients across Europe** information family Screening  
 centres of excellence Rare diseases supporting patients' disorders treatment recommendations  
 patterns of inheritance **databases** Orphan drugs national plans for rare diseases prevention



Directorate-General for Health & Consumers



Executive Agency for Health and Consumers

**Further information on the projects can be found on the Executive Agency for Health and Consumers database at:**

EAHC website <http://ec.europa.eu/eahc/projects/database.html>,  
on the DGSANCO Health Portal EU <http://health.europa.eu> and on  
SANCO Web Site <http://ec.europa.eu/health/>

The Executive Agency for Health and Consumers (EAHC) implements the EU Health Programme, the Consumer Programme and the Better Training for Safer Food initiative.

ISBN 978-92-79-19453-5

doi:10.2772/58184

Catalogue N° ND-31-11-046-EN-C

© European Union, 2011

Reproduction is authorised provided the source is acknowledged.

# Table of contents

<b>Introduction</b>	<b>5</b>
<b>Projects</b>	<b>8</b>
EUROPLAN	8
EURORDIS	12
ORPHANET	16
ECORN-CF	20
CARE-NMD	24
RARECARE	28
EUROCAT	32
European Newborn Screening practices	36
<b>Glossary</b>	<b>40</b>



### Rare disease sufferers: isolated yet not alone

A rare disease is a life-threatening or chronic, debilitating disease that occurs infrequently or rarely in the general population.

In the European Union (EU), a rare disease is defined as one occurring in less than 5 in 10,000 individuals. This apparently small number can mean as many as 250,000 sufferers of a distinct rare disease across the 27 Member States.

For any given disease in a single country, the numbers may be quite small, leaving patients feeling isolated and vulnerable. Rare diseases are characterised not only by their low prevalence but by their heterogeneity and complexity. There is a genetic origin for at least 80% of rare diseases and in 50% of cases the onset occurs in childhood.

### The paradox of rarity

Paradoxically, rare disease patients as a collective group are not rare. There are estimated to be 5–8,000 different rare diseases that affect 6–8% of the EU population (27–36 million people).

Rare diseases carry a high burden to affected individuals, their families and the community in terms of quality of life, participation in society and the need for services. EU policy is driven by a need to reduce this burden by promoting action through networks of patients and health professionals across Europe.

### What is the EU doing?

The focus on rare diseases is a relatively new achievement in most EU Member States. It has been increasingly recognised that, whilst rare diseases represent single entities with specific pathogenic and clinical features, they share common issues from a public health perspective and require specifically targeted policies.

This booklet focuses on various EU initiatives that signpost the way forward for rare diseases in Europe.

Taken individually, each patient with a rare disease is, by definition, in a minority. Taken as a whole, even though rare diseases affect millions of people across Europe, there is still a lack of public awareness; rare diseases often do not represent a public health priority, resources are fragmented across individual countries and the economic incentives to fund research and promote new treatments are seemingly poor.

The work done in the past few years has demonstrated that European collaboration and the common development of solutions are the key elements to improve health and social care of rare disease patients.

A number of EU projects are now in place to pool resources and to provide both patients and health professionals with improved access to medical information, treatment centres, patient support groups and epidemiological/research data. By enhancing



networking across European countries, joint actions are enabling patients and professionals to share expertise and information across borders.

Some projects have been running for decades, others are more recent. All of them share the common aim of improving the lives of families of patients with rare diseases.

### EU strategy on rare diseases

The projects described in this booklet stem from the following texts which drive the European strategy on provisions for patients with rare diseases.

## EC texts which guide the funding of rare disease projects in Europe

Text	Date of Adoption
Regulation of the European Parliament and Council on orphan medicinal products	16 December 1999
Communication from the EC – rare diseases, Europe’s challenge	11 November 2008
Council Recommendation on action in the field of rare diseases	9 June 2009
EUROPLAN selected indicators to evaluate the achievement of RD initiatives	10 January 2010
EUROPLAN guidance document – draft recommendations for the development of national plans for rare diseases	Recommendations being finalised 2010/2011

The **Council Recommendation on action in the field of rare diseases (June 2009)** is a driving force behind many of the projects described in this booklet. It is important because it calls for concerted action at the EU and national level to:

- Ensure that rare diseases are adequately coded and classified
- Enhance research in the field of rare diseases
- Identify centres of expertise by the end of 2013 and foster their participation in European Reference Networks
- Support the pooling of expertise at the European level
- Foster patient empowerment by involving patients and their representatives at all stages of the decision-making process
- Ensure the sustainability of infrastructures developed for rare diseases

The European Council Recommendation highlights the increasing recognition of rare diseases as a public health priority and as an area of unique European added-value for community action. Co-ordinated European action on rare diseases will lead to the most efficient use of the available resources and a greatly improved level of individual patient health, quality of life and survival, as well as significant wider socio-economic benefits.

Eight projects are described, which receive funding from the EU, to illustrate some of the specific measures that are being undertaken:

- **EUROPLAN** is supporting and guiding the development and implementation of **national plans for rare diseases** in EU Member States.

- The patient advocacy and support organisation **EURORDIS**, promotes cooperation between rare disease patient organisations across the EU, with a myriad of educational and advisory activities that promote the **empowerment of patients**.
- **ORPHANET** is **improving the recognition and visibility of rare diseases** by offering patients and health care professionals up-to-date, relevant information on rare diseases, orphan drugs and expert services.
- The creation of **European Reference Networks**, linking centres of expertise and professionals in different countries, is essential to both share knowledge and to identify where patients should go when expertise is unavailable in their home country. **ECORN-CF** and **CARE-NMD** are two projects where treatment recommendations and a consensus in clinical care are being promoted for cystic fibrosis and Duchenne Muscular Dystrophy respectively.
- Many EU-funded projects encourage more research into rare diseases. Understanding the scale and scope of rare diseases is often an issue, particularly when clinicians and patients struggle to find the right diagnosis and treatment. Two projects **EUROCAT** and **RARECARE** present detailed European **epidemiological data** on congenital anomalies and rare cancers respectively.
- Projects like EUROCAT promote wide-ranging **networks** of expert knowledge to better understand rare diseases and support evidence-based action. For example, the review of **European Newborn Screening** practices will guide future European policy, enabling the appropriate diagnostic and preventative measures to be put into action in all Member States.



### **Harnessing the power of the online community**

Patients are not alone in feeling isolated. Although health professionals and policy makers are united across Europe in their desire to understand and treat rare diseases, many struggle with the level of knowledge that is required.

Reaching out and connecting rare disease patients and health professionals is designed to improve the lives of patients with rare diseases. Providing a centralised knowledge database is a key feature of European collaboration on rare diseases, allowing the pooling and comparison of data, the sharing of expertise and a joint approach to European public health questions.

All eight projects described have developed, or are in the process of developing, extensive websites, encouraging the kind of synergistic networking and interaction that is at the heart of EU rare disease policy.

Long term sustainable infrastructures are now being developed in the fields of information, research and health care for rare diseases.

Coordinated European action on rare diseases is the way forward. Linking and sharing available resources across Europe will lead to an enormous impact on the quality of life and survival for millions of patients with rare diseases.

# EUROPLAN

European Project for Rare Diseases National Plans Development

EUROPLAN is a three year project funded by the European Union, which began in April 2008. Coordinated by the National Center on Rare Diseases of the Italian National Health Institute (Istituto Superiore di Sanità – ISS, Roma) the project involves partners from thirty-three Countries, representing other EU Member States, candidate countries, non-EU countries, as well as EURORDIS, the European organization for rare diseases patients.

The project's main goal is to support the EU Council recommendation to establish a national plan or a strategy for rare diseases in each Member State by 2013. Focusing on current policies, actions and experiences in each country EUROPLAN aims:

- To implement consistent national actions within a common EU strategy
- To facilitate the coherence of national initiatives with identified priority issues and good practices, as well as
- To prepare the ground for possible synergies and co-operative approaches in the future

EUROPLAN also aims to share information, models and data on effective strategies to address rare diseases.

EUROPLAN takes stock of and integrates activities performed in the past years at European level, as well as the experiences of countries where public health initiatives for rare diseases are enacted. Thus, EUROPLAN is an operational tool within the EU strategy on rare diseases, with a view to facilitate the implementation of effective national approaches within a coherent European collaborative framework. Sharing of knowledge and expertise to develop common solutions are key elements to improve the provision of health and social care to rare disease patients in Europe.

### Developing national strategies for rare diseases

EUROPLAN involves stakeholders from 33 countries: ministries and other, decision makers, health care professionals, researchers and patients represented by EURORDIS. Dr Domenica Taruscio is the director of the Italian National Centre for Rare Diseases (ISS) and EUROPLAN's project leader. She explains how EUROPLAN sets out to help rare disease patients: 'In order to ensure that all patients across Europe have equal



***'By the end of 2013, every EU country should have a national plan in place for rare diseases.'***

access to high quality care, the EC Recommendation on Rare Diseases (2009) stresses the importance of establishing national plans or strategies. Recommendations and indicators developed by EUROPLAN provide tools to Member States to develop their plans or strategies within a common European framework.' Dr Taruscio highlights that 'this will allow countries to tailor plans or strategies to their specific needs and public health requirements, whilst ensuring consistent outcomes in terms of, for example, patient care across the EU'. EUROPLAN outcomes may pave the way for Member States to develop and implement consistent and effective policies.

EUROPLAN has defined a national plan or strategy as a set of integrated and comprehensive health and social policy actions for rare diseases to be developed and implemented at national level; actions are characterized by identified objectives to be achieved within a specified timeframe. Appropriate resources for its development, monitoring and evaluation should be allocated.

EUROPLAN **Recommendations** are tools to guide stepwise efforts for elaborating national plans or strategies for rare diseases, including priority areas for actions.

