RARE DISEASE PATIENT SOLIDARITY

Centres of Expertise

EUROPEAN WORKSHOP

ON CENTRES OF EXPERTISE AND REFERENCE NETWORKS FOR RARE DISEASES

REPORT

PRAGUE
12 – 13H JULY 2007

EUROPEAN WORKSHOP on CENTRES of EXPERTISE and REFERENCE NETWORKS for RARE DISEASES

CREDITS 4

EXECUTIVE SUMMARY 5

Rationale 5

Facts – EurordisCare survey – preliminary results 5

Outcomes 6

FORWORDS 9

WORKSHOP OBJECTIVES AND PROGRAMME 10

THE EU CONTEXT – THE HLG ON HEALTH SERVICES AND MEDICAL CARE AND RDTF 12

High Level Group on health services and medical care (HLG-HSMC) 12

State of the art and recommendations from the rare disease task force 17

PRESENTATION OF SELECTED NETWORKS 21

Establishing a European Reference Network supported by DG Sanco: practical experience 21

Euro-SCA, a network supported by DG research 27

Debate 28

EURORDIS SURVEY OF PATIENTS' EXPERIENCES AND EXPECTATIONS 30

Debate (in direct relation with the EurordisCare survey) 34

FEEDBACK FROM NATIONAL WORKSHOPS 37

Question 1: Needs and expectations 38

Question 2: proposals for the evaluation of centres of expertise 43

Question 3: Cooperation with other countries 45

Debate 48

SUMMARY PROPOSAL (DRAFT FOR DISCUSSION) 51

Debate **53**

METHODOLOGY TO ASSESS THE OUTCOMES OF EUROPEAN REFERENCE NETWORKS **55**

Discussion based on the proposals to the High level group **55**

Assessing centres of expertise for rare diseases **57**

Debate **59**

THE WAY FORWARD FROM THE COMMISSION'S PERSPECTIVE **61**

ANNEXE1: PARTICIPANTS **66**

ANNEXE 2: OVERALL PRESENTATION OF NATIONAL WORKSHOPS **69**

CREDITS

A WORKSHOP ORGANISED IN THE CONTEXT OF THE RAPSODY PROJECT CONDUCTED BY

The European Organisation for Rare Diseases **(EURORDIS)**

AND ITS PARTNERS

Association Francaise contre les myopathies AFM-Telethon, France

Barretstown, Ireland

Climb (Children Living with Inherited Metabolic Diseases National Information Centre for Metabolic Diseases), United Kingdom

Frambu, Norway

Fundacio Doctor Robert, Spain

Orphanet/ Inserm, France

Rare Disorders Denmark, Denmark

State Institute for Drug Control (SUKL) , Czech Republic

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Groupe Initiatives Mutuelles UGIM, France

EXECUTIVE SUMMARY

On 12th and 13th July 2007, eighty patient, health care, EU and national policy maker representatives, all involved and committed to rare diseases, brainstormed approaches to improve the delivery of care for patients living with a rare disease. The central theme was the creation and development of national centres of expertise, and European reference networks for rare diseases.

RATIONALE

The workshop was hosted under the auspices of the Czech State Institute for Drug Control, SUKL. It was an achievement of the Rare Disease Patient Solidarity project, conducted by Eurordis and its partners, and supported under the DG SANCO European Community Public Health Programme.

It followed a series of national workshops organised in the Czech Republic, Denmark, France, Germany, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and United Kingdom on the same theme. A wide survey among patients themselves from twenty three European states gathered information about the expectations and experiences of patients and families regarding the organisation of care for sixteen different rare diseases (EurordisCare survey).

It was an opportunity to learn more publicly about the concepts of centres of expertise and reference networks as developed by the High Level Group on Health Services and Medical Care, and to discuss the findings of the DG SANCO Task Force on Rare Diseases which published its latest report on the subject in November 2006.

From this catalogue of facts, figures, ideas, comments, suggestions, and proposals, participants were invited to detail what they expected from a European policy in this area and how they envisaged the designation of such centres, the cooperation between them both at national and European level and the evaluation of their outcomes.

This exercise is a very real effort to improve the lives of people living with a rare disease, through improving the organisation of care, improving communication between various health care professionals involved in daily care management, reducing the time take to obtain accurate diagnosis, agreeing treatment and care guidelines, providing expert advice and ensuring patients are treated at specialist centres where the best possible care is available.

FACTS – EURORDISCARE SURVEY – PRELIMINARY RESULTS

2,853 questionnaires were received from 60 patient organisations in 13 countries: Austria, Belgium, Denmark, France, Germany, Hungary, Ireland, Italy, Slovakia, Spain, Sweden, Switzerland and United Kingdom.

The authors are recommending not disseminating these results. Only results from the final analysis that will be presented in November 2007 at the European Conference on Rare Diseases.

When a rare disease is diagnosed: **18% of families move to a different location** following diagnosis; 60% to find a better adapted house, **11% to live closer to a specialist, another 11% to live closer to a care centre**, and 18% to live closer to relatives.

12% of patients do not have access to the medical service they need: not so much due to lack of adequate care (~24%), as to the fact that they were **not referred to the appropriate consultant or treatment centre (~59%)**. Other reasons included waiting time, distance and cost of journey.

Most families and patients need assistance to travel to the care centre: this was reported by 63% of respondents.

On accessing the required treatment centre or consultant, **19% of patients faced immediate rejection** by the health care professionals they were visiting: in 80% of cases due to the complexity of the disease, and in 10% of cases, according to the patient, due to the physical symptoms of the disease.

For 30% of patients, it was difficult, very difficult or impossible to get access to a social worker.

The most widespread demand was for **coordination within centres (between different health services and professions)** (essential for ~75% of respondents), for communication with other centres for expert advice (~70%), for coordination with and between local care centres (~70%), and for a closer link with research (~65%).

OUTCOMES

Expectations and needs

Only **multidisciplinary approaches** can be effective in providing adequate care. Rare diseases are complex diseases involving different medical specialties and a wide range of paramedical healthcare professionals working in close collaboration with social workers. Centres and networks that succeed in organising care through a multidisciplinary approach are on the right track.

To be effective, close **communication** is vital:

- within centres, between all professions
- between centres, highly specialised ones and less specialised ones that are easier to access or closer to where the patient lives
- within networks, combining European and international knowledge of rare diseases to adopt consensus guidelines on how best to treat individual rare diseases and to co-ordinate research

No patient should feel neglected because he cannot be treated at a well-known highly specialised centre led by a leading international expert which is situated hundreds or thousands of kilometres from where he or she lives. No patient should think that the local hospital where he or she can be treated rapidly when the need arises is a stopgap or second-best. Other medical teams could instead give better care to their patients by learning from care centres designated as expert. Any centre applying for qualification or accreditation in line with a set of standards established for the care of a given disease or group of diseases would thus ensure that patients benefit from the **network's expertise** of care. It will no longer be necessary to travel long distances to see an expert, in fact the expert will communicate with the treating practitioner and medical team via telemedicine, training seminars, treatment consensus conferences and medical staff exchanges etc.

Health care professionals need time to communicate properly between them. This time has to be recognised and rewarded accordingly:

- Development of best practices, standards and guidelines for diagnosis, treatment and care of rare diseases at international level
- Dissemination of European reference diagnostic and therapeutic protocols will ensure equity at EU level by reducing the impact of the "post code lottery" and will increase trust in local services
- Provision of expert opinion, confirmation of diagnostic and therapeutic options

Main criteria for the designation of centres of expertise

1. Two essential pre-conditions:
   - Professional qualification: both clinical and scientific experience. Proven qualification documented by publications and grants and pre-existing certification or accreditation.
   - Commitment to cooperate and share information.
2. Patient access to a multidisciplinary team of experts
3. Combine research and care
4. Report volume of relevant activity
5. Importance of coordination between professionals
6. Importance of global approach (holistic, comprehensive) integrating medical and social aspects
7. Participation in research activities at European and international level
8. Perform education, information and communication outreach activities with the public and primary health care professionals
9. Perform training activities for health professionals
10. Perform activities to empower patients and collaborate with patient organisations

Additional criteria for the funding of European reference networks

- 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
- Involvement in epidemiological surveillance, such as registries
- Close links and collaboration with other expert centres at national and international level and capacity to network
- Appropriate arrangements for referrals of patients from other Member States established within a framework

Methods for evaluation

A general agreement is that European reference networks should be:

- Initially evaluated and accredited at EU level via an agreed set of criteria (minimum set of standardised criteria and objectives)
- Regularly assessed on common indicators with soft values and hard values

Centres should define their goals when applying for designation and these goals should serve for the evaluation of their activities: have they met their objectives after three or five years?

Common standardised criteria for evaluation

Soft values	Hard values
Co-operation with patient organisations	Time to diagnosis
Patient-orientated approach	Waiting time
Improved outcomes	Genetic consultancy
Improved atmosphere	Multidisciplinary approach
Improved quality of life	Co-operation with other centres (clinical and laboratory)
Avoiding unnecessary complications	Registries
Awareness and knowledge dissemination (to patients and to society)	Care guidelines and recommendations
Information provision to local centres	Quality control
	International and national networking
	Economic assessment

It will always be very difficult to dissect out whether improved outcomes (reduced mortality or morbidity, improved quality of life) are a result of the network or of the centre of expertise where care is provided.

Birthe Holm, Rare Disorders Denmark – leader of the work package on centres of expertise / Rapsody project

A warm welcome to you all in the wonderful city of Prague! I am from RDD, the Rare Disorders Alliance in Denmark, and partner in the Rapsody project, with the leadership of Work Package 8 about centres of expertise and reference networks. This workshop is one of the many activities of the Rapsody project.

After having read all the reports of the national workshops, I am convinced we shall have a very good workshop these next two days. I would like to thank both Martin Benes and Maryna Krenkova for their precious help in organising this workshop, and also the Eurordis team.

Martin Benes, director SUKL, Czech Republic

Just a few words from the representative of the State Institute for Drug Control, SUKL. This is the first patient-orientated activity of this institute that I have the pleasure to be hosting, as most of the institute's activities generally involve health care professionals. Patients' needs are not always at the centre of our preoccupations, but they should be.

We are facing various challenges, as SUKL is gaining new competences. In the next few months, our institute will also be responsible for the pricing and reimbursement of new drugs. This will be particularly important for orphan drugs, and I am confident patient organisations will become our day-to-day partners in the near future.

Welcome again, and I wish you a fruitful workshop.

Jiri Hruda, Huntington Disease Association, Czech Republic

Dear Birthe Holm, dear Mr. Beneš, dear Maryna, Ladies and Gentleman,

My name is Jiri Hruda and I am a member of the Board of the Czech Huntington Disease Association.

Allow me to welcome you all as participants at this congress on behalf of the Czech HDA and the organising committee, especially Birthe Holm and Mr Beneš, the director of State Institute for Drug Control.