A national health and social policy for rare disease should include:

- Fair and equal access to diagnosis of rare diseases and subsequent treatment and care
- Adequate definition, codification and inventories of rare diseases
- The establishment of centers of expertise and European reference networks
- The development of research and researchers' networks into rare diseases
- An emphasis on the empowerment of patients
- Sustainability of the national plan or strategy

In order to develop EUROPLAN recommendations, **best practice** experiences and case studies are being collected. This framework will help each Member State to identify priority areas and actions to be included in its strategic plans. 'In addition, EUROPLAN is facilitating the cooperation among countries as well as among stakeholders, raising awareness and identifying priority areas for action where countries can work together,' says Dr Taruscio.



**Indicators** are selected to support the monitoring of the implementation of national strategies and to evaluate their impact. Common and agreed indicators will ensure compatibility of data among the Member States and monitor progress towards implementing the Council Recommendations on Rare Diseases (2009) in the EU countries.

**National Conferences**, held throughout 2010 and 2011 in 15 Member States and Candidate Countries, allow national stakeholders to discuss the overall European strategy, the EUROPLAN recommendations and the applicability to their own country's specific needs. The national conferences are coordinated by EURORDIS and organized by its National Alliances, in collaboration with national authorities. All partners are involved and the role of the advocacy group EURORDIS highlights the vital input of patients in the design of national plans.

### Putting national plans into action

The scheduled project's work plan is nearly complete, but the role of the EUROPLAN Consortium will not finish there. Collaboration on an EU level will continue, mainly providing scientific and technical support to countries without dedicated policies on rare diseases, as well as assisting Member States in implementing their national plans.

## National Conferences Organization

Country	City	Date – 2010/11	Organiser
Bulgaria	Sofia	28–29–30 May	NAPRD National Alliance of People with RD
Romania	Bucarest	18–19 June	RONARD Romanian National Alliance for RD
Croatia	Dubrovnik	17–18–19 September	Hrvatska udruga bolesnikas rijetkim bolestima
France	Paris	30 September	Alliance Maladies Rares
Germany	Berlin	13–14 October	ACHSE Allianz Chronischer Seltener Erkrankungen
Hungary	Budapest	15–16 October	HUFERDIS Rare Disease Hungary
Poland	Krakow	22 October	Polish Cystic Fibrosis Foundation MATIO
Spain	Burgos	5–6 November	FEDER Federación Española de Enfermedades Raras
Sweden	Stockholm	11 November	Sällsynta diagnoser
Italy	Florence	11–12–13 November	UNIAMO Federazione Italiana Malattie Rare
United Kingdom	Manchester	16 November	Genetic Interest Group – Rare Diseases UK
The Netherlands	The Hague	19 November	VSOP Dutch Genetic Alliance
Denmark	Copenhagen	19 November	Rare Disorders Denmark
Greece	Athens	26–27 November	PESPA Greek Alliance for RD
Ireland	Dublin	20 January 2011	GRDO Genetic and Rare Disorders Organisation

As Dr Taruscio identifies, 'we are providing a remarkable contribution to help Member States shape their policies under a common European framework and to increase awareness. Up to now, only a few countries have adopted a national plan or a strategy for rare diseases.<sup>1</sup> By the end of 2013, every country should have one in place and we will support them in their start-up, development and implementation phases.'

Ultimately, EUROPLAN will ensure that all rare disease patients across Europe have access to high quality health care, thereby improving strategies on prevention, diagnosis, treatment and surveillance. As Dr Taruscio points out, 'I am confident that EUROPLAN is a successful project. These are exciting times for those who care about people with rare diseases. We are working in such a way across EU countries that we are really collaborating for the benefit of all patients.'

<sup>1</sup>Taruscio D, Vittozzi L, Stefanov R. National plans and strategies on rare diseases in Europe. In Posada M & Groft SC (eds). Rare Diseases Epidemiology book, 1st edn. Springer, The Netherlands.





## EUROPLAN: The story so far ...



## CONTACT

**Dr Domenica Taruscio**  
**National Centre for Rare Diseases**  
**Istituto Superiore di Sanità**  
**Viale Regina Elena, 299**  
**00161 – Roma**  
**Italy**

## EUROPLAN

**Tel: +39 0649904016**  
**Fax: +39 0649904370**

**Email: [europlan@iss.it](mailto:europlan@iss.it)**  
**[www.europlanproject.eu](http://www.europlanproject.eu)**



Patient organisations are key players in EU initiatives to improve the lives of patients with a rare disease. One organisation that speaks out on behalf of the 30 million people affected by rare diseases in Europe is EURORDIS. This is a non-governmental patient-driven alliance of patients' organisations and individuals active in the field of rare diseases.

EURORDIS' mission is:

- To build a strong pan-European community of patient organisations and people living with a rare disease
- To be their voice at the European-level and to fight against the impact of rare diseases on their lives

EURORDIS' Chief Executive Officer, Yann Le Cam, explains how EURORDIS began: 'We were set up to advocate the adoption of the EU Regulation on Orphan Medicinal Products. Since then rare diseases have moved up the EU policy agenda and are now recognised as a public health priority in Europe and an area of unique European added-value for community action. We are proud of our contribution to this.'

Founded in 1997, EURORDIS is supported by its members, the French Muscular Dystrophy Association (AFM-Téléthon), the European Commission, corporate foundations and the health industry.

### Spreading the net wide

EURORDIS represents more than 434 rare disease organisations in 43 different countries (of which 24 are EU Member States) covering more than 4,000 rare diseases.

Yann Le Cam feels passionately about the work that EURORDIS does. As a parent of a child with cystic fibrosis, he knows the importance of locating the right resources. 'I know how we felt when we found out our child had a rare condition. It is a difficult time and meeting with other people, affected by the same disease, was the best way of getting information and much needed support.'

EURORDIS recognises that patients need a strong voice. With the isolation of many rare diseases, families need help. As Le Cam argues, 'people affected by rare diseases face common problems, such as long delays in diagnosis, misdiagnosis and lack of information or support in everyday life. Due to the low prevalence of these diseases, medical experts are also rare, knowledge is scarce, care is often inadequate and research is limited. However, because rare diseases share a number of common characteristics, it is possible to develop public policy across more than 5,000 different diseases and across Europe.'

### Improving the lives of patients

EURORDIS helps patient organisations and individuals rise to the challenges of rare diseases in a number of ways. Broadly, its activities fall into four groups:

- Information and networking
- Advocacy
- Health policy and health care services
- Therapeutic development and research

EURORDIS aims to improve the quality of life of people living with rare diseases in Europe through advocacy at the European level, support for research and drug development, networking of patient groups, raising awareness and other actions designed to fight against the impact of rare diseases on the lives of patients and their families.

EURORDIS undertakes various activities on behalf of its members, a selection of which are presented here:

***'The voice of rare disease patients in Europe'***

Activities	Examples of achievements
<p>Information and networking</p> 	<p>434 members in 43 countries</p> <p>Website and monthly <b>e-newsletter</b> in 6 languages</p> <p>Creation of the <b>Council of National Alliances</b> (22) and the <b>Council of European Federations</b> (30) of rare disease patient groups</p> <p>Organisation of five <b>European Conferences on Rare Diseases</b> (every two years)</p>
<p>Advocacy</p> 	<p>Contribution to the adoption of EU <b>Regulations on Orphan Medicinal Products</b> (1999), Paediatric Drugs (2006) and Advanced Therapy Medicinal Products (2007)</p> <p>Promotion of the <b>Clinical Added Value of Orphan Drugs</b> and Risk-Benefit Effectiveness Management</p> <p>Contribution to the promotion and maintenance of rare diseases as a priority in <b>EU Public Health Policy and Research Framework programmes</b></p>
<p>Health policy and health care services</p> 	<p>Scientific <b>surveys</b> on delay in diagnosis, access to care and patient access to orphan drugs in the EU</p> <p>Networking of specialised services for rare disease patients at European level (<b>Respite Care Services, Therapeutic Recreational Programmes and Help Lines</b>)</p> <p><b>Patient training sessions</b> on internet information searching, patient databases and clinical trial protocols</p>
<p>Therapeutic development and research</p> 	<p>Contribution to the <b>designation of over 800 orphan drugs</b>, by participating in the Committee on Orphan Medicinal Products</p> <p>Creation of a European network of rare disease Biological Resource Centres (<b>EuroBioBank</b>) for DNA, cells and tissues</p> <p>Support patient representatives in various <b>scientific committees of the European Medicines Agency</b> (Orphan Drug, Advanced Therapies and Paediatric Use, Protocol Assistance)</p>



*Discussions at a EURORDIS summer school for patients*

EURORDIS' achievements are many and varied. A number of EURORDIS projects, co-funded through EC grants highlight the power of EURORDIS to harness expertise across Europe.

#### Novel initiatives

- The European Network of 22 Rare Disease National Alliances has been consolidated with the organisation of two European Workshops of its Council. These focused on the organisation of the Rare Disease Days awareness-raising campaign and on the development of National Plans for Rare Diseases (see EUROPLAN). 'The Council of National Alliances is very important because it allows for coordinated actions and facilitates the exchange of best practice,' says Le Cam.
- A 'Wiki-style' **good practice guide to help create and develop new disease-specific European Rare Disease Federations**.
- A major initiative since 2008 is **Rare Disease Day**, which involved 46 countries last year and 'has been very successful in raising awareness on rare diseases and the problems faced by the people affected by them, worldwide,' says Paloma Tejada, Communications Manager at EURORDIS.
- Creation of an **Online Patient Communities portal** for specific rare diseases in order to meet, learn and share.
- The structuring of the **European Network of Rare Disease Help Lines** with a view to reserving a single European 116 number.
- EURORDIS produces a number of publications including one entitled '**The Voice of 12,000 Patients**.' This was

the result of two surveys (EurordisCare2 and EurordisCare3) which investigated patients' experiences and expectations regarding access to diagnosis and to health services, for a variety of rare diseases across Europe. 'The Voice of 12,000 Patients is intended as an information and advocacy tool for patients, patient organisations, health professionals, and health authorities,' explains Flaminia Macchia, Director of European Public Affairs at EURORDIS.

- A wide-scale consultation project to allow optimal patient input in both EU policy and the development of specific plans on rare diseases at national level, through deliberative debates (Play Decide) and an evaluation of patients' satisfaction regarding the implementation of **European Reference Networks**.
- **Summer schools** cover the **training of patients** in issues such as drug development, the regulatory process and what is involved in clinical trials.

#### Joining forces

Patients with rare diseases often feel isolated and vulnerable. 'That is why our role is so important,' says Le Cam. 'EURORDIS provides a platform for rare disease patients to benefit from each other's experiences, share concerns and join forces in order to shape the public policy that affects them.'

EURORDIS now covers approximately two-thirds of the known rare diseases and more patient organisations join every year. 'Patient organisations that come to us represent patients that are scattered across a country and across Europe; the benefits of being part of an enormous network are huge,' says Anja Helm, Manager of Relations with Patient Organisations at EURORDIS.



EURORDIS summer school for patients

'We allow their voices to be heard and their needs, viewpoints and hopes, to be expressed and acted upon.'

'With the support of the EC, EURORDIS has been able to make an increasing impact,' says Yann Le Cam. 'Rare diseases exemplify the benefits to citizens and added value of working at the EU level to address the health challenges of the most vulnerable.'

**'A patient-driven  
alliance'**

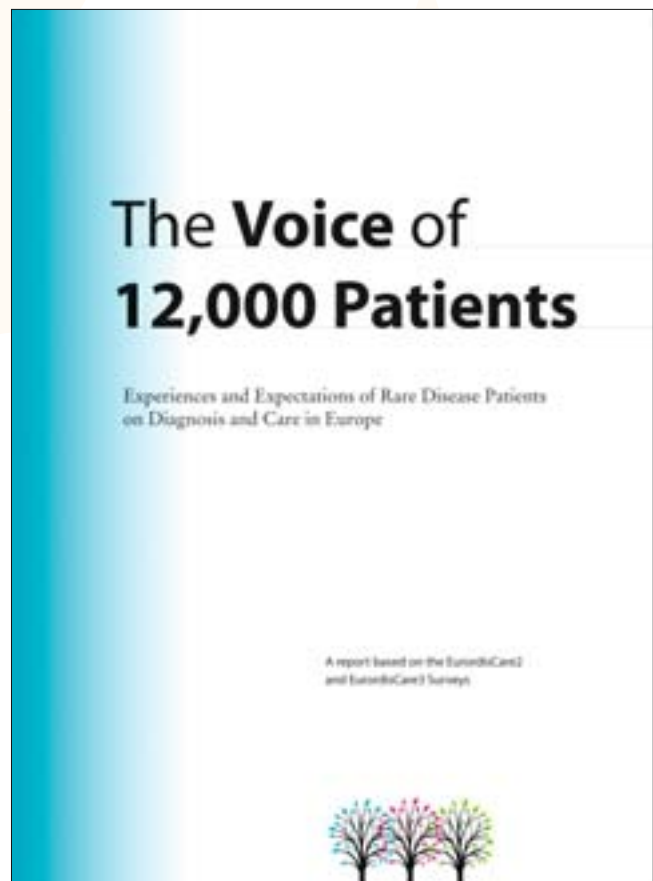
#### CONTACT

**EURORDIS**  
**Plateforme Maladies Rares**  
**96, rue Didot**  
**75014 Paris**  
**France**

**Tel: +33 156535210**

**Fax: +33 156535215**

**Email: [eurordis@eurordis.org](mailto:eurordis@eurordis.org)**  
**[www.eurordis.org](http://www.eurordis.org)**



# orphanet

Orphanet is the reference portal of information on rare diseases, orphan drugs and expert services throughout the EU. Its aim is to contribute to the improvement of the diagnosis, care and treatment of patients with rare diseases. Orphanet includes an inventory of rare diseases, a Professional Encyclopaedia, written by experts and peer-reviewed, a Patient Encyclopaedia and a Directory of Expert Services (expert clinics, clinical laboratories, research activities, technical platforms and patient organisations).

## A European leader

Orphanet is one of the longer-standing projects in the field of rare diseases in Europe. Established in 1997, as the European database of rare diseases and orphan drugs, Orphanet is currently funded by the French Ministry of Health, INSERM and the European Commission (DG SANCO and DG Research).

Orphanet was started in recognition of the particular problems in dealing with rare diseases, namely that the rarity of many of these conditions means information, expertise and resources are scarce.

Its founder and director, Dr Ségolène Aymé, is based at the French Institute of Health and Medical Research (INSERM). With her background as a medical geneticist, she understood from the start how vital Orphanet was. 'At the beginning of my career in medical genetics, I always felt very isolated. How could I respond to the needs of rare disease patients considering how much knowledge I was expected to have? I dreamt of having a system where the information was readily available,' says Dr Aymé.

Orphanet has led the way, both in Europe and globally, in providing comprehensive information on a large number of rare diseases. In supporting EU policy, Orphanet sets out to improve the quality of medical care by presenting a range of services for the rare disease community.

## Making rare disease information freely available

Orphanet provides an extensive inventory of rare diseases. Each disease is described in detail with information such as its name and synonyms, prevalence, age of onset and the genes that are involved.

## Orphanet grows year on year



An **encyclopaedia** is also published in English in an electronic open-access journal, the **Orphanet Journal of Rare Diseases**. Here, it is possible to search for information by either disease name and/or category of diseases. The journal is published in English, but the abstracts are available in French, German, Italian and Spanish. 'Although this encyclopaedia is predominately aimed at health professionals,' says Dr Aymé, 'we are now starting to develop an encyclopaedia for patients. Currently only available in French, demand is phenomenal, with 400,000 downloads/month.'

The website provides an inventory of **orphan drugs** at all stages of development, from EMA orphan designation to European market authorisation. 'I am delighted to see that drugs are now being developed for these rare diseases and we are unique in providing a wealth of information to help that process,' says Dr Aymé.

A free-access electronic bimonthly **newsletter** keeps the rare disease community informed of policy decisions, the latest scientific developments and progress on orphan drugs.

**Policy makers** are supported by the production of reports entitled 'Orphanet Report Series'. These cover such areas as 'Prevalence of Rare Diseases', 'Patients Registries', 'Research in Europe' and 'Orphan Drugs' and are regularly updated.

### Supporting efficient diagnosis

Orphanet allows physicians to enter rare disease symptoms as five key words. Possible diagnoses are listed in order of priority. Although many of the Orphanet website users are health professionals, patients also access this section of the website. 'We know that many patients have used the **'search by sign'** facility to establish their own diagnosis,' says Dr Aymé.

Unnecessary delays in obtaining a diagnosis can be an issue with rare disease patients. Orphanet seeks to alleviate this by providing a continuously updated **directory of expert clinical centres and laboratories**. These can be searched by disease name, category or associated genes as well as by region or country. 'This is so important,' says Dr Aymé, 'because it's impossible for a single country to offer all the diagnostic tests. Cross-border access to highly specialised services is vital and Orphanet has revealed how important it is to collate this information in a single database.'



### Helping researchers connect with industry

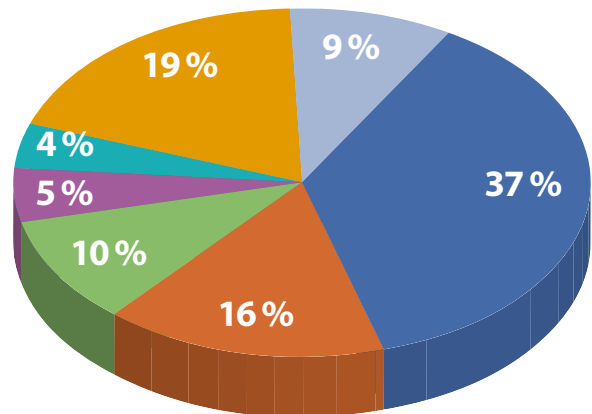
To facilitate collaboration between researchers and industry, Orphanet lists national and EU-funded research projects. These projects are listed under their institution, funding agency or type of disease with any associated licensing opportunities displayed. 'Increasingly pharmaceutical companies are turning to us to access our data set on rare diseases then using the information available to establish their strategy,' says Dr Aymé. 'We see that more and more pharmaceuticals companies are investing in the field of rare diseases and that can only be good for patients.'

### Connecting patients

Giving patients the opportunity to contact other sufferers is vital, particularly when they are likely to be geographically isolated. Orphanet promotes this by providing information on patients' organisations across Europe. If no such organisation exists, Orphanet allows patients to register and be put in contact with others with the same disease.

The Orphanet website is aimed at health professionals, researchers and patients and is visited by 20,000 users daily. Surveys have shown 53% of the users are health professionals and researchers, whilst patients and their families account for 19% of the users; the remaining 28% comprises teachers, students, journalists, industry managers or interested observers.

### Orphanet website users



Source: Orphanet Activity report <http://www.orpha.net/orphacom/cahiers/docs/GB/ActivityReport2009.pdf>

Orphanet's remit is broad and far reaching. Its range of services has been instrumental in contributing to the establishment of research networks and it has a measurable effect on the referral of patients to expert clinics and of samples to expert laboratories. 'In France, we have seen that when we put the address of a clinic on the website, the number of patients who visit this specific clinic can increase by up to 40%,' says Dr Aymé. 'That is also a big responsibility and we are delighted that the concept of national expert centres is being increasingly accepted and developed.'

#### Orphanet's future

Looking forward, Orphanet will concentrate on its main asset and area of expertise, the inventory of rare diseases and their classifications. The number of languages available will also be expanded. 'One of our biggest successes is also a key focus for future action,' says Dr Aymé. The World Health Organisation (WHO) is currently revising the International Classification of Diseases (ICD) and Orphanet is in charge of this process for rare diseases. 'We are now analysing the current edition and the next edition, due in 2014, will encompass all rare diseases, with their specific codes,' says Dr Aymé.