I want to thank you very much Mr. Beneš for providing this venue and for all the necessary background support. Many thanks to Maryna Křenková for her role in organising this workshop and thanks to the former director of SÚKL, Mr. Milan Šmíd too.

As I remember, I was contacted by Maryna Křenková in October 2006 and soon after by François Houÿez and Birthe Holm. Czech HDA was the only member of the European Organization of Rare Diseases from Czech Republic. We were invited to take part in the organisation of the national workshop on national centres of reference and European networks of centres of reference for rare diseases.

Yes, this was something special that I could hardly have imagined. But since then we have met several times at meetings of the organising committee. I am very glad to have the opportunity to meet people from different patient organisations having the same interest in doing something for the future of patients, family members and people at risk of disease.

The Czech national workshop was held 3rd March this year and altogether there were 39 participants. Most importantly, there were representatives of 13 different patient organisations as well as professionals and representatives from the Ministry of Health, Ministry of Labour and Social Affairs, Health Insurance Company and State Institute for Drug Control. The whole workshop was very interesting. I do believe that everything said there will be acted upon.

You will hear the conclusions of the individual national workshops soon, and so allow me to wish you well in today's and tomorrow's discussions.

Have a nice time here at the congress and in Prague too.

WORKSHOP OBJECTIVES AND PROGRAMME

1. To address the needs and expectations primarily of patients and families and also of health professionals and policy makers regarding:

    a. Centres of expertise for rare diseases

    b. European reference networks of centres of expertise

2. To develop recommendations for:

    a. Principles and criteria for the identification of such national centres of expertise and European reference networks

    b. The evaluation of their respective outcomes

First day
Introduction 11.00 to 12.00 am Co-chairs: Birthe Holm (Rare Disorders Denmark) , Martin Benes (SUKL State Institute for Drug Control) ▪ Welcome speech: **Jiri Hruda**, Czech patient representative ▪ Workshop objectives: **François Houÿez**, Eurordis, EU ▪ Presentation of the proposals of the High Level Group on Health Services and Medical Care: **Dr Alexandra Fourcade**, Ministère de la Santé France ▪ Presentation of the DG Sanco Rare Disease Task Force report: **Dr Ségolène Aymé** , DG Sanco Rare Disease Task Force, EU **Presentation of selected networks 12.00 – 1.00 pm** Co-chairs: Birthe Holm (RDD), Maryna Krenkova / Martin Benes (SUKL) ▪ Establishing A European Reference Network: practical experience: **Dr Laura Fregonese**, Patients' Association and AIR Registry, Netherlands ▪ Cystic fibrosis, a network supported by DG Sanco: **Prof Thomas Wagner**, Goethe University Frankfort, Germany ▪ EuroAtaxia, a network supported by DG Research: **Prof Olaf Riess**, Tübingen University, Germany
EurordisCare Survey results, 2.30 – 4.30 pm Co-chairs: Yann Le Cam, Eurordis and Rosa Sanchez de Vega, FEDER, Spain ▪ Survey on patient experience and expectations in access to health services (EurordisCare3): **Dr Pierre Chauvin**, (Inserm), France
Second day
Synthesis of national workshops 9.30 am – 1.00 pm Chair person: Terkel Andersen / Maryna Krenkova ▪ Overall Presentation national workshops: **Yann Le Cam**, Eurordis, EU ▪ Summary responses to question 1: **Christel Nourissier**, Prader Willi France ▪ Summary responses to question 2: **Melissa Winter**, Genetic Interest Group, United Kingdom ▪ Summary responses to question 3: **Birthe Holm**, RDD, Denmark ▪ Summary of proposals: **Yann Le Cam**, Eurordis
Methodology to assess the outcomes of European Reference Networks, 2.30 to 4.00 pm Chair person: Prof Olaf Riess ▪ Discussion based on the proposals to the HLG June meeting: **Dr Edmund Jessop**, NCG UK ▪ Description of the evaluation plan as proposed by the French policy: **Marie-Claude Hittinger**, Haute Autorité de Santé France
Closing remarks 3.45 to 4.00 pm ▪ The way forward from the Commission's perspective: Toni Montserrat, DG Sanco, EU

HIGH LEVEL GROUP ON HEALTH SERVICES AND MEDICAL CARE (HLG-HSMC)

The political process that inspired the reflection on centres of expertise and reference networks for rare diseases at the European level started in 2003, with a High-level reflection process on patient mobility and healthcare. Among other developments, it was concluded that European centres of reference could provide healthcare services for conditions requiring a particular concentration of resources or expertise and also contribute to medical training and research, information dissemination and evaluation.

A recommendation to the Commission was made: the Commission, in collaboration with the Member States, should carry out a mapping exercise relating to centres of reference and to explore how to foster networking and cooperation on these issues, including the organisation, designation and development of centres.

The following year in 2004, a Commission Communication 'Follow-up to High-level reflection process' – confirmed the importance of the work on European centres of reference. A High Level Group on Health Services and Medical Care (HLG) was established, consisting of meetings of senior officials from health ministries, to be held approximately four times a year.

A HLG working group on European reference networks was created: chaired by France, with the European Commission providing secretarial support, composed of senior officials from the national health ministries and, with external input (Rare Diseases Task Force, European Hospital and Healthcare Federation, EURORDIS and health professionals working in this area, invited on *ad hoc* basis).

A first meeting took place in September 2004, with the agreed objective to work towards a common approach on the organisation, designation and development of European centres of reference, which could then be implemented through pilot activities, taking into account ongoing activities at national level.

A questionnaire on the situation in Member States highlighted very different situations. The area of rare diseases was identified as a starting point for discussions in the 'experimental stage'. However, the overall aim was to develop a general system of European reference networks, not limited to the area of rare diseases only.

In 2005, the Task Force on Rare Diseases (RDTF) was mandated by the HLG Working Group on ERN to provide technical and scientific input which resulted in the 2005 RDTF report on European centres of reference for rare diseases (including a mapping exercise on national centres of reference/expert centres for rare diseases), followed by a second RDTF report on European centres of reference for rare diseases in 2006.

Agreed general principles (2005 HLG report)

- Networking of reference/expert centres rather than isolated centres should be favoured.
- Hierarchy between national (or regional) reference/expert centres and networks versus European reference networks should be avoided.

- In principle, expertise (professionals, samples, information) should travel rather than patients themselves. However, it should be possible for patients to travel to centres where this is necessary.

Criteria to be fulfilled by centres of expertise

In 2005, the following criteria for European centres of expertise were agreed (2005 HLG Report):

- appropriate capacities to diagnose, to follow-up and manage patients with evidence of good outcomes so far as applicable;
- sufficient activity and capacity to provide relevant services and to maintain quality of services provided;
- 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;
- demonstration of a multi-disciplinary approach;
- high level of expertise and experience documented through publications, grants or honorific positions, teaching and training activities;
- strong contribution to research;
- involvement in epidemiological surveillance, such as registries;
- close links and collaboration with other expert centres at national and international level and capacity to network;
- close links and collaboration with patient organisations where they exist.

Criteria to be fulfilled by European reference networks (ERN)

- Although European reference networks should fulfil most of the above criteria, the comparative relevance of those various criteria will depend on the particular disease or group of diseases covered.
- This list of criteria could also be revised following the outputs coming from the pilot projects on ENR.

Areas to be covered by ERN

2005 HLG report: priority areas should be determined at EU level, drawing on national experiences, on the basis of the following indicators:

- Diagnosis (when the diagnosis is difficult and is necessary for informing clinical management, to prevent complications and to set up treatment).
- Therapeutics and management (when treatment requires expertise and specialist intervention).
- Outcome (when patients are at high risk of developing severe complications or disabilities which are preventable).
- Technology and therapeutic innovations.
- Organisational and governance issues.
- Main focus of the work of WG ERN in 2006.

- ‘Options for a procedure for identification and development of ERN’ have been developed and submitted to ministers for consideration.
- These options could be used to identify already existing EU networks and to support their development as well as to support the establishment of new networks.
- Whichever proposed option is chosen, the necessary standards of transparency should be ensured throughout the process.
- Continuing compliance with criteria and evaluation of ERN should be ensured.

Organisational and governance issues

- **Option 1 – Adaptation of existing EU mechanisms (such as Programme of Community action on public health)**

Pros

- does not require major structural change
- relatively easy to execute in the short-term

Contras

- very limited in terms of budget and time
- does not guarantee long-term sustainability for the networks
- does not address related practical, financial and legal issues specific to ERN

- **Option 2 - New specific EU mechanism for European reference networks (including distribution of tasks between national authorities and a Committee of Member States)**

or

- **Option 3 – New specific ‘concentrated’ procedure at EU level (most of the competences concentrated in a Committee combining Member States, the Commission, health professionals and patient representatives)**

Pros

- provide long-term sustainability for the networks
- opportunity to address specific practical problems, including financial and legal issues

Contras

- require new specific instrument, so lengthy EU inter-institutional negotiations
- require specific allocation of resources from the Community budget

These options may still be modified on the basis of the outcomes of the pilot projects on ERN, and on the outcomes of the Rapsody project (national and European workshops on ERN).

These options should be now discussed thoroughly at the political level, i.e. by the Council of EU health ministers - a political orientation on whether these principles and options represent a good basis for future work would facilitate further progress on this issue.

Pilot projects

Objective

- To test feasibility of the general principles, criteria, areas and processes agreed so far.
- To see how this approach could be applied in practice for a specific disease, group of diseases, group of Member States or other focal principles, building, where appropriate, on existing centres, expertise or networks.
- To identify any specific (practical) problems for further consideration.

Supported under the Commission's Public Health Programme (2006 call for proposals), and with rare diseases as a priority area.

Pilot projects

- European Network of Centres of Reference for Dysmorphology (Project leader - University of Manchester, UK)
- European Centres of Reference Network for Cystic Fibrosis (Project leader - Klinikum der Johann Wolfgang Goethe-Universität, Germany)
- Establishment of a European Network of Rare Bleeding Disorders (Project leader - Università degli Studi di Milano, Italy)
- European Porphyria Network: providing better healthcare for patients and their families (Project leader - Assistance Publique - Hôpitaux de Paris, France)
- Patient Associations and Alpha1 International Registry (Project leader - Stichting Alpha1 International Registry, the Netherlands)

More details on the projects at:

http://ec.europa.eu/health/ph_threats/non_com/rare_8_en.htm#4

2006 Recommendations

- The name of the working group should be changed to "Working group on European reference networks". This better reflects the concept on which the working group is working.
- The definition of common principles and criteria for the identification and development of European reference networks should be adopted at the European level and should be based on the principles and criteria as defined in the 2005 report of the High Level Group, supplemented by additional details specifically related to networks.
- The development of a methodology to assess the benefits of establishing and supporting European reference networks from the perspective of different stakeholders should be supported by the Commission, e.g. within the Public Health Programme, Research Framework Programmes or other structures.
- The Council should discuss thoroughly the options for identification and development of European reference networks developed by the working group. These options may still be modified on the basis of the practical outcomes of the pilot projects. From a long-term perspective, however, a political orientation on whether these principles and options represent a good basis for future work would facilitate further progress on this issue.