'When we started,' says Dr Aymé, 'we were in charge of producing information', now we are also slowly evolving towards identifying what others have done in the field and putting our stamp on it. Review articles produced in other journals will be assessed for relevance and promoted on the website.'

Clinicians, like patients, can feel very isolated but Dr Aymé feels the internet has 'changed my dreams into reality. I am a great believer in networking and the ability to work with other countries and provide such detailed information on rare diseases through Orphanet is fantastic. It provides such a positive environment for our future work.'





***'Cross-border access to highly specialised services is vital and Orphanet has revealed how important it is to collate rare disease information in a single database.'***

#### **CONTACT**

**Orphanet – INSERM SC11  
Plateforme Maladies Rares/  
Rare Disease Platform  
96, rue Didot  
75014 Paris  
France**

**For further information: [contact.orphanet@inserm.fr](mailto:contact.orphanet@inserm.fr)**



### Providing answers

- **Information on both medical and psychosocial aspects of cystic fibrosis**
- **Expert advice irrespective of country or language**
- **Advice for patients, health professionals and patients' relatives**

ECORN-CF was initiated in 2007 with funding from the EU as a pilot project, to build a model of a 'European Centres of Reference Network for Cystic Fibrosis' (ECORN-CF). The network provides patients, family members, doctors and other care professionals with easy access to expert knowledge and advice on cystic fibrosis. Question and answers are detailed on the ECORN-CF website.

As Professor Thomas Wagner, ECORN-CF's project leader, explains, 'as part of DG SANCO's Public Health Programme (2008–2013), ECORN-CF's mission has been to help improve public health by developing and co-ordinating a health information system. By uniting professional expertise across the EU we have built a multilingual web-based network of local expert advice and a quality-assured central archive in English.' This not only encourages the sharing and development of expertise but increases the availability of knowledge to patients.

### Cystic fibrosis – a debilitating disorder

Cystic Fibrosis is one of the more frequent metabolic diseases in the European population. It is a serious inherited disease which mainly affects the lungs and pancreas.

Cystic fibrosis arises when an individual inherits a copy of the defective gene from both parents. This autosomal recessive heritage means that 5% of the total population who carry just one defective gene, are healthy and unaware they are carriers.



Mukoviszidose e.V.



The genetic mutation in cystic fibrosis sufferers results in a defect in an important cellular mechanism – the ion transport channel. This is located in cell membranes and is responsible for the transport of chloride ions. As a result, secretor glands produce a very viscous fluid, resulting in obstruction of their ducts, excessive mucus production and chronic inflammation.

The illness presents predominantly with lung and digestive system symptoms. In the lung, high levels of mucus production, which need to be constantly cleared, are accompanied by a chronic cough and recurring infections. In the digestive system, there is an impaired secretion of digestive enzymes, from the pancreas, which results in problems with digestion and maintenance of weight.

### ECORN-CF as a model reference network

- **Advice for patients, relatives and health professionals**
- **Implementation of accepted European guidelines and evaluation of adherence to these**
- **Quality assurance measures to raise expertise to the highest levels across Europe**
- **Expertise provided irrespective of residence or language**
- **Referral to patient organisations**
- **Information on medical and psychosocial aspects of the disease**

There is no cure for cystic fibrosis and daily treatment regimes are relentless, often taking up several hours of a patient's day. With recurrent infections, there is a progressive deterioration in lung and digestive function. Nevertheless, the prognosis has improved greatly over the last few years due to the development of more effective therapies involving, for example, physiotherapy, inhalation treatments and IV drugs.

Thanks to improved clinical management, life expectancy for cystic fibrosis has increased during the last 20 years by more than 20 years. As Prof. Wagner explains, 'in Germany, for example, only 2% of the patients were adults in 1982, whereas now almost 50% are 18 years or older. This is a good situation, in many ways, but it means we face a different set of clinical challenges.'

The impetus to develop ECORN-CF arose out of the need to ensure that all patients, young and old, across the EU receive equal access to the highest level of care. 'This is only possible with the dissemination of knowledge and expertise and ECORN-CF, as a pilot project, will guide the way for other such projects,' says Prof. Wagner.

'Cystic fibrosis was chosen as a model rare disease for networking in Europe,' says Wagner, 'because it fulfils several criteria.'

- The diagnostic criteria are simple and unequivocally accepted
- Cystic fibrosis is a chronic deadly disorder requiring a high level of expertise
- Centre-oriented care has been shown to improve prognosis
- Therapeutic intervention has dramatically improved prognosis over the last 20 years
- Costly therapies call for evidence-based decision making; this evidence is much better with cystic fibrosis than with other rare diseases

### A central archive of questions and answers

All collaborating partner-countries provide expert advice to their patients and care team members in their mother tongue on a local website. 'By providing this service in the native language,' says Prof. Wagner, 'we are ensuring ease of access. This really empowers the patients.'

The website currently exists in 10 language zones across the EU – Czech, Dutch, English, French, German, Greek, Lithuanian, Polish, Romanian and Swedish. ‘We have observed,’ says Prof. Wagner, ‘that the patients and other interested people use the website most frequently when the moderators of the expert advice cooperate closely with the patients organisations and there is therefore an efficient, local expert advice service.’

Relevant questions and answers (from the local websites) are translated into English and published in the ‘Central Archive’. In the future, there are plans to locate ECORN-CF on the homepage of ‘CF Europe’, the federation of cystic fibrosis associations.

### Quality control

Before a question/answer pair (Q/A pair) is published, the English version of it is checked by a quality assurance team. Q/A pairs are only published in the ‘Central Archive’ if the answers are in accordance with European guidelines or, in the absence of this, with the consent of experts.

If there are different opinions about the appropriate answer to a question, it is made clear that there are several opinions and that each expert has his/her personal opinion. Difficult topics that have been raised, such as ‘travelling with cystic fibrosis’ are being further researched and published in scientific journals.<sup>1</sup>



Mukoviszidose e.V.

## **‘Providing patients, family, doctors and other care professionals, with easy access to expert knowledge and advice on cystic fibrosis’**

Feedback loops, through the moderators, ensure that the answers can be updated in the original language. This system ensures that experts are continuously able to expand their knowledge.

### Open access

ECORN-CF is available for anybody who is interested in cystic fibrosis. All areas of cystic fibrosis care are covered. Website visitors can search the archive by key words, the most frequent being general aspects of cystic fibrosis care, genetics, pseudomonas infections and travelling. ‘Although there is a special registration mode for care team members, it has become obvious that the lay person’s need for expert advice is much higher,’ says Prof. Wagner. ‘Only about 5 % of the incoming questions are from health care professionals.’

For individuals who want to ask a question guidance is given.

### A model of help for sufferers of a specific rare disease

Projects like ECORN-CF facilitate access to specific health care aids for patients with cystic fibrosis. ECORN-CF will help to extract data on deficits in existing guidelines or lack of evidence based guidelines and to find a European Consensus for care of cystic fibrosis patients, where it is necessary. ‘This will eventually help to bridge the gap between those countries where the quality of care is not as good as others,’ says Prof. Wagner. ‘The hope is that ECORN-CF will act as a model for other rare diseases.’

ECORN-CF facilitates the transfer of knowledge and expertise throughout Europe. This helps to ensure the same level of expert advice in all partner countries and reduces the need for lengthy travel to a cystic fibrosis centre. ‘What we are most pleased about,’ says Prof. Wagner, ‘is that we managed to establish cross-border quality management of expert advice. This is the start of a more European approach to quality of care.’

<sup>1</sup>Hirche, T.O. et al. (2010). Travelling with cystic fibrosis: Recommendations for patients and care team members. *Journal of Cystic Fibrosis* 9/6, pp. 385-399.



Mukoviszidose e.V.

***Questions answered ... 'Our 6 month granddaughter lives in South-Africa and has Cystic Fibrosis. Her parents are planning a trip to Holland during the month of April. Is flying possible or does it cause problems?'***

#### **CONTACT**

**Goethe University Hospital  
Medical Clinic I, Pneumology/Allergology  
Theodor-Stern-Kai 7  
D-60590 Frankfurt am Main  
Germany**

**Tel: +49 6963013824  
Fax: +49 6963016335**

**Email: [info@ecorn-cf.eu](mailto:info@ecorn-cf.eu)**



***'We don't only want to address professionals.  
We're convinced we have to address families as well.'***

CARE-NMD is an EU-funded project to implement best-practice standards of care for Duchenne Muscular Dystrophy (DMD) across Europe, by bringing together a network of leading care centres.

Set up in May 2010, the project will evaluate existing treatment practices, implement newly agreed international consensus care recommendations and evaluate their impact on patients' quality of life.

Other rare diseases may benefit from this focused networking approach to optimising care for DMD.



*DMD only affects boys*

**Duchenne Muscular Dystrophy – a complex clinical picture**

DMD is the most common neuromuscular disorder in childhood, affecting only boys. It is caused by a mutation in the X chromosome, affecting the production of a crucial muscle protein dystrophin.

About 1 in 6,000 newborn boys will develop the disease. They appear normal at birth but at the age of 3–5 years the first symptoms will appear. Boys have difficulty rising from the floor and standing up. Progressive muscle weakness results in loss of ambulation and therefore dependence on a wheelchair, at around 10 years of age. Additional problems also develop later on with respiratory failure and heart disease.

The nature of the disease involves many organ systems, so DMD patients need a multidisciplinary clinical care team. With the introduction of non-invasive ventilation and corticosteroid drugs, life expectancy has risen in recent years from 20 to approximately 35 years.