Plans for future work

- To follow closely the ERN pilot projects supported under the 2006 call for proposals and to use the practical experience gained from these pilot projects in future work.
- To consider how the principles developed and the experience gained so far, mainly in the context of rare diseases, could be applied to other areas beyond rare diseases (for example to therapeutic and technology innovations).
- To focus further on outstanding legal and financial aspects of ERN.
- To examine whether and how the work on ERN could benefit from or could be linked with the upcoming EU 'Community action on health services' (Public consultation closed on 31 January 2007, proposals to follow in 2007; more info at http://ec.europa.eu/health/ph_overview/co_operation/mobility/patient_mobility_en.htm).
- The working group should continue to work in close cooperation with other actors involved in this issue, such as the Task Force on Rare Diseases, EURORDIS, patient representatives and hospital and health professionals.

More information can be found on the following websites:

- HLG on Health Services and Medical Care (including working group on European reference networks) (http://ec.europa.eu/health/ph_overview/co_operation/mobility/high_level_hsmc_en.htm)
- EU co-operation on rare diseases (http://ec.europa.eu/health/ph_threats/non_com/rare_diseases_en.htm)
- Task Force on Rare Diseases (http://www.rdtf.org)

STATE OF THE ART AND RECOMMENDATIONS FROM THE RARE DISEASE TASK FORCE

Dr Ségolène Aymé, leader of the DG SANCO Task Force on Rare Diseases.

Centres of reference have always existed in practice, as a hierarchy of knowledgeable experts, teachers and authors of articles, leaders of opinion, with technical platforms in the richest institutions with developed services and/or research institutions with innovative services.

Historically however, the information has been restricted to a few professionals and resources allocated without objective criteria.

The rationale to push for a more formal approach to designate centres of expertise for rare diseases was:

1/ Budget constraints in university hospitals: an annual budget to serve the area population, strict budget for research activities and analytical budget.

2/ New regulation of clinical research: increased administrative constraints and higher costs

3/ Accessibility of information via the Internet: medical second opinions possible by phone, fax and e-mail in an environment where patients have more opportunity to travel and enlarge their choice of medical services

Though patients are rare, experts are rare too, and the need to identify them has always been a priority. Necessary expertise often may be found only at international level, and it is impossible for most countries to offer appropriate services to all patients.

Clinical research with large cohorts of patients and the systematic collection of data is needed to develop treatment and care guidelines and recommendations.

Travelling from one centre to another presents many drawbacks for patients:

1. Financial constraints: cost of travel and accommodation;
2. Communication constraints: more than 20 European languages and cultural differences;
3. Logistical constraints: hospital services have a limited number of beds and clinics.

The Rare Diseases Task Force was asked to provide an overview in a report to the High Level Group for Health Services and Medical Care based on these factors:

1. The rationale for developing European collaboration is well established
2. The concept of centres of reference is understood as a centre to which patients may be referred and implies that:
   - distance between home and the centre is not too far
   - costs are covered by the health care system
   - doctors, physicians and patients speak the same language
   - the centre is able to accommodate referred patients

“Centre of reference” is a term used only by a few Member States:

Specific to rare diseases: Sweden (1990), Denmark (2001), Italy (2002), France (2004), Bulgaria (2007) and Spain (?).

Not specific to rare diseases: Belgium, Czech Republic, Finland, Greece, Ireland and United Kingdom.

"Centre of reference" is recognised as a concept in all Member States:

Countries with identified, unofficial "centres of reference" include Austria, Cyprus, Estonia, Germany, Hungary, Lithuania, the Netherlands, Poland, Portugal, Romania, Serbia, Switzerland and Turkey.

The definition of a centre of reference differs from one country to another based on differences in:

- The definition of a rare disease
- Size of the population served
- Mission/task
- Number of diseases covered
- Identification process of a centre of reference
- Financial support
- Purpose of the establishment of a centre of reference

Areas of disagreement within the Task Force:

1. Risk/benefit analysis
   - In favour of centres of reference: improved access for EU citizens, maximised cost /effectiveness, facilitated shared knowledge and training
   - Not in favour of centres of reference: distant referral and long waiting lists, psychological burden in respect of differing languages and isolation, loss of trust in local services, loss of interest by professionals not part of the centre of reference
2. Activity
   - Disease centred: by disease, by medical specialty
   - Technology centred: surgery//highly specialised treatment
   - Social support centred: multiple handicap/familial dimension
3. Geographical coverage of centres
   - European centres
   - National centres
   - Regional centres

     And at which respective level to designate and fund the centres? European, national or regional level?
4. Structure
   - Centres of reference: national and regional centres to which patients may be referred

- Or networks of centres of reference, with highly developed communication, good practice guidelines and sharing of expertise.

From concept to reality

The Task Force envisaged different solutions to ensure the European dissemination of these concepts, the publication of experiences, a follow-up of national initiatives and a definition of responsibilities: European networks (European Commission and/or bilateral contracts between countries), centres of reference (Member States or regions).

Recommendations from the RDTF expert group

Recommendations to Member States

1. Explore all possible forms of cooperation between MS in the field of health services and medical care for patients with a rare disease
2. For MS having official centres of reference:
   a. Agree on their definition, mission and evaluation
   b. Share experiences and outcome measures
3. For MS not having official centres of reference:
   a. Establish centres of reference or find other appropriate methods to meet the needs of patients (by contracting with centres of reference)
   b. Develop electronic communication with centres of reference
4. Contribute to the identification of their expert centres and support them as much as possible
5. Organise health care pathways for their patients
   a. through the establishment of cooperation between all necessary expert centres on a national level
   b. and when necessary on an international level
6. Recognise and fund the activity of expert opinion

Recommendations to the European Commission

1. Avoid using the term “centre of reference” when referring to expert centres collaborating within a network and favour “centre of expertise”
2. Play an important support role in identifying centres of expertise and in diffusing information about them
3. Identify and fund collaboration between centres of expertise via “European networks of centres of expertise”
4. Continue financial support of networks of centres of expertise for rare diseases until outcomes of the networking process are evaluated
5. Open the call for proposals to the development of a methodology to assess the benefits of such networks from the perspective of the different stakeholders
6. Encourage the development of electronic tools necessary to further the use of telemedicine in the field of rare diseases

Plans for 2007

7. New report to be issued autumn 07
8. Workshop to be held
9. Workshop topic: Methods to assess the added-value of
    a. Centres of expertise
10. Reference networks of centres of expertise

ESTABLISHING A EUROPEAN REFERENCE NETWORK SUPPORTED BY DG SANCO: PRACTICAL EXPERIENCE

Dr Lara Fregonese, Leiden University, the Netherlands

Pilot reference networks (centres of reference) for rare diseases

The Work Plan 2006 for the implementation of the EU Public Health Programme introduces, as a priority in the area of rare diseases, the development of European networks of centres of expertise[1] for rare diseases. In line with this priority the following projects have been selected for funding after the call in 2006:

- European Porphyria Network: providing better healthcare for patients and their families with the Assistance Publique - Hôpitaux de Paris (FR) as Project Leader,
- Establishment of a European Network of Rare Bleeding Disorders, with the Università degli Studi di Milano (IT) as Project Leader.
- Patient Associations and Alpha1 International Registry with the Stichting Alpha1 International Registry (NL) as Project Leader,
- European Network of Centres of Reference for Dysmorphology with The University of Manchester (UK) as Project Leader,
- European Centres of Reference Network for Cystic Fibrosis with the Klinikum der Johann Wolfgang Goethe-Universität (DE) as Project Leader.

Consistent with the High Level Group recommendations, the criteria that drove their selection were as follows:

- appropriate capacities to diagnose;
- sufficient activity;
- capacity to provide expert advice;
- demonstration of a multi-disciplinary approach;
- high level of expertise & research activities;
- close links and collaboration with expert groups and support groups.

Do the projects actually meet these criteria?

To respond this question, Prof Thomas Wagner developed a questionnaire that was presented at the most recent High Level Group meeting. The first six questions addressed the establishment of the network. Telephone interviews with each project leader provide interesting answers.

[1] Centres of reference in the text of the Work Plan

1.1 How were the network partners identified in the initial stage, and how was the network formally established?

1.2 Is the network open to new partners and how are potential new partners being identified or selected?

1.3 What are the criteria for becoming a network partner?

1.4 How to assess centres and their capacity to become partners?

1.5 How to disseminate the information about the network to potential partners and patients?

1.6 Can the network be easily expanded/transferred to other diseases?

1.1 How were the network partners identified in the initial stage, and how was the network formally established?

- Established scientific/clinical collaboration (2)
- Pre-existing networks (3)
- Crucial role of scientific bodies
- Willingness to participate/commitment
- Self-sustainability (4)
- Primary/secondary partners (2)
- Attention to geographical coverage

1.2 Is the network open to new partners and how are potential new partners being identified or selected?

Yes, within the next three years of the project

1.3 What are the criteria for becoming a network partner?

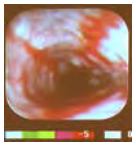
- Specific interest in the disease
- Spontaneous interest ("spreading the word")
- Geographical coverage (EU): the network should be as broad as possible, however the issue of having a centre in each Member State for each project is a difficult one. Strategies to enlarge the network rely on scientific bodies, non-specialist networks for rare diseases, patient organisations and ministries/national rare disease institutions.
- Willingness to collaborate
- Self-sustainability
- Level of competence? (minimal requirement: diagnosis)

Specific criteria:

European Porphyria Network

The main criterion is the ability to diagnose all forms of the condition. As the diagnosis is mainly biochemical, there is a model for all specialist porphyria laboratories that would apply in order to become a partner: ability to distinguish various forms of the disease, using biochemical testing; ability to offer detailed specialist interpretation of results with clinical advice, and participation in network quality assurance schemes.

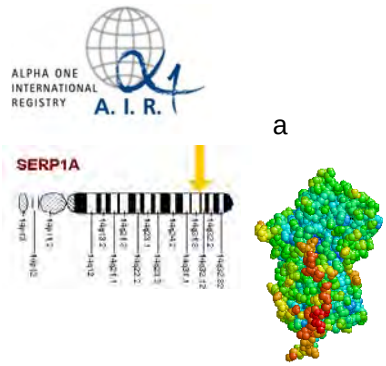
Laboratory analyses must be documented: approximate numbers of analyses per year, numbers of diagnosis per year, accreditation system, quality assessment scheme followed and numbers of inhabitants covered by the centre. In addition, recent publications relevant to porphyria (since Jan 1999) must be listed.



European Network for Rare Bleeding Disorders EN-RBD (www.rbdd.eu)

Centres dealing with RBD (reference in their country/already screened for international project) are already identified worldwide, and some will participate in the European network, provided they can transfer data into a web database, to compile an RBD registry which is a pre-requisite for FP6 project. A major exercise is to formulate an agreement on patients' data and informed consent (privacy).

PAAIR: Patients' Association and Alpha1 International Registry



This project is a collaboration between US and EU. It aims at generating a data-set of clinical items for the AIR database. Participating centres must be able to transfer data into a web-based database, register a certain number of doctor visits per year, fill-in Health Status questionnaires, store plasma and blood, perform spirometry, CO diffusion, obtain certification for biomarker detection in the lungs and measure liver function.

Dyscerne: a European network of centres of reference on dysmorphology

Primary partners: are centres with good working experience (track records on clinical diagnosis, training in dysmorphology), commitment, and self-sustainability.

Secondary partners (Submitting Nodes): are centres that will receive training on how to use the electronic system, with the aim of ensuring the largest possible geographical coverage without overlapping with each other.

In summary, the criteria common to all projects for the selection of partners were the following:

- Centres already having clinical (scientific) experience in the disease
- Or committed centres with little experience (tutorial role of the network)
- Capability to make a proper diagnosis (genetic/biological/clinical)
- Adequate geographical coverage (self-containment of the network)
- Specific sets of criteria per each disease/cluster of diseases
- Capability to join the network's web-based system

1.4 How to assess centres and their capacity to become partners?

- Steering committees
- Criteria sheets/guidelines
- Minimal set of requirements (reliability in making diagnosis)
- On-site visits possible
- Training for potential centres when necessary

1.5 How to disseminate the information about the network to potential partners and patients?

- Specific web site for each project
- Communications at international scientific meetings
- Guidelines, publications, brochures
- Patient organisations connected to the network
- RDTF and Orphanet
- Health ministries/national health agencies

1.6 Can the network be easily expanded/transferred to other diseases?

Dyscerne could be used as a model for skeletal dysplasias (diagnostic), EN-RBD as a database of monogenic rare diseases, porphyrias are different clinical entities but the expansion to other diseases are part of the pilot project, PAAIR: possible expansion to other rare respiratory diseases, and cystic fibrosis as a two-level model.

Recommendations

- Identify pre-existing realities: ongoing
- Multidisciplinary approach/clusters of diseases: whenever possible!
- Establish necessary geographical coverage (on the basis of prevalence?)
- Identify specific quality criteria when not existent (clinical and/or scientific)
- Two levels of centres?

EUROPEAN CENTRES OF REFERENCE NETWORK FOR CYSTIC FIBROSIS ECORN-CF

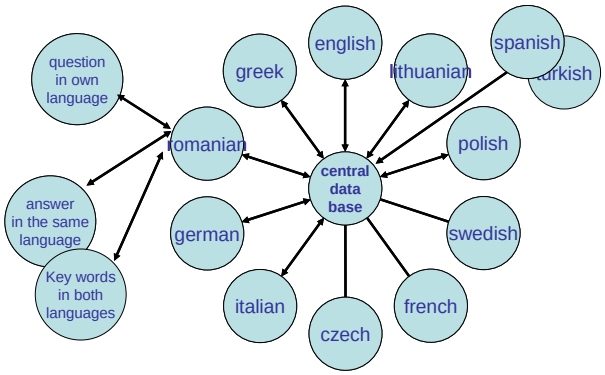
Prof Thomas Wagner, Johann Wolfgang Goethe-University, Frankfurt am Main, Germany

This project is a practical approach aimed at improving quality wherever possible in the treatment of cystic fibrosis (CF). CF is a rare disease. It is the most common (mono) genetic inborn error of metabolism in Caucasian people, making it possibly more accessible for physicians and clinicians. Twenty years ago, only 2% of patients reached the age of 18, but today approximately 50% of patients are 18 years or older. Patients still die early from pulmonary failure. Specialist care increases survival rates. Costly drugs are widely used. A European consensus of care has been established

The project: ECORN-CF: 16 associated partners from the CF care team and from patient organisations (GER, UK, BE, NL, SWE, ROM, POL, LIT, CZE) and collaborating partners (ITA, FRA, ESP, SLO, AT, DK, GR, TUR etc.). It is funded by the European Commission and Christiane Herzog organisation.

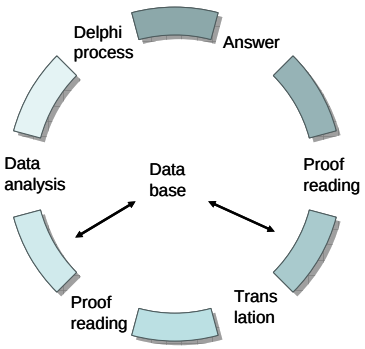
It consists of 7 work packages (3 standard WPs) with the objectives of providing expert advice to patients and to care team members, quality control measures, evaluation of quality of life, utilisation of health care provision (duration of doctor visit, nurse consultation, etc.) and implementation of the European consensus. It started 1st May 2007.

It is an expertise network, it is not a referral network: “only the information travels, not the patient”.



The exchange of information is web-based. The quality of information provided is monitored according to guidelines and rules set for the network. Patients can contact the network through the web site or via their support groups (support groups can be partners) or via their doctors.

Everyone can ask a question in their own language: for example, when a question comes in Romanian, the answer is given in Romanian and also translated for the purpose of quality assessment by the expert panel to check that it respects the guidelines. It is stored in the frequently asked questions section of the database.



It is a virtual type of expert system: it is not about care, about seeing the patient, it is responding to medical questions in compliance with guidelines and recommendations. The original question and answer are read by a second expert, then translated to English and proof read again. All questions and

answers are evaluated, key words extracted, quality assessed, and eventually a Delphi process is used to decide which question/topic needs a consensus.

In conclusion:

ECORN-CF will give equally good advice to each participating Member State and act as a model for other rare diseases.

- ECORN-CF will help harmonize levels of expertise throughout the EU
- ECORN-CF has just begun
- No kick-off meeting, so communication has been slow to start with
- ECORN-CF will only provide part of the necessary service
- Many collaborating partners want to join (full rights, full duties, no cost)

EURO-SCA, A NETWORK SUPPORTED BY DG RESEARCH

Prof Olaf Riess, Tübingen University, Germany

This project is supported through Priority 1 (Life Sciences, Genomics and Biotechnology for Health) of European Union's FP6 Contract number: LSHM-CT-2004-503304.

The Hereditary Ataxias are a group of rare diseases characterised by degeneration of the cerebellum, brain stem and spinal cord. They vary in age of onset, mode of inheritance and severity of symptoms. The most common recessive ataxia is Friedreich's Ataxia. The dominant ataxias are mostly known as Spinocerebellar Ataxia (SCA), type 1, 2, 3, 4, 5, 6 and so on. Other names used for forms of SCA are ADCA (Autosomal Dominant Cerebellar Ataxia) or OPCA (Olivo Ponto Cerebellar Atrophy).

EURO-SCA is a European integrated project on spinocerebellar ataxias: pathogenesis, genetics, animal models and therapy.

22 European groups from 9 countries with excellent reputations for clinical, clinical-genetic and basic research on spinocerebellar ataxias (SCA) jointly form an “Integrated project” to develop a treatment for patients suffering from this rare, late manifesting, and autosomal dominant inherited group of neurodegenerative diseases.

To attain this goal, an international standard on clinical evaluation in the form of a “Core Assessment Program for Interventional Therapies of SCA” (CAPIT-SCA) will be developed, based on clinical rating scales, structural imaging, and electrophysiology. The generation of the world’s largest collection of information on SCA, the European SCA Registry (EUROSCA-R), will ensure standardized data acquisition. This powerful tool will facilitate continuous recruitment of SCA patients throughout Europe for linkage analysis, identification of novel ataxia genes and natural history studies. Subsequently, for the first time such a combined effort will offer a systematic large-scale search for genetic modifier factors in SCA allowing a better comprehension of factors accounting for wide clinical variability with application for prognosis and to identify new potential targets (modifier genes) for delaying the age at onset or disease progression.

The disease provokes a dramatic situation: patients are suffering. Patients are not socially integrated, they cannot go to restaurants, they lose their friends, they have difficulty finding work, and they can even lose the confidence of the family.

The project has an important clinical aspect: to help assess the disease. The evolution of the disease is not known for most of the subtypes.

When pathogenesis is better characterised, then new tools for drug development will be available. Thus, the project proposes:

- a scale for assessment and rating of ataxia
- patient registry, natural history
- central DNA and RNA depository
- animal models
- pre-clinical treatment studies

DEBATE

Prof Vives Corron, Spain, insisted on the existence of other networks that existed prior to the call in 2006. Enerca, the European Network of Rare Anemias, is one.

Prof Joao Lavinha, Portugal, asked about the longer term sustainability of the support for European reference networks, and whether European policy would be useful to ensure their long term operation. In her response, Dr Alexandra Fourcade highlighted the importance of the Commission Communication on rare diseases, which makes the respective roles of Member States and European bodies explicit. Of the projects presented, it seems that some activities could be funded at the European level, and others would remain the responsibility of local and national authorities.

Dr Edmund Jessop expressed his personal opinion that rather than pushing for a common health policy for all diseases, that a push for a common policy for rare diseases only would be less alarming for taxpayers and health authorities alike

Inge Christensen, Denmark, highlighted the absolute necessity to include social and psychological care in the multidisciplinary approach presented by the speakers. In addition, Europe should offer instruments to help patients get together and form groups at a European level (European federations of rare disease organisations).

In her response, Dr Lara Fregonese reminded participants that most of the pilot projects started with a scientific objective. As each project proceeds, patients' expectations are measured through questionnaires and interviews, and the issue of focusing on support for patient organisations and social and psychological care has come almost automatically out of this dialogue. Prof Jean Charles Deybach seconded this view, and pointed out that it is often difficult to transform a scientific collaboration into a multidisciplinary one, even though quality of life measurement is an important outcome. The higher the numbers, the easier it is, but even for very rare diseases such as Günther's disease, it has been possible to conduct a quality of life survey among the 100 diagnosed patients in Europe.

Prof Deybach questioned the feasibility of centres of expertise in Member States such as Germany where it seems impossible to create a federal centre of expertise, due to the political organisation of the country. Prof Wagner acknowledged the difficulty, and responded that the situation has forced teams to work via networks. This has been done, there are several active research networks in Germany, and they can be the basis for clinical research networks. For Germany, a national network of regional centres of expertise is probably the solution.

As Dr Ségolène Aymé explained that some 200 specialist networks already exist, of which 5 are supported by the European Commission DG SANCO and Yann Le Cam, Eurordis, expressed the wish to continue the exercise and to further analyse the criteria used, the processes for identification and other key factors involved in the development of networks for rare diseases

REGARDING ACCESS TO HEALTH SERVICES IN EUROPE (EURORDISCARE)

Pierre CHAUVIN, MD PhD, Director for Research, Public Health and Social Epidemiology Unit, Inserm, Paris, France

IMPORTANT NOTE: These are preliminary results of an on-going survey among patients. The overall study will include 6 000 questionnaires disseminated via 120 patient organisations in 24 countries. At the time of this preliminary results, 2 853 responses from 13 countries had been received. Therefore the authors are recommending not to disseminate the current report and its related slides. Only results from the final analysis that will be presented in November 2007 at the European Conference on Rare Diseases will be broadly disseminated.