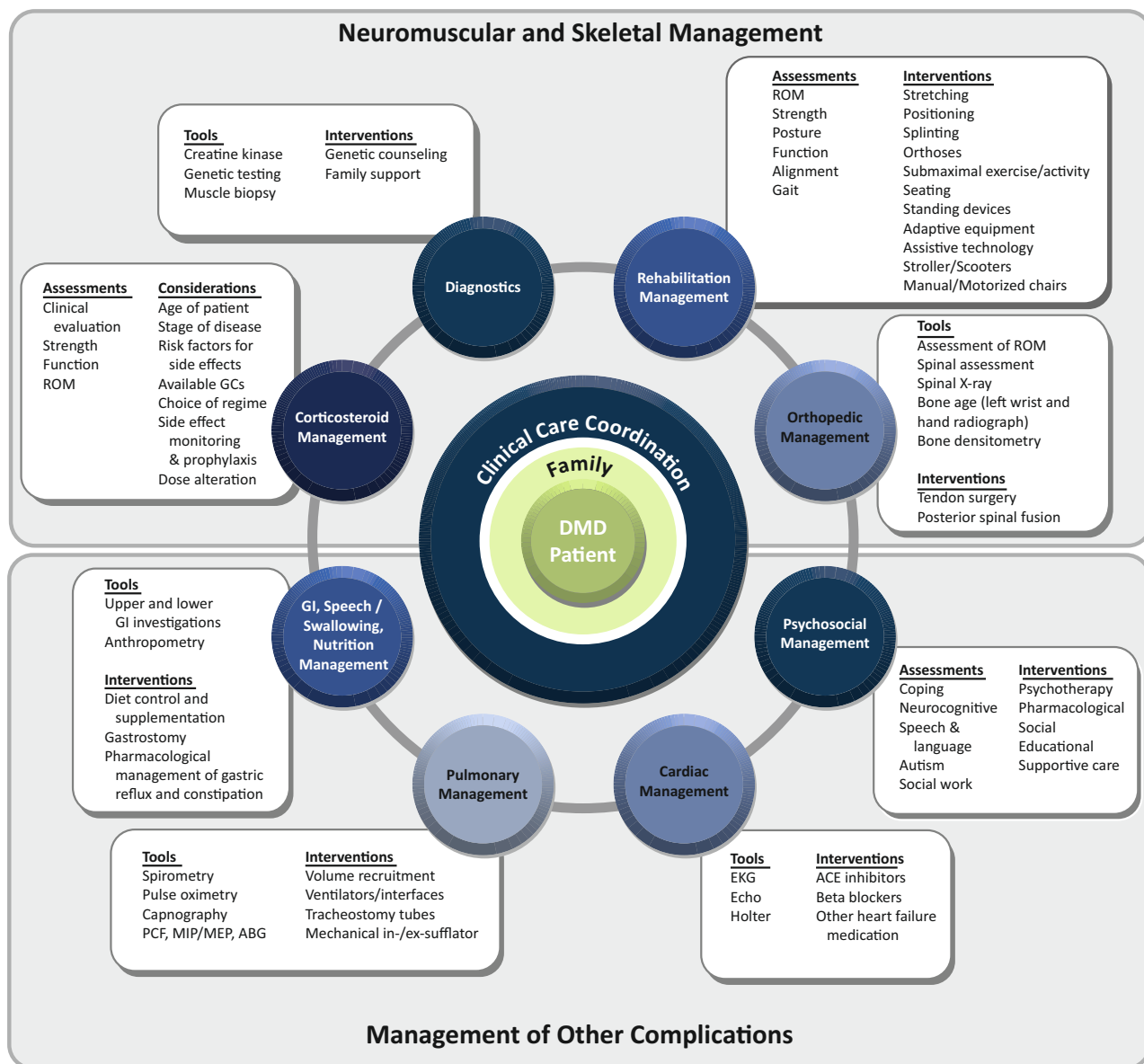
The degree of complications from, for example, pneumonia and heart failure, varies widely. Much depends on the provision of appropriate clinical services to manage the complex clinical picture. Although there is currently no specific cure for DMD, a multidisciplinary approach to care can significantly improve both patients' quality of life and life expectancy.

Provision of the appropriate care varies widely across Europe.

# 'Duchenne Muscular Dystrophy patients need a multidisciplinary clinical care team.'

## Interdisciplinary management of DMD (adapted from Busby et al – Part 1, 2010<sup>1</sup>)

Coordination of clinical care is a critical component to the management of DMD. This care is optimally provided in a multidisciplinary care setting where the individual and family can access expertise for the required multisystem management of DMD in a collaborative effort. A coordinated clinical care role may be provided by a wide range of healthcare professionals depending on local services, including (but not limited to) neurologists or pediatric neurologists, rehabilitation specialists, neurogeneticists, pediatricians, and primary care physicians. It is critical that the person responsible for the coordination of clinical care is aware of the available assessments tools and interventions to proactively manage all potential issues involving DMD.



### Linking rare disease research and quality of care

Dr Janbernd Kirschner (Consultant Paediatric Neurologist, Freiburg University Medical Centre, Germany) is the leader of the CARE-NMD project. He explains how the project arose: 'An international consensus process was started in 2006, by 84 international experts in DMD diagnosis and care, to establish treatment recommendations for patients. The result was the publication in the journal *Lancet Neurology* (2010)<sup>1</sup> of a very extensive set of recommendations for the clinical management of DMD patients. These form the basis of the CARE-NMD project.'

In conjunction with this set of treatment recommendations, CARE-NMD is set to build on the progress made by TREAT-NMD. This was founded in 2006, as an EU-funded network of excellence. Its focus is on translational research – the development of new therapies and getting them to the patients. Part of that process involved the establishment of a network of treatment centres, where clinical trials could take place.

TREAT-NMD provides an infrastructure to launch CARE-NMD. Treatment recommendations, access to health professionals, a database of care and trial sites and patient registries are all available. 'Now we can contact professionals and patients and

try to find out whether the recommendations are being carried out and if not, why not?' says Dr Kirschner.

### European coverage

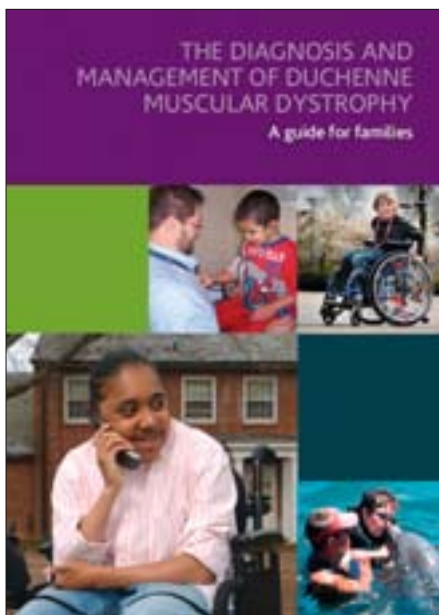
CARE-NMD is in its infancy but is already active in a number of European countries. Seven countries (UK, Germany, Poland, Hungary, Czech Republic, Bulgaria and Denmark) are active participants receiving funding as primary partners. In addition, many organisations in other European countries are collaborative partners, so the project website will disseminate resources and information in as many languages as possible. As Dr Kirschner explains, 'they are interested in the project and are supporting it, but are not currently receiving funding. Extending the coverage of the network is part of our future plans.'

### Duchenne Muscular Dystrophy guide for families

The Lancet recommendations for treatment are published in an academic journal which is not easily intelligible to people without a medical background. Now, a guide has been produced for families, which presents the guidelines in a comprehensive and accessible style. The family guide will be available in print and online formats in a number of different languages.



*Young DMD wheelchair user with health professional*



Family guide to DMD

It is hoped that patients and their families can use it in collaboration with their care providers to discuss their specific needs. 'Our idea,' says Dr Kirschner, 'is that we don't only want to address professionals. We're convinced we have to address families as well. Families have to be empowered to understand the condition and be able to request potential treatments.'

#### **A care model for other rare diseases?**

The publication of the extensive treatment recommendations represents a unique opportunity to implement the highest quality of care for DMD patients. By adopting an inclusive networking approach, targeting both care providers and patients, CARE-NMD will improve accessibility to best-practice care for DMD patients throughout Europe.

CARE-NMD is working towards implementing the recommended treatments across Europe. 'This is a long-term process and in the first instance is all about raising consciousness of the programme. We would like to highlight the kind of treatment that is possible for DMD and the possibilities available to improve patients' quality of life,' says Dr Kirschner.

CARE-NMD is divided into 4 phases: outreach, evaluation, implementation and impact assessment. For example, questionnaires are being sent to patients and professionals to assess the care needs across Europe. 'The information we obtain could influence future policy decisions about national treatment plans,' says Dr Kirschner. 'By looking at the gaps in the needs for each country, we are able to direct specific training sessions for treatment recommendations in that country.'

Developing up-to-date, relevant and feasible care guidelines for rare diseases is a focus of EU policy, ensuring that best practices are updated and providing all patients with access to the best possible levels of care across Europe. CARE-NMD is a project that will guide the way for future initiatives in the field of rare diseases. Funding such a project for all rare diseases is not feasible but Dr Kirschner echoes the hopes of many 'that this type of networking approach may be applicable to other rare diseases.'

## **CONTACT**

### **CARE-NMD**

**Dr Janbernd Kirschner**

**Division of Neuropaediatrics and Muscle Disorders  
University Medical Centre Freiburg, Germany**

**Tel: +49 76127043750 (direct)**

**Tel: +49 76127044970 (secretariat)**

**Fax: +49 76127044460**

**Email: [janbernd.kirschner@uniklinik-freiburg.de](mailto:janbernd.kirschner@uniklinik-freiburg.de)**

**[www.care-nmd.eu](http://www.care-nmd.eu)**

<sup>1</sup>Bushby,K et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *Lancet Neurology* 2010; 9: 1–17



**RARECARE provides data on European rare cancer incidence, survival, prevalence and mortality.**

The RARECARE project was initiated in 2007, with funding from the EU, in response to the need for surveillance of rare cancers in Europe. Based at the Fondazione IRCCS, Istituto Nazionale dei Tumori (Milan, Italy), RARECARE has 14 European Institutions and Organisations as participating partners.