The objectives of the survey are:

- To describe and compare the experiences and expectations of patients and patients' relatives regarding access to health services in Europe
- To make the patient's voice heard at a time when several European countries are involved in the reorganisation of health services for rare diseases
- When the survey is completed, to produce comparisons:
  - between diseases
  - between countries
  - and/or between social groups

Immediately after Pierre Chauvin's presentation, these preliminary results were commented on and discussed, in the presence of several patient representatives who participated in the survey: Aniridia Italy, Prader Willi France, Prader Willi Romania, Sarcoidosis Germany, Williams syndrome Hungary, Myasthenia gravis France, Epidermolysis bullosa Spain, Ehlers Danlos France, 11Q network Netherlands, Tuberous sclerosis United Kingdom, Fragile X United Kingdom, and Osteogenesis imperfecta Denmark.

Diseases involved

The diseases involved in the survey are as follows:

- Marfan syndrome (3.00 / 10,000)
- Fragile X syndrome (1.42 / 10,000)
- Williams syndrome (1.33 / 10,000)
- Ehlers-Danlos syndrome (1.25 / 10,000)
- Cystic fibrosis (1.20 / 10,000)
- Prader-Willi syndrome (1.07 / 10,000)
- Epidermolysis bullosa (1.00 / 10,000)
- Tuberous sclerosis (0.88 / 10,000)

- Myasthenia (0.85 / 10,000)
- Osteogenesis imperfecta (0.65 / 10,000)
- Huntington disease (0.62 / 10,000)
- Ataxias (0.22 / 10,000)
- Aniridia (0.17 / 10,000)
- Pulmonary arterial hypertension (0.15 / 10,000)
- Chromosome 11q disorders (150 published cases)
- Alternating hemiplegia (about 330 families in the world, 130 in Europe)

Preliminary results of data received as of 8th July 2007

2,853 questionnaires have been received from 60 organisations in 13 countries: Austria, Belgium, Denmark, France, Germany, Hungary, Ireland, Italy, Slovakia, Spain, Sweden, Switzerland and United Kingdom. France and Spain are over-represented in the interim analysis.

By the end of the survey, questionnaires from 120 organisations in 21 countries will have been received. Diseases will be represented by at least 8 countries, allowing for country comparisons.

See table 1 below for the distribution of the questionnaires that are part of this preliminary analysis:

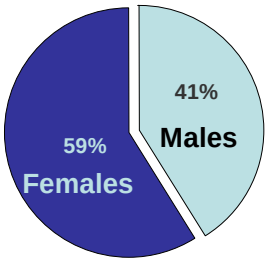
Tableau 1: origin of first 2,853 questionnaires

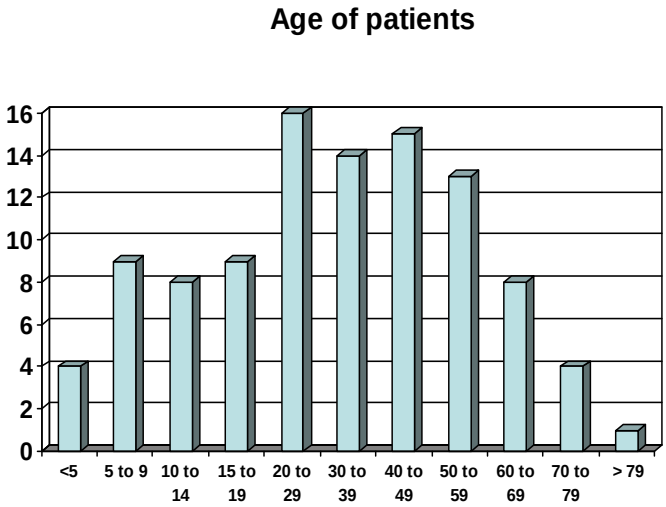
Disease	Number of questionnaires	Countries
Aniridia	43	Denmark, France, Italy
Ataxia	416	France, Ireland, Spain
Chromosome 11q disorders	5	
Cystic fibrosis	170	France, Hungary, Sweden
Ehlers Danlos syndrome	497	Austria, Belgium, Germany, Denmark, France, Spain, Sweden
Epidermolysis bullosa	90	Belgium, France, United Kingdom
Fragile X syndrome	197	Belgium, France, Italy, Spain, Switzerland, United Kingdom
Huntington disease	112	Austria, Belgium, France, Italy, Switzerland
Marfan syndrome	250	Belgium, France, Sweden, Switzerland
Myasthenia	192	France, Hungary, Italy, Spain
Osteogenesis imperfecta	112	France
Prader Willi syndrome	294	France, Hungary, Italy, Spain, United Kingdom
Primary pulmonary arterial hypertension	121	Austria, France
Tuberous sclerosis	191	Germany, France, Hungary, Spain, Switzerland,
Williams syndrome	163	Belgium, France, Hungary, Slovakia

Importantly, the response rate was over 90% for all questions, indicating that respondents filled-in the questionnaire almost entirely; there were few withdrawals during the questionnaire. No systematic biases were seen in the response distribution.

Age and gender of respondents

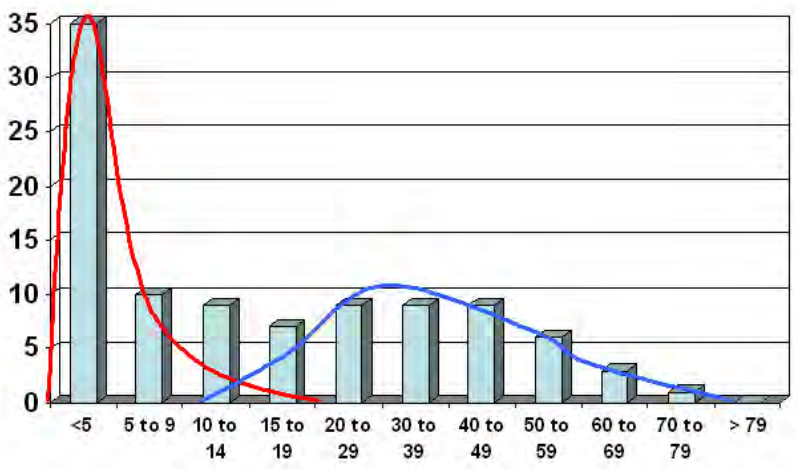
32% of respondents were under 20 years old. Age distribution was normal. Females were slightly higher represented than males (see below).





Age of patients at the time of diagnosis

62% of patients were diagnosed before the age of 20.

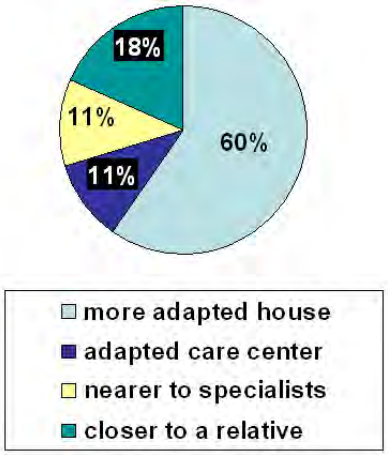


Place of residence

The place of residence is a widely debated result.

From the sample population, it appeared that most of the respondents lived in small cities of less than 100 000 inhabitants. This was unexpected, and will be analysed again when all responses will be obtained.

Importantly and strikingly, 18% of families had to move to a different location following the diagnosis of a rare disease: 60% to find a better adapted house, 11% to live closer to a specialist, another 11% to live closer to a care centre, and 18% to live closer to relatives.



Other characteristics

Other characteristics that will be part of the final analysis include: family structure (number of siblings, number of adults, and number of patients), working status and occupation class, financial resources, education level, and reduction of activity.

In terms of reduction of capacity, in 60% of families, at least one family member works less or has completely stopped his/her professional activity (in 49% of cases, this family member is the patient himself, in 51% of cases, he/she is the patient's carer).

Responses on experiences and expectations regarding the organisation of care

Failure and difficulty in accessing medical care

12% of patients do not have access to the medical service they need: (8% for cystic fibrosis patients, 17% for Ehlers Danlos patients): not so much due to lack of adequate care (~24%), as to the fact that they were not referred to the appropriate consultant or treatment centre (~59%). Other reasons included waiting time, distance and cost of journey.

However, for the 88% of patients who managed to access adequate medical services, overall patients' expectations were met to a relatively high degree: ~56% fully met, ~32% partly met, ~8% poorly met, and ~3% not at all met.

Distance to medical sites was surveyed in great detail: the distance from home to the place of treatment was found acceptable in 88% of situations but assistance was required for the majority of journeys, with 63% of patients needing help to travel to a medical centre.

Rejection by care centres

High numbers of patients reported rejection by health care professionals because of the disease: this is a clear indication of stigma within the medical community against patients with rare diseases, as rarely seen for common diseases. Here, up to **19%** of patients reported having being rejected: in 80% of cases this was due to the complexity of the disease, and in 10% of cases, according to the patient, due to physical symptoms of the disease.

Specific health services

For 30% of patients, it was difficult, very difficult or impossible to get access to a social worker. Information on social services was generally well provided, but more technical and specific social services were generally more difficult to access: financial support, personal assistance, integration programmes etc.

Expectations in relation to specialist centres, and to the implementation of such centres

The most widespread demand was for coordination within centres (between different health services and professions) (essential for ~75%), for communication with other centres for expert advice (~70%), for coordination with and between local care centres (~70%), and for a closer link with research (~65%).

The demand for more acute and routine care or for registers and surveys was less important.

Overall, demand for better coordination of medical and social care was greater than for care itself.

In terms of the implementation of specialist care centres - whether centres of expertise or not - respondents requested strong involvement of patient organisations in the process (for ~80% of respondents), many centres rather than one national one (~70%), identified on the basis of their active file (~60%), their specialisation and their capacity to transfer knowledge (~57%).

Preliminary conclusions

- High demand for structures that welcome patients with a specific disease (disease-related rejection remains frequent)
- Better communication between professionals (integration of the multidisciplinary aspect of rare diseases)
- Better social services
- Right balance between specialisation (critical mass) and proximity from home on a case-by-case basis.

DEBATE (IN DIRECT RELATION WITH THE EURORDISCARE SURVEY)

With reference to the distance between home and medical centre, 88% of respondents declared this distance to be acceptable. Patients might well be willing to travel for a consultation at a specialist care centre, if they do not have a choice. This should be taken into consideration in the definition of a policy for centres of expertise, as it has already been established that medical information, not the patient, should travel. In reality patients are willing to travel.

The lack of availability of specialists was also discussed: respondents who reported that specialists do not exist for their disease had perhaps been badly informed; it might be more an issue of referral and information within the medical community. The specialist may be located at the other end of the country but if the patient is not referred to him/her, then the patient may well believe that he/she does not exist. Not all doctors are linked up to the

appropriate network of specialists, and this is what the exercise on centres of expertise should address.

Gabor Pogany, Hungary, and other participants commented on the survey population. A frequent question was about place of residence, with only a small minority of respondents living in cities of over 100,000 inhabitants. These results are surprising and need to be controlled by country and compared to the general European population census. This will be carried out as part of the final analysis.

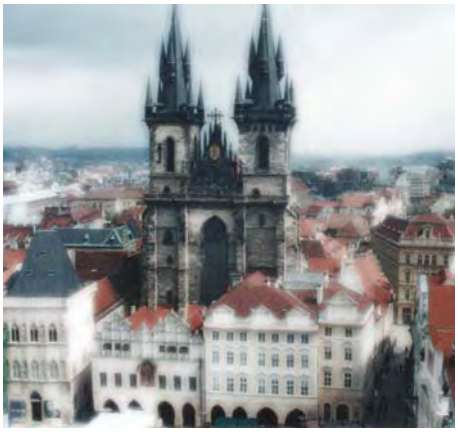
Michaela Damin, United Kingdom, asked about patients who are diagnosed but not affiliated to any support group. It may be assumed that patients who are affiliated get immediate better access to care. As unaffiliated patients are not part of the survey, maybe the results do not fully reflect the issues. Undiagnosed patients also may have acute difficulty finding the right experts and acute problems accessing care. Their experience is also not assessed in this survey.

Martin Johnson, United Kingdom, stressed the importance of this survey and its results: it is important data for the purpose of service delivery and for improving the existing situation. The important issue is perhaps less about life expectancy - this principally changes as medical and scientific knowledge progress – and more about what will change when care and service delivery are better organised: the quality of life experienced by patients through the full term of their lives. This is common to every rare disease group benefiting from a network of expert centres. Properly managed we could change the quality of life of all people living with a rare disease, however long their life, and that in turn will change their own expectations of the life available to them. And that will give outcomes that we cannot begin to predict.

Terkel Andersen, Denmark, emphasised the need to identify cohorts of people that could be followed up prospectively in order to measure changes and the evolution of their experiences and expectations. Recent surveys in Denmark showed divergence between results and expected data, as patient population is changing all the time and members of patient organisations may not represent or reflect the overall patient population.

Lynne Zwink, United Kingdom, was concerned by the question about the distance to access a specialist doctor. For the care of fragile X syndrome, paediatricians, psychiatrists, therapists and other health care professionals that are not experts in Fragile X do see the patients; there is no one medical speciality that holds the expertise for fragile X. All the professionals that may become involved in the care of Fragile X patients are found in all regional hospitals; so there is no real need to cross the entire country to visit for example, a psychiatrist who would have more experience of Fragile X, and this should be considered in the final analysis.

Yann Le Cam, France, insisted on two results: a) 67% of respondents require the assistance of a social worker, and b) the poor levels of satisfaction regarding assistance for infrequent needs. These results highlight the need to identify and train social workers within networks to ensure that not only are they information providers but also and principally that they are of real help in daily life. This specificity should become a priority perhaps in national plans for rare diseases and in the reflections of the High Level Group.



Prof Thomas Wagner, Germany, commented that social services are part of primary care and it is the responsibility of the health care system to provide that service. Prof Wagner sees no European added value in social services aiming at solving local issues. Therefore, European networks should not have a role to play in social services and these services should not be addressed at the European level. There is agreement that a deficit of social services exists in the case of most diseases, even in cystic fibrosis, but this is not a European issue.

In reply, Terkel Andersen explained that health outcomes rely partly on the adherence of patients to their treatments, and the way they cope with their diseases. Available resources distributed by social services should also be used to motivate families and patients. Thus, the dimension of social services should be integrated in overall care and patient management.

Furthermore, Alan Summerside, United Kingdom, reported a patient using the European E112 form to get care in a Member State other than his country of residence, and failing to obtain reimbursement on his return, as the decision-maker on reimbursement in one country was someone other than the person prescribing care in the other. This is another example of poor coordination between health and social services and this specific case now needs a solution at the European level.

Dr Alexandra Fourcade, France, stated that expertise on patient empowerment and adherence support programmes could be part of the expert centres' activities. This has not been considered in France but, as this is a real competence that brings great benefit to patients, this task could be added to the criteria used to designate centres of expertise.

In response to a question from Edmund Jessop, United Kingdom, the questionnaire cannot distinguish between rejection due to the objective complexity of the disease and situations where the doctor says that nothing can be done when in fact there is still something that medicine can do.

Inge Christensen, Denmark, suggested the creation of focus groups of patients to tell their life stories to build arguments to support these figures.

FOR NATIONAL CENTRES OF EXPERTISE AND EUROPEAN NETWORKS OF REFERENCE

In March and April 2007, eleven workshops took place in Europe with the objective of opening or continuing dialogue between patient representatives, health policy makers and health care professionals about national centres of expertise and European reference networks of centres of reference for rare diseases.

All the workshops had the same agenda, the same format, the same audience (20 patient representatives, health care professionals, health care system experts and health authority representatives), and the same preparatory materials. After each meeting, a synthesis was written and the responses to the three main questions addressed were presented at the European workshop in Prague.

Dates, names of local organisers, and numbers of participants are listed below (PO for patient organisation representatives, HCP for health care professionals, PM for policy makers and Pharm for pharmaceutical industry representatives).

Member State	Date	Lead contact person	Organisation	
Czech Rep.	2nd March	Maryna Krenkova	SUKL	21 PO, 12 HCP, 4 PM = 37
Denmark	26th March	Torben Grönnebaek	RDD	10 PO, 7 HCP, 2 PM = 19
France	29th March	Françoise Antonini	Alliance Maladies Rares	12 PO, 6 HCP, 7 PM, 1 Pharm = 26
Germany	19th March	Mirjam Mann	ACHSE	11 PO, 6 HCP, 5 PM = 20
Italy	24th March	Simona Bellagambi	UNIAMO	10 PO, 7 HCP, 1 PM = 18
Luxembourg	22nd March	Bettina Vogel	ALLAN asbl	2 PO, 8 HCP, 1 PM = 11
Spain	23rd March	Rosa Sanchez de Vega	FEDER	17 PO, 16 HCP, 4 PM = 37
Sweden	16th March	Elisabeth Wallenius	Swedish Alliance	11 PO, 10 HCP, 7 PM, = 28
Netherlands	11th April	Pauline Evers	VSOP	9 PO, 11 HCP, 2 PM = 22
United Kingdom	28th March	Alastair Kent & Melissa Winter	GIG	16 PO, 12 HCP, 1 PM = 29
Portugal	30th March	Ana Rita Dagnino	Ass. Haemophil Portugal	14 PO, 10 HCP, 1 PM = 25
				Total 272 participants

FOR NATIONAL RARE DISEASES CENTRES OF EXPERTISE

Christel Nourissier, Prader Willi France

Participants at the workshops were first asked to respond to the following questions:

- What are the expected benefits for patients?
- How does the concept of centres of expertise meet these requirements?
- How does the concept of centres of expertise apply to the national health care system?
- What criteria to use to identify/designate them? How is it done already or how would you like to do it?
- What cooperation between centres of expertise and other specialist care centres? Are national networks of centres of expertise the solution?
- How to ensure long term sustainable funding?
- What critical view do you have of the risks and benefits of the approach, expected advantages and potential risks?

Expected benefits for the patients

A satisfaction survey conducted in Denmark, and so far the only survey of centres of expertise conducted in Europe, showed overwhelmingly positive results, with 72% of patients feeling improvement as regards care and treatment, and 67% more consistent treatment.

The main expectations were:

- **Global approach**: multidisciplinary team with coordinated care
  - GBr, Cz, Fra, Por, Spa, Nld, Ger, Swe, Lux[2]
- **Earlier and more accurate diagnosis**
  - Ita, GBr, Cz, Nld, Ger, Lux, with psychological support in Spain
- **Data collection, registers: records of natural history and of effects of treatments**
  - Ita, Dnk, Cz, Fra, Nld, Lux
- **Coordination of research, care and development of new therapies**
  - Fra, Ita, Nld, Spa, Swe, Lux. Advocacy for drug reimbursement Cz, Lux
- **Training and education of health professionals**
  - Ita, GBr, Cz, Spa, Fra, Lux

As a comment, data collection and registers come up as the third priority, slightly in contradiction with the preliminary results of the EurordisCare survey where registries were not defined as a high

[2] Cz: Czech Republic, Dnk: Denmark, Fra: France, Ger: Germany, Ita: Italy, Lux: Luxembourg, Nld: Netherlands, Por: Portugal, Spa: Spain, Swe: Sweden, GBr: Great Britain

priority. Probably the composition of the national workshops reflected different views, with more insight into research and the tools that can serve research purposes.

Secondary expectations were for:

- Equitable and easy access to appropriate and continuous care and treatment
  - GBr, Por, Fra, Spa, Lux
- Protocols for care and therapies
  - Fra, Nld, Ita, Spa, Lux
- Connection with local medical care, social system, home services, access to insurance, loans
  - Dnk, Ita, Cz, Spa
- Easy access to information for patients and general public
  - Ita, Cz
- Contact and cooperation with patient organisations, contact between patients, especially if no patient organisation exists yet
  - Cz, Nld
- Medical alerts for "acute attacks"
  - GBr
- Second opinion on therapeutic choices
  - Ger

How does the concept of centres of expertise meet these requirements?

The centre should be:

- **Assembling multidisciplinary professionals, data, diagnosis, treatment and care** (Nld, Por) adapted to the needs of the specific disease or group of diseases (Ger)
- **Truly a centre of expertise** and not a point of reference defined at political/bureaucratic level (Ita) documented through publications, grants and training activities (Por)
- **Recognised by Ministries of Health, Labour and Social Affairs and health insurance companies** (Cz, Nld)
- **Sharing laboratory resources for costly and complex diagnosis for all** and exchanging best practices, protocols, recommendations, using the expertise of other pre-existing centres and networks (GBr, Ita, Por)
- **Closely linked with patient organisations where they exist** (Fra, Por)

And also:

- The centre should use telemedicine: virtual networks and IT systems to avoid travel (GBr)
- Its laboratory procedures should be accredited (Ita)
- it should implement outcome measures of capacity to diagnose and follow up patients and quality control (Por)

Is the concept of centres of expertise applicable to national health systems?