Data from population-based cancer registries have been used extensively for the RARECARE project. These registries are essential to monitor rare cancers and to guide cancer prevention and treatment. As Dr Gemma Gatta, RARECARE's project leader, comments, 'these population-based cancer registries are so important, without their data the project would have never achieved the results it has.'

RARECARE's data have revealed the true numbers of patients living with rare cancers in Europe. Like many rare diseases, each rare cancer taken individually has a low burden, but together rare cancers have been shown by RARECARE to add up to 19% of all cancers diagnosed and 22% of the total cancer prevalence.

**Surveillance of rare cancer patients**

Historically, the burden of patients with rare cancers in Europe was largely unknown and no generally accepted definition existed. Rare cancers are often inadequately diagnosed and treated, due to lack of both knowledge and clinical expertise. Survival rates vary greatly, with poorer outcome among older patients and in Eastern European countries.

Improving the quality of care for these cancers is a public health priority. This is difficult to achieve without reliable data on the incidence, prevalence and survival of rare cancers. Such data can be provided by population-based cancer registries and by large international databases that pool data from cancer registries.

As Dr Gatta explains, 'when we started, there was no epidemiological data on rare cancers. Since I work in cancer epidemiology, looking at, for example, survival rates, this was of great interest to me and I applied for EU funding. RARECARE was the result.'

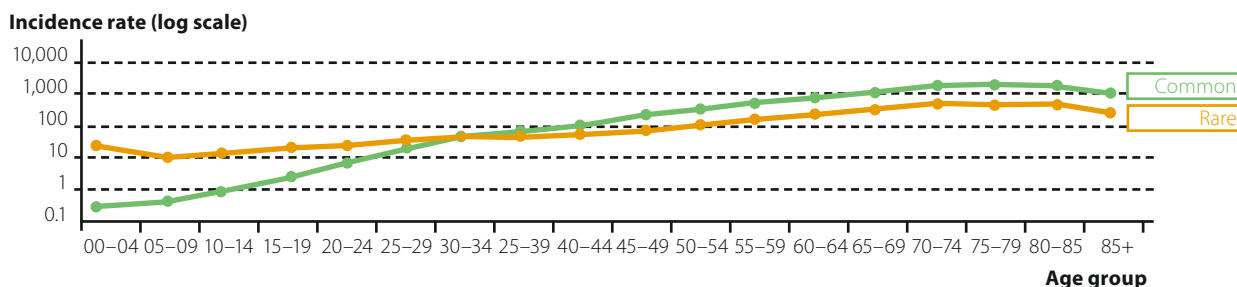
RARECARE set out to:

- Provide a definition of 'rare cancers' and a list of cancers that meet this definition
- Estimate the burden of rare cancers in Europe
- Improve the quality of data on rare cancers
- To disseminate information among all the key players involved in Europe-wide surveillance and treatment of rare cancers

RARECARE has collected data on rare cancers, diagnosed from 1978 to 2002, from 89 population-based cancer registries in 21 European Countries. This has made it possible to study the epidemiology of these cancers, as a whole, in a large and heterogeneous population.

The RARECARE project included 32% of the EU population. Estimates of incidence, survival, prevalence and mortality were provided for Europe and EU regions.

**RARECARE estimates of age-specific incidence rates (x 100,000) for rare and common cancers in the 27 EU Member States.**



**List and definition of rare cancers**

An international consensus group was established including epidemiologists, clinicians, pathologists and patients' associations, to develop the definition and list of rare cancers. The international experts agreed that rare cancers are those cancers that present specific problems in clinical decision making, health care organisation and clinical research because of their low frequency. The group agreed to define rare cancers on the basis of an incidence cut-off of < 6 patients/100,000 people/year. This identified 194 cancers as rare and 34 cancers as common.

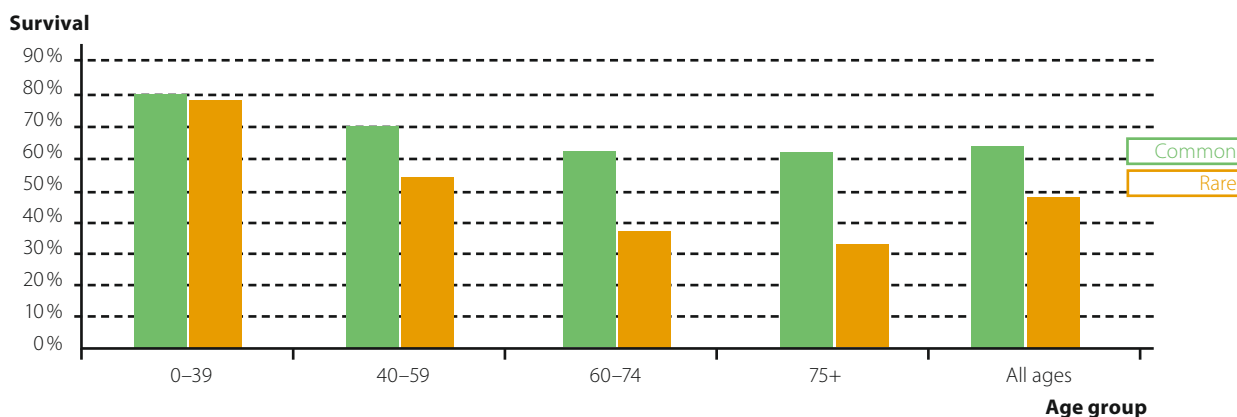
**Age-specific incidence rates for rare and common cancers**

The annual incidence rate of all rare cancers was approximately 97 patients/100,000 people, corresponding to 486,000 new diagnoses annually or 19% of all cancer diagnoses. The incidence of rare cancers in the youngest sections of the population was higher than the incidence of common cancers; the reverse was true for the older age groups.

**Age-specific survival rates for rare and common cancers**

Five year survival was 48% for rare cancers and 64% for common cancers, with marked differences between age groups. Survival rates in the older age groups are poor for rare cancers, compared with common cancers.

**RARECARE estimates of five-year relative survival of rare and common cancers classed by age, in the 27 EU Member States.**



### Prevalence for rare cancers

Four million people in Europe live with a previous diagnosis of a rare cancer, 22% of the total cancer prevalence.

### Improving data quality for rare cancers

One of the aims of the RARECARE project was to improve the data quality in rare cancers. For selected rare cancers considered a high priority, 38 cancer registries participated in a data quality study to develop recommendations to improve rare cancer registration. The resulting improvement in data quality will improve the comparability of incidence, prevalence and survival of rare cancers among European populations and across time periods.

To promote the standardisation of coding procedures for rare cancers, RARECARE is organising training courses in collaboration with the European School of Oncology. The first course on 'rare solid cancers' will take place in Stresa (Italy), 31 March to 1 April 2011.

***'Our data has shown the reality of the rare cancer problem in Europe. Now we have to use the knowledge we've obtained to improve the care of patients.'***

### RARECARE's information resources

RARECARE is a scientific research programme on rare cancers in Europe. By defining rare cancers, their characteristics and incidence, it is paving the way for better diagnosis, treatment and prolonged survival rates.

Patients and health professionals are being kept up-to-date with the latest findings through the website ([www.rarecare.eu](http://www.rarecare.eu)), patients' associations, scientific meetings and journals.

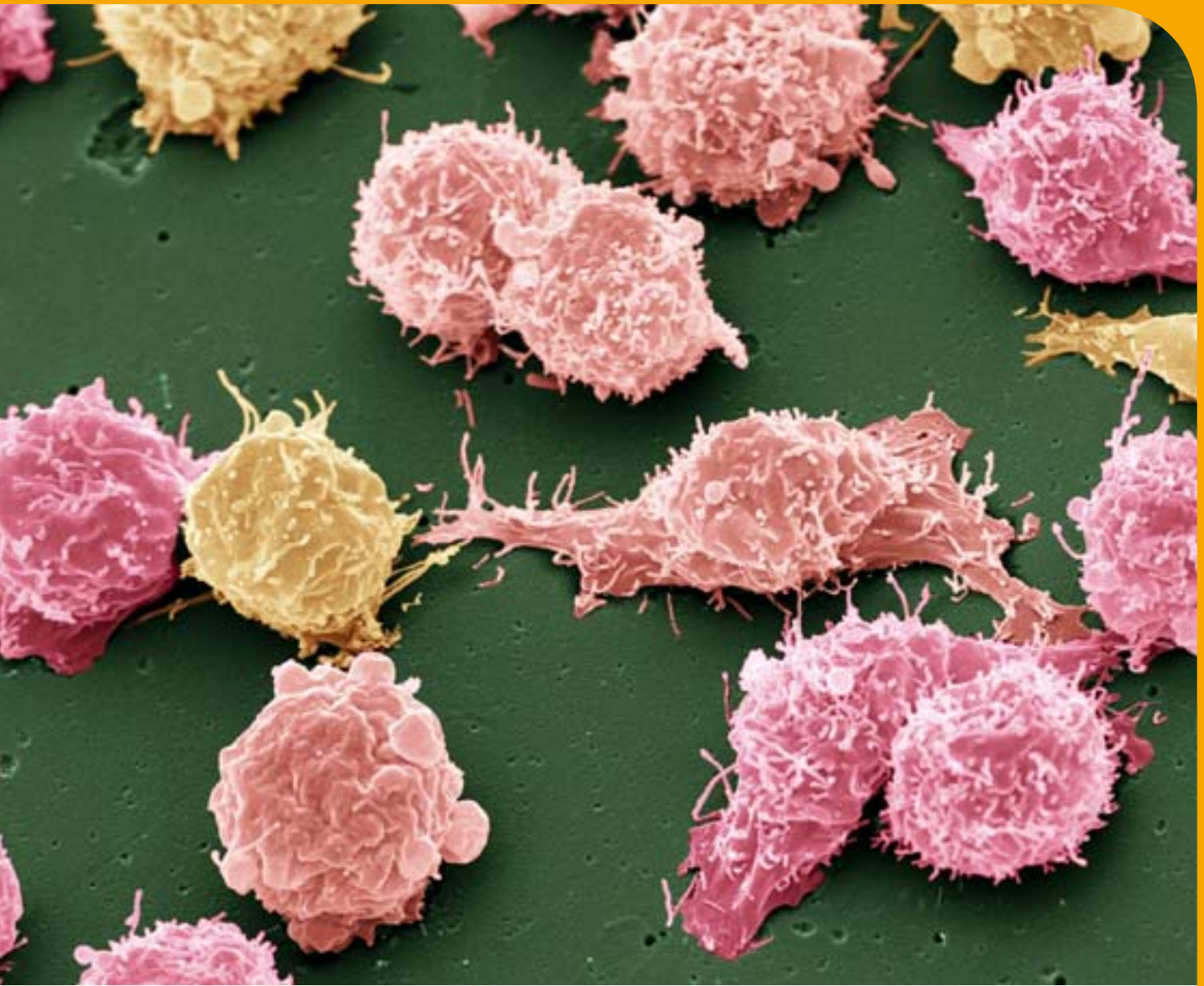
- The project website was launched in March 2008 and is constantly updated to include new results, information and relevant documents. The main pages are available in 8 different languages (English, Italian, French, German, Polish, Spanish, Dutch and Portuguese). The number of visitors has steadily increased over the course of the project.
- More than 300 cancer patient organisations have been kept up-to-date with RARECARE's findings through the European Cancer Patient Coalition (ECPC).
- In addition, 'scientific publications, are now being prepared by a team of epidemiologists and clinicians for a number of scientific journals,' says Dr Gatta. Recently, a chapter was published in the book 'Rare Diseases Epidemiology.'<sup>1</sup>