- **High relevance in decentralised health care systems**
  - Need for a lower number of centres with high expertise (Ita)
  - Allow mobility of patients and reimbursement (Spa)
  - Evaluation and benchmarking at EU not federal level (Ger)
- **High relevance in EU Member States with a smaller population**

    - Exchange of experiences (Lux, Cz)
    - Easier, more rapid and effective orientation of patients (Lux)
- **Existing experiences in countries with centralised health care systems**
    - In Denmark: centres for diagnosis and treatment of rare diseases and a national information centre already exist
    - In France: 132 centres of reference designated and funded
    - In UK: for some diseases only, group similar conditions together
    - In the Netherlands and Portugal: in some general hospitals and for some rare diseases, approach which matches some of the criteria. However historical, unplanned, vulnerable approach
- **Need for a comprehensive national plan: Denmark, Spain, Portugal**

Which criteria are being used or should be used to identify/designate centres?

The main criteria could be:

- **Appropriate capacity to manage patients, a multidisciplinary approach, bringing together social and medical care**
    - Spa, Por, Ita, Fra, Nld
- **Use a bottom-up approach (Spain)**, dialogue and cooperation with patient organisations and scientific bodies to build a consensus (Ita, Dnk, Nld, Ger)
- **Combine research and care**
    - Fra, Nld, Ger, Swe
- **Volume of relevant activity**
    - Fra, Por, Nld, Ger, however difficult to prove (Ger)
- **Link to patient organisations**
    - GBr, Fra, Nld
- **High level of expertise, publications, grants**
    - Fr, Por, Lux

Identification and designation could be processed through:

- Call for proposals issued by Ministry of Health
    - Fra, Por, and progressive designation in Spain
- With participation of patient representatives in the decision
    - Ger, Fra
- Impartial standards to be met (Ita)
- Independent evaluation panel (Por)
- Not taking into account regional and political aspects, financial benefits (Spa, Ita)
- Group similar diseases together
    - GBr, Spa, Swe
- Periodic efficiency assessment (Fra, Spa)
- Quality control (Nld, Ger)
- Based on monitored and documented clinical results, capacity for expanding, capacity for research (Spa)
- Creating a legislative framework reflecting current status, after a critical review and comparison of results, respecting international standards when they exist (Cz)

- Not necessary to concentrate experts under one roof (Cz)

How do centres of expertise and other specialist centres co-operate? Are national networks of centres of expertise the right solution?

- Yes
- National networks are essential for sharing information and for the dissemination of expertise both at a national and international level
    - Ita, Spa, Ger, Lux, Por, Nld
- Multidisciplinary cooperation is possible by sharing expertise, linking healthcare, social welfare, educational systems etc. (Cz, Sp) with patient organisations (Lux) and research networks (Spain)
- For very rare diseases: there is a need for a European approach (Dnk, Nld, Fra), with professional networks linked to patient groups (UK, Nld)
- For more common diseases: organisation at national or regional level
- Assignment of responsibilities at national, regional and local levels necessary (Dnk)
- Long term sustainability of networks is crucial (Spain)

On this last point, how to secure economic support in the long term?

- Legal recognition of existing centres to improve their visibility (Spain), but avoid creating completely new structures (Ita, Spa)
- Centres driven by patient groups and goodwill of clinicians. Need for permanent funding by state budgets and health insurance funds, not by 2- or 3-year grants
    - Cz, Nld, GBr
- Specific funding to support additional activities linked to the duties of the centres of expertise, at national or international level
    - Fra, Por, Spa, Ger
- Take into account the cost of diagnosis and treatment (Ita) and the extra time needed to treat rare disease patients (Ger, Fra)
- Demonstrate that centres are cost effective and provide improved care (GBr, Por)
- All Member States should contribute (Lux)
- Ad hoc funding for rare diseases based on model of drug agency for clinical research independent from companies (Ita)
- Grants for research and development, awareness of possible existing funds (Por)
- Ensure transfer from research to care (Spain)
- Orphan drugs should be included in hospital services, central policy suggested (Spain)
- Funding from EU is complex and time consuming (GBr)

In conclusion: expected benefits from centres of expertise for rare diseases?

- Earlier and correct diagnosis
- More accurate epidemiological picture, better knowledge of the disease via databases and registries (Por, Spa)
- Proper disease management programmes and guidelines (Dnk)
- Improvement of care through coordination from basic science to clinics, training, care (Ita, Por, Spa)
- Following approval of treatment by centre of expertise, application by field doctors (Ita, Cz)

- Individual empowering plans for patients (Dnk)
- More efficient use of resources and research (Spa)

Potential risks and issues?

- Lack of financial resources to work properly
    - Spa, GBr, Ita, Cz, Por, Fra, Nld, Ger, Swe
- Lack of information: need to publicise centres, activities and research to end users and clinicians
    - GBr, Spa, Dnk, Fra, Lux
- Close coordination with patient organisations required to diffuse information (Ita)
- Monopoly situation of the centre of expertise, work load increase
- Centre too dependent on a single person (GBr, Nld)
- Lack of collaboration with other professionals, demotivation of non designated centres (GBr, Fra, Lux)
- Necessity for local or national centres providing proximity healthcare, supervised by centre of expertise, to be properly recognised and funded (Fra, Dnk, Por, Lux)
- Lack of objectivity and criteria for designation (Spa, Ita)
- Inappropriateness of developing an artificial network for completely different diagnoses (Cz)
- Methods for provision of care can become too rigid (Fra, Ger), not adapted to the needs of patients (Lux)
- Databases: data not always standardised, and comparing or sharing data has to respect legal and ethical issues (Nld)
- Passage from paediatric to adult care (Ger)
- Links between centres and patient organisations not taken into account in the evaluation (Fra)
- Problems of communication in national networks, and with social welfare (Fra)
- Language, travel, reimbursement problems for patients and families (Lux)

QUESTION 2: PROPOSALS FOR THE EVALUATION OF CENTRES OF EXPERTISE

Melissa Winter, Genetic Interest Group, United Kingdom

The participants in the national workshops were invited to discuss how they would measure whether the centres of expertise actually responded to their expectations, and how to ensure that patients really benefited from them.

This assessment could first rely on the following factors:

- Increased number of diagnoses/time reduced to get a diagnosis (GBr, CZ)
- Improved quality of life (Swe, GBr), evaluation of the physical environment in cared patients (Swe)
- Outcome of treatments (Swe) and improvement of healthcare services for rare diseases (Por), annually monitored (CZ, Dnk), efficiency of the care of the whole network (Fra)
- **Involvement of patient organisations** (PO), health professionals and local management in establishing criteria (different needs) of the patients and health professionals (Spa)
- Patient/health professional satisfaction (Swe, Ger), quality control evaluated with the PO (Nld, GBr, Por, Spa) through periodic surveys (Ita, Dnk, Fra) (common standardised questionnaire)
- Establishment of multidisciplinary team to approach the disease (Cz-Ita) and experts to have continued professional development skills and practices (GBr)
- **Effective cooperation with other national, regional and international centres** (Cz, Ita, GBr), skills centres (Fra), building up shared database (Dnk) and new protocols and models
- Development of regularly updated patient registry: determination of patient numbers – natural course of disease (Swe, Cz, GBr, Ger, Fra)
- National and international certification of centres and labs for quality control and assurance on common criteria (Swe, Cz, GBr, Ita)

To ensure centres of expertise meet patient expectations, the following information could be monitored:

- Health economic evaluation (Swe), availability of adequate human and economic resources (Ita, Spa), economic assessment of the operation of the centres of expertise. (Fra)
- System to analyse/monitor the cost benefit (GBr)
- Develop regulations for hospitals and professionals to have an obligation to prioritise rare disease patients (Spa)
- In France the centres perform self- assessment 3 years after certification to assess if they have met their objectives. After 5 years, external assessment to renew their certification. Both assessments performed on the indications of the French National Authority for Health manual (see below)
- Including centres of expertise in the national health system structures (Spa)
- Give the economical means to regional councils to ensure they send patients to the centres (Swe, Por)

- Ensuring access to care 24 hours a day 7 days a week (Cz)
- Provision by the centres of expertise of international treatment plan and recommended procedures for local health carers (Cz, Por) and continuous exchange of information and data (Ita, Por)
- Mechanisms for referral of new patients such that local professionals do not feel de-skilled and patient access is timely and appropriate (GBr)
- Formal collaboration between PO and centre for contribution to database (Nld, Ger, GBr), involvement in formulating evaluation criteria and indicators (Nld, Spa, GBr)
- Ensuring prenatal diagnosis - timely diagnosis (Ger), genetic consultancy for family (Cz), children and adult care (Fra)
- Matters of attitude (Swe), holistic coverage including biomedical care, psychological and social care (Spa)
- In-service training (Swe), increasing the ability to prevent complications

Common standardised criteria for evaluation surveys

Soft values	Hard values
Co-operation with patient organisations	Time to diagnosis
Patient-orientated approach	Waiting time
Improved outcomes	Genetic consultancy
Improved atmosphere	Multidisciplinary approach
Improved quality of life	Co-operation with other centres (clinical and laboratory)
Avoiding unnecessary complications	Registries
Awareness and knowledge dissemination (to patients and to society)	Care guidelines and recommendations
Information provision to local centres	Quality control
	International and national networking
	Economic assessment

Centre designation and assessment: where do we go from here?

- The French model? Could this work in other EU Member States?
- National or international collaboration?
- How could we learn from networks that are currently in place? E.g. cystic fibrosis, dysmorphology?
- Should we create minimum standardised criteria and objectives?
- Certification to be periodically renewed? External evaluation?

QUESTION 3: COOPERATION WITH OTHER COUNTRIES

AND RECOMMENDATIONS FOR EUROPEAN REFERENCE NETWORKS

Birthe Holm, Rare Disorders Denmark, leader of the work package on centres of expertise and reference networks, Rapsody

The final questions addressed by the national workshops were: How do you see your centres cooperating at the EU level? What role would European reference networks play? Which specific added value can you identify when networking your national centres of expertise at European level? On which criteria to identify/designate European reference networks? And what would the specific expected benefits for patients be?

Elements to establish European cooperation:

- National/regional networks of specialist care centres/centres of reference (Ger, Ita)
- Already established networks (Cz, Fra, GBr)
- Patient-hosted networks and voluntary activity (GBr)
- Specialist health care professionals (Lux)
- Forum-like meetings/conferences (Nld, GBr, Swe)
- Websites/information, databases/registries (GBr ,Fra, Dnk, Ita, Por, Spa)
- Equal access for patients to services from EU networks (Ger, Dnk)
- Long-term funding needed (Fra)

Remarks and recommendations

- Expert teams for very rare diseases/different approach needed (Fra, Dnk, Spa)
- Holistic approach (social aspects/quality of life, how to cope with the disease, habilitation programmes) (Fra, Dnk, Cz)
- Reimbursement systems to be adapted (Ita, Spa, Fra, Swe)
- Interaction with stakeholders including patient organisations (Dnk, Por)
- European research projects to be developed to networks (Fra, Por, Lux)
- Risk of creation of a disproportionate bureaucracy relative to numbers of patients (GBr)

What role would European reference networks play?