### Translating rare cancer research into improved patient care

'Pooling data from population-based cancer registries has been central to RARECARE'S work, allowing us to achieve reliable indicators of the burden of rare cancers in Europe,' says Dr Gatta. 'Our experience has really demonstrated the benefits, to all the disciplines in the field of rare cancer, of networking across Europe.'

'This has been such a great experience,' says Dr Gatta. 'I usually just work with other epidemiologists but RARECARE has involved interactions with oncologists and pathologists and so on. It was interesting, for me, to see how clinicians define rare cancers. And how difficult it is to diagnose and treat the majority of rare cancers. They need our epidemiological indicators to monitor progress in diagnosis (incidence) and treatment (survival and prevalence).'

RARECARE's extensive epidemiological research has placed rare cancer firmly on the European map. Taking this forward, the EU will use RARECARE's data to support the establishment of networks of national and regional centres of excellence for rare cancers. RARECARE will continue to encourage such initiatives. 'Our data has shown the reality of the rare cancer problem in Europe,' says Dr Gatta. 'Now we have to use the knowledge we've obtained to improve the care of patients.'



*A close up photo of cancer cells*

## **CONTACT**

**Dr Gemma Gatta, Project Leader**  
**Fondazione IRCCS Istituto Nazionale dei Tumori**  
**Department of Preventive and Predictive Medicine**  
**Evaluative Epidemiology Unit**  
**Via Venezian 1**  
**20133 Milano**  
**Italy**

**RARECARE**  
**Tel: +39 0223903518**  
**Fax: +39 0223903522/3516**

**Email: [gemma.gatta@istitutotumori.mi.it](mailto:gemma.gatta@istitutotumori.mi.it)**

**[www.rarecare.eu](http://www.rarecare.eu)**

<sup>1</sup>Gatta G, Capocaccia R, Trama A, Martinez Garcia C and the RARECARE working group (2010). The burden of rare cancers in Europe, In Posada M & Groft SC (ed). Rare Diseases Epidemiology book, 1st edn, Springer, The Netherlands.



EUROCAT is a European network of population-based registries for the epidemiological surveillance of congenital anomalies. It was started in 1979 and now surveys more than 1.5 million births per year across 20 European countries. An extensive website ([www.eurocat-network.eu](http://www.eurocat-network.eu)) presents the latest findings on prevalence data, prevention and risk factors, prenatal screening and diagnosis, and clusters/trends.

Population-based registries are particularly powerful tools to monitor the prevalence of congenital anomalies and for the evaluation of health services, as they represent the experience of a whole community, not just individual specialist units.

#### **Congenital anomalies: a hard start in life**

Congenital anomalies are structural defects due to chromosomal abnormalities, single gene mutations or multifactorial causes that arise in utero and are therefore present, if the foetus survives, at birth. They are a major cause of foetal death, infant mortality, childhood morbidity and long-term disability.

Congenital anomalies carry a high burden to affected individuals, their families and the community in terms of quality of life, participation in society and need for services.

#### **Why register congenital anomalies?**

Professor Helen Dolk (University of Ulster, Northern Ireland) is the European Project Leader of EUROCAT. She explains the origins of EUROCAT and the two factors that drove its creation: 'It really arose when thalidomide was still fresh in the mind of health policy makers – the need to prevent another tragedy on the scale of thalidomide, by improving surveillance of congenital anomalies.' Ever since thalidomide and rubella (German measles) were discovered as powerful teratogens, registries have been set up to facilitate research and surveillance concerning environmental causes of congenital anomalies, and to give early warning of new teratogenic exposures.

At the same time, in the late 1970s, 'there was also a need to try and find some kind of prototype of European health surveillance and the two factors came together to produce EUROCAT,' says Prof. Dolk. 'Here was something that was badly needed in terms of monitoring the rate and causes of congenital anomalies.'

'Working together for health surveillance on a European basis was the driving force behind EUROCAT,' says Prof. Dolk. Now, the objectives are wider and more extensive, with a large number of registries (each with their own set of interests) and more birth coverage. With 41 registries in 21 countries, 31 % of the European birth population is covered.

#### **Influences of EUROCAT on planning and evaluation of health services and prevention of congenital anomalies.**

<b>Levels of prevention</b>	<b>Examples</b>
Primary prevention – tackling the causes and risk factors for congenital anomalies	<ul style="list-style-type: none"> <li>• Pre-conception folic acid supplementation to prevent neural tube defects</li> <li>• Vaccination against rubella to prevent congenital rubella syndrome</li> <li>• Foetal Alcohol Syndrome</li> </ul>
Secondary prevention – early detection to improve the treatment opportunities	<ul style="list-style-type: none"> <li>• Prenatal screening, for example, to detect congenital heart defects in time for corrective surgery at the earliest opportunity</li> <li>• In the future, foetal surgery may also be increasingly possible for some congenital anomalies</li> </ul>
Tertiary prevention – reducing disability and its consequences	<ul style="list-style-type: none"> <li>• Medical services including paediatric surgery and rehabilitation</li> </ul>



Specialist scanning in Foetal Medicine

***'Like the rest of the rare diseases field, we're better off joining forces and sharing resources and expertise across Europe.'***

#### **Essential epidemiological information database**

EUROCAT gives essential epidemiologic information on congenital anomalies in Europe. It collects high quality data from multiple source registries, including all pregnancy outcomes (livebirths, stillbirths and terminations of pregnancy), in its central database. Although primarily aimed at health professionals, the EUROCAT website is also accessed by patient organisations who are, for example, interested in data on the prevalence of conditions.

EUROCAT is principally used as a basis for surveillance using routinely collected data. In addition, it can be used for case-control studies of environmental causes including, for example, medicines taken early in pregnancy, or exposure to environmental pollutants. Recent published studies from EUROCAT have concerned the risks of antiepileptic drug exposures.

#### **Uniting Europe**

At the heart of the drive behind EC-funded rare disease projects is the fact that rare disease projects, like congenital anomalies surveillance, do not attract a lot of attention or funding in individual countries.

'Like the rest of the rare diseases field, we're better off joining forces and sharing resources and expertise across Europe,' explains Prof. Dolk. 'In particular the expertise is just as important as the financial resources that are put into it. In our network, we have medical geneticists in some countries working with obstetricians in others and epidemiologists in yet others, and so on, all with a common interest in congenital anomaly surveillance. It would be really difficult to get a team like that together on a national basis.'

#### **EUROCAT Objectives**

- **To facilitate the early warning of new teratogenic exposures**
- **To evaluate the effectiveness of primary prevention**
- **To assess the impact of developments in prenatal screening**
- **To act as an information and resource centre for the population, health professionals and managers regarding clusters, exposures or risk factors of concern**
- **To provide a ready collaborative network and infrastructure for research related to the causes and prevention of congenital anomalies and the treatment and care of affected children**
- **To act as a catalyst for the setting up of registries throughout Europe collecting comparable, standardised data**

Once there is support from clinicians and other health professionals, any country can establish a registry. 'Part of the networking process is that we have guidelines available on how to implement, what data set to collect, the appropriate software to enter their data, validate it, produce reports and do statistical monitoring – much of it at the push of a button.'

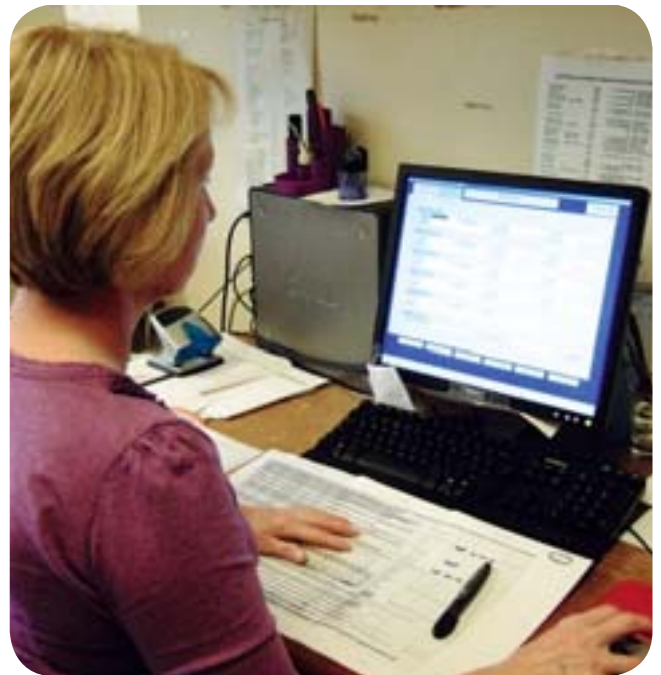
'Our reasons for networking are clear,' says Prof. Dolk. 'By so doing, we can share resources and expertise to tackle EU health problems together, pool data for greater statistical power, and compare data between countries. New countries are set to join in the near future and we are hoping that we will be represented in at least every EU country.'

### **Building on a long-standing network**

EUROCAT is an example of a registry project where the power of surveillance and networking across Europe, particularly through online databases, has become evident.

Originally conceived in 1974 at an EC workshop to improve 'the methodology of population studies throughout the Community', the EUROCAT database was established in 1979. The central registry was transferred from Brussels in 2000 to the University of Ulster, Northern Ireland.

Financial support from the EU (Public Health Programme) is ongoing, with EUROCAT recently receiving funding as a Joint Action between the European Commission and the Member States. 'As part of that, we really want to put the primary



*Data entry at one of the congenital anomaly registers in the UK*

prevention of congenital anomalies into national plans for rare diseases in collaboration with EUROPLAN so that we're taking the information and evidence about risk factors we produce a step further and we're making sure it converts to action on primary prevention,' Prof. Dolk explains.

Preventing congenital anomalies pre-conception can be quite a challenge. Campaigns that promote pre-conception care, for example, folic acid supplementation, do not always reach their target audience.

***'Our hope for the future is that we can have a real impact on the primary prevention of congenital anomalies.'***





EUROCAT Registry Leaders' Meeting, Dublin 2010

***'Every year in the European Union 120 000 babies are diagnosed with a major congenital anomaly.'***

Professor Dolk explains that 'our registry network has made a difference, in showing, unfortunately, that the folic acid opportunity for prevention of neural tube defects, such as spina bifida, has not been realised and new and more effective policies are therefore needed. That's why you need registries, to monitor the impact of prevention policies.'

As Prof. Dolk stresses, EUROCAT focuses on the prevalence, primary prevention and pre-natal screening of congenital anomalies. Our role is around epidemiologic information and scientific evidence, not advocacy, but we also try to make sure that our information and evidence reaches the policy makers. Our hope for the future is that we can have a real impact on the primary prevention of congenital anomalies,' says Dolk.

## **CONTACT**

**EUROCAT Central Registry is at:  
Room 12L09, University of Ulster  
Newtownabbey, Co Antrim  
Northern Ireland, BT37 0QB**

**Tel: +44 2890366639**

**Fax: +44 2890368341**

**Email: [eurocat@ulster.ac.uk](mailto:eurocat@ulster.ac.uk)**

**[www.eurocat-network.eu](http://www.eurocat-network.eu)**

# Evaluation of population Newborn Screening practices for rare diseases in the EU

This project, awarded in 2009 sets out to identify and evaluate all aspects which influence the implementation of a public health action in Newborn Screening (NBS). This tender has been commissioned by the European Commission (DG SANCO) and has been awarded to the Italian National Centre for Rare Diseases (National Institute for Health, Rome).

Antoni Montserrat is the EU Policy Officer for Rare and Neurodevelopmental Diseases. He explains why he feels this project is so important: 'There is currently a wide variety of practices related to NBS across the EU, primarily as a result of the development of new diagnostic tests. This results in very different situations, whereby an EU citizen may be screened for a widely varying number of diseases, depending on the country of residence.'

The impact on inequalities is self-evident. In the absence of clear criteria, EU citizens will want to access the tests that they are unable to find in their own countries.

The widely referred to 'Wilson and Junger' criteria, for decision-making on screening, date back to 1964, before dramatic developments occurred in diagnostic techniques. Several other criteria have been debated since then, but there is no commonly used set of criteria. It is time to make a step forward to cope with the new challenges posed by both the current diagnostic possibilities and the integration of quality NBS in different health systems.'

NBS practices and policies will be mapped in the whole European Union and analysed on the basis of current expert methodologies and stakeholders' views. As a public health initiative, NBS should be feasible and sustainable and demonstrably improve individual and population health.

Challenges and opportunities resulting from NBS implementation will be identified and solutions proposed, accompanied with the information necessary to let national authorities make informed choices. Finally, the feasibility of supporting actions at the Community level will be explored.

Ultimately this work will deliver a consensus on the development of European policies in NBS practices for rare diseases.

## EU NETWORK OF EXPERTS ON NEWBORN SCREENING



### Screening for rare diseases early in life

NBS is the process of testing babies for treatable genetic, endocrinological, metabolic and haematological diseases. Screening for phenylketonuria was introduced in the late 1960s and primary congenital hypothyroidism in the 1970s; both screenings were rapidly adopted across Europe. The development of new techniques in the early 1990s led to a large expansion of potentially detectable congenital metabolic disorders.

Additional tests have been added to many countries' screening programmes over the last two decades. NBS has been adopted by many countries around the world, although the list of screened diseases varies widely from country to country.

A number of factors should influence the decision to screen newborns for rare diseases:

- The screened condition should be regarded as an important health problem
- Diagnosis before the onset of clinical symptoms allows a reduction in the health consequences



- A treatment or intervention is available that will make a difference if the disease is detected early
- A simple and reliable test is feasible, which is acceptable to the general public
- The cost of screening should be balanced against the cost of medical care

Although the consensus is that all these factors should be taken into account, this is often not the case. More and more diseases

are screened for at birth, which do not fulfil all these criteria. Having the technology to perform the early diagnosis does not necessarily correlate with an ability to treat the condition.

#### **Understanding Newborn Screening practices in Europe**

There is a need to identify the current practices for Newborn Screening in EU Member States. The priorities will be to address the policies that underlie NBS, its integration as a key mechanism in national health care systems and the impact NBS has in the wider public health context.

### Expected Outcomes of the Newborn Screening tender

NBS Tender Expected Outcomes	Aims
Report on the practices of NBS for rare disorders.	This report will describe the main features of the existing NBS practices, including the number of centres, estimates of the number of infants screened, numbers of disorders screened and the reasons for their selection.
Expert opinion, including a decision-making matrix, on the development of European policies in the field of Newborn Screening for rare diseases.	This document is intended to provide a reference set of criteria, encompassing both general issues and specific health system conditions, which the national health authorities in EU may use to influence their decisions on the development of national NBS programmes.
Establishment of a European Union Network of Experts on Newborn Screening (EUNENBS).	This network of experts will analyse the information and make recommendations on best practices.
A European Experts Consensus Workshop on Newborn Screening.	This Workshop will be organised with the participation of experts and the competent authorities of the EU Member States with the main aim of reaching a consensus on the Expert Opinion document and the decision-making matrix.

Key questions that arise are:

- On what basis are rare diseases screened?
- What influences the decision to add a disease to the list?
- Which technologies are used?
- What organisation is in place to ensure comprehensive screening of all newborns and to evaluate the performance of the programmes?

It is early days for this initiative but the signs are encouraging. A first meeting has been convened with experts active in European scientific and professional associations (who are involved in NBS) and representatives of the key European alliances of rare disease patients.

With the collaboration of these participants, a comprehensive survey is being carried out on current NBS practices. Member States have been invited to set up the health authority component of EUNENBS and the criteria for the selection of additional experts to be included in the EUNENBS directory have been agreed.

‘We are certain that this work will lead to a change in the way NBS is carried out across Europe,’ says Antoni Montserrat. ‘By establishing a consensus amongst experts, NBS can be rationalised across Europe to minimise inequalities in access to health services. Newborn health is, and should be, a prime focus of European health policy.’



***'Newborn health is,  
and should be, a prime  
focus of European  
health policy.'***

#### **CONTACT**

**Antoni Montserrat Moliner**

**Health and Consumers General-Directorate (DG SANCO)  
Directorate C: Public Health and Risk Assessment – Unit C2  
European Commission  
HTC 00/071, L-2920 Luxembourg**

**Tel: +352 430133249**

**Fax: +352 430131050**

**Dr Domenica Taruscio  
National Centre for Rare Diseases  
Istituto Superiore di Sanità  
Viale Regina Elena, 299, I-00161 – Rome, Italy**

**Tel: +39 0649904016**

**Email: [tendernbs@iss.it](mailto:tendernbs@iss.it)  
[http://www.iss.it/cnmr/prog/cont.  
php?id=1621&lang=1&tipo=64](http://www.iss.it/cnmr/prog/cont.php?id=1621&lang=1&tipo=64)**

**CARE-NMD**

An EU-funded project to implement best-practice standards of care for Duchenne Muscular Dystrophy (DMD) across Europe, by bringing together a network of leading care centres.

**ECORN-CF**

European Centres of Reference Network for Cystic Fibrosis.

**EUNENBS**

Establishment of a European Union Network of Experts on Newborn Screening.

**EUROCARE**

EUROpean CAncer REgistry – based study on survival and CARE of cancer patients – is a cancer epidemiology research project on survival of European cancer patients.

**EUROCAT**

EUROpean Concerted Action on Congenital Anomalies – a European network of population-based registries for the epidemiologic surveillance of congenital anomalies.

**EUROPLAN**

European project for rare diseases national plans development.

**EURORDIS**

EUROpean Organisation for Rare DISeases – EURORDIS is a non-governmental patient-driven alliance of patient organisations representing more than 434 rare diseases patient organisations in over 43 countries.

**Orphan Drugs**

Medicines that are intended for the diagnosis, prevention or treatment of rare diseases. Pharmaceutical companies are reluctant to develop such drugs under normal market conditions. Without EU incentives, the cost of bringing such drugs onto the market is not recovered by the expected sales.

**Orphanet**

A portal of information on rare diseases and orphan drugs.

**RARECARE**

Surveillance of rare cancers in Europe.