- Improve knowledge by sharing information/databases (Dnk, Cz, Nld, Por, Fra, GBr)
- Establish research projects, studies, trials (increase cohorts) and develop registries and databases (Por, Spa, Dnk, Ita, Ger, Fra, Swe)
- Develop best practices/protocols (Por, Cz, Dnk, Swe, Fra, Spa, Ger, Ita)
- Grouping diseases (GBr, Ita)

- Defining quality/recommendations for care services/standard of care (Nld, Por, Fra, GBr)
- Training, exchanging resources, twinning between centres (Cz, Dnk, Spa, Ita, Por, Swe)
- Encourage networks between patients (Nld), educating patients and families (Por)

Remarks and recommendations

- Expertise should "travel" to the patients, health care professionals may have to visit the patients where they are, and it should also be possible for patients to travel to centres if necessary (Por, Dnk)
- Accrediting national centres of expertise (recognised centres of expertise)/list of centres (GBr, Spa)

Which specific added value can you identify if your national centres of expertise belonged to a European network?

- Creation of critical mass for research and clinical trials (Ger, Swe, Fra, Por, Cz, GBr, Spa)
- Shared databases and registries (Fra, Cz, Dnk, Lux, Spa)
- Creation of a multidisciplinary approach (Ita, Fra)
- Pool knowledge for protocols and state of the art treatment (Ita, NId, Por, Cz, Lux, GBr, Spa)
- Training of professionals (Swe, Por, Cz, Dnk, Lux)
- Better surveillance of medicines concerning efficacy and safety (Ita)
- Creation of a greater and better link between health care professionals and patients (GBr)

Remarks and recommendations

- Long term resources/funding needed, as it takes at least 10-15 years to build a register (Fra)
- Improvement of care and services on national level when benchmarking on European level (GBr, Ger, Por, Fra, Cz, Dnk). Diversity of European cultures has not been mentioned as an obstacle.
- Uniform approach might better integrate rare patients in the healthy population (Cz)
- Support network for people who have to travel (Cz, Fra)
- For very rare diseases substitute a missing national centre (Cz)

On which criteria to identify/designate European reference networks?

- Flexible criteria depending on complexity, rarity and development in the specific country (Fra, Cz, Dnk)
- Clear objectives and visions for each network (Swe, Dnk)
- Ability to share information and to benchmark (disclose procedures and results) (Ger, Swe, Cz)
- Groups of diseases rather than single diseases (Ita, GBr)
- Minimum standards and common procedures (Dnk)

- Same criteria as national centres of expertise (Ger, Por, Nld)
- Quality of care, number of patients, publications issued (Spa)

Remarks and recommendations

- "Leading" centres and "associate centres" should be identified on the basis of acquired and proved experience (Ita)
- Clear leadership needed (Swe)
- Each Member State should identify its experts for rare diseases (Fra)
- Some networks regulate themselves (EuroWilson) (Fra)
- Creation of a European monitoring body (Fra)
- Credits should be allocated to criteria e.g. effective cooperation (Fra)

What would the specific expected benefits for patients be?

- Improved quality of information, care and services (Spa, Lux, GBr, Cz, Fra, Por, Ita)
- Earlier diagnosis and recognition of its importance (Spa, Lux)
- Creation of multidisciplinary teams (GBr)
- Harmonisation and standardisation of best practices/guidelines (Spa, Lux, Cz, Por, Swe, Ita)
- Access to the best European resources for rare diseases (Cz)
- Better incentives for research by pooling patients/registries (Spa, Lux, Cz, Swe, Ita)
- Recognition of rare diseases and thus of their specificities as regards care (Fra)
- Fewer journeys (Spa)

Remarks and recommendations

- Opportunity for a second opinion (Ita)
- Improved quality of life (Lux, Nld, Cz)
- Better access to care in the poorest countries (Fra)
- Contacts between patients on the European level (Cz, Nld)
- Reimbursable care when travelling in Europe (Fra)
- Progress resulting from comparison of systems and cultures (F, Dnk)
- Better access to orphan drugs (Swe)

DEBATE

Prof Deybach, France, mentioned the Porphyria network that was selected by EC DG SANCO following the call for proposals in 2006. The network was in fact created in 2002 with the support of Association Française contre les Myopathies, with partners in United Kingdom and Czech Republic. It then expanded step by step to twenty European states. In his opinion, centres are too fragile, and often competing: they rely on one hospital doctor who may retire or move to another region or country, and the centre will close. In many countries, regions are competing; this is particularly sensitive in Italy, where north, south and Roma have their own structures, and in Spain with competition between Madrid and Barcelona. Prof Deybach then emphasised three important issues:

- Quality control for diagnosis. His experience shows frequent errors in DNA assays.
- Importance of joint ventures with the pharmaceutical industry: research on gene therapy and protein and enzyme replacement will continue to produce outcomes. Networks are in a better position to work with industry than isolated centres.
- Databases based on family histories are rare. One product is marketed, but too costly for most rare diseases.

Inge Christensen, Denmark, proposed applying the European principle of subsidiarity to the debate, as it was shown yesterday that rare diseases face geographical diversity and inequality. Subsidiarity should be the basis for coordinating effort at the European level in order to abolish this diversity and decrease inequalities.

Prof Olaf Riess, Germany, called for lessons to be learnt from existing centres and networks: for example, when centralised centres exist, they could serve as a supervisory body for centres that are not formally part of the network but that are making efforts to meet the criteria. It would be rational to group diseases together, as it will be impossible to create networks for each individual rare disease. Lastly, we should define the minimum funding these networks and centres of expertise should receive, as a tool to advocate their cause with taxpayers and health authorities.

Christel Nourissier, France, explained that in fact each centre will decide what activities it will pursue, and while some will decide to develop efforts to train health care professionals, others may decide to support social services and others will invest in medical equipment etc. It will therefore be difficult to estimate minimum funding for centres of expertise, as their activities will probably continue to vary greatly.

Dr Domenica Taruscio, Italy, reported on the Italian model for centres of expertise: in Italy, the regional health authorities are the

designating bodies. In almost all Italian regions, centres of expertise lack resources to fund all activities and to satisfy all patients' needs. The federal/central government cannot act directly. Even though European funding would be welcome, it is still the Member States' responsibility to ensure appropriate funding for these centres.

Dr Ségolène Aymé commented on the French model. A few years after its implementation, changes can already be envisaged.

- Firstly, the call for proposals was a solution to obtain an expression of interest from health care professionals. However, this mostly favoured those who were prepared to apply immediately and who were not necessary the best. And once a disease benefited from a designated centre of expertise, it was really difficult to add a new one as other diseases were prioritised.
- Secondly, funding was initially the same for all centres, whether they were dealing with a single disease and just a few patients, or several diseases with thousands of patients.
- Thirdly, expert bodies were left out of the designation system. In fact, expert bodies are perhaps the best partners to make national level proposals.

A survey has just been conducted: 95% of rare diseases are covered by one of the 132 centres of expertise for rare diseases as of today, and this is a great achievement.

Importantly, recommendations should distinguish between care centres that are close to the patient, and care centres that can benefit the patient but remotely, mostly through expert advice, second opinion, telemedicine and the development of care and management guidelines. Such guidelines can be translated and shared.

It is also equally important to distinguish between the three different kinds of European Member State: large, medium and small.

Mirjam Mann, Germany, identified a potential risk: specialising too much could limit the views of the health care professionals. Doctors need to continue learning from people outside their specialty and see new patients and new diseases all the time.

Prof Flora Payvandi insisted on the importance of standardising data prior to exchanging it; and this may be the main role of the networks. A condition for centres to join a network may even be their agreement to use standardised data.

Hanne Love, Denmark, reported the difficult transition from childhood to adulthood, where paediatricians stop being the treating physicians and feel that they are losing a patient, and doctors who take over the patient's treatment do not have the medical history and the experience with the individual.

Lene Jensen, Denmark, insisted that all the efforts we are proposing consist of concentrating, gathering, building up information

- generally acting as if everybody is eager to share it. However, that is not necessarily the case, and there are barriers to tackle convincing all actors to actually share information. In addition, rare diseases are not at the top of the agenda of all Member States. Major competition between teams is an obstacle to any collaborative initiative.

Regarding the reluctance to share information, Evanina de Morcillo, Spain, expressed her concern that if medical publications serve as a criteria for the designation of centres of expertise, some health care professionals will continue to withhold information for their own publications.

Michaela Damin, United Kingdom, asked whether a database of specialists and experts for rare diseases already exists. Terkel Andersen answered that Eurordis is working with COMP to identify patients as experts, and Yann Le Cam further explained that Orphanet is the first source of information to look for medical experts.

Dr Martin Johnson, United Kingdom, brought to the attention of the participants that different rare disease groups have different abilities to attract the attention of the general public and gain advantage for themselves. Dr Johnson illustrated this by the story of two diseases affecting the same number of patients in the area covered by a hospital he served in twelve years ago. Out of a population of 290,000 inhabitants, there were about 35 people affected by each of these two diseases. The life expectancy from diagnosis to death was almost identical. The nursing needs were moderate for one disease and considerable for the other. The government funded centres in every city for patients with the first disease, and everybody thought that was normal. The second disease group received no government funding; and although the care support needs were considerable, they had to be provided through charitable funding. The first disease group was categorised as AIDS, and the second as motor-neurone disease. We have to look at how it is that a particular patient group can divert attention to its own interest, away from other disease groups. If there is something to be done here, it is to try and prevent individual rare disease groups from taking advantage over the others.

In reply, Terkel Andersen, Denmark, stated that there is no such thing as objectivity and in the rare disease community where there is a high degree of solidarity this exercise is very much about recognising the right to equality of access to care.

EXPECTATIONS AND ELIGIBILITY CRITERIA FOR EUROPEAN REFERENCE NETWORKS OF CENTRES OF EXPERTISE FOR RARE DISEASES – ERNCOE

1. Two essential pre-conditions:

- Professional qualification: both clinical and scientific experience. Proven qualification documented by publications and grants and pre-existing certification or accreditation
- Commitment to cooperate and to share information

Importance of the general "atmosphere and attitude": trust rather than competition among experts to ensure effective cooperation.

2. Patient access to a multidisciplinary team of experts:

- both at the level of centres of expertise and European reference networks
- full competence does not exist in a single Member State
- a cross-disciplinary approach is needed to tackle rare disease patients' needs for diagnosis, care, treatment, therapeutic research

3. Importance of coordination between professionals:

- Coordination within and between centres of expertise, within European reference networks, between centres of expertise and proximity/primary care
- Coordination between care and research activities
- An intelligent way of circulating information and organising the continuum of activities (care, follow up care, research), placing the patient at the centre, making better use of existing expertise and resources
- In order to improve quality of care and to reduce thepsychological burden of the patient (feeling of being lost in the system, lack of support, language barriers, etc)

4. Importance of global approach (holistic, comprehensive) integrating medical and social aspects

- At all levels (primary care centres, centres of expertise, European reference networks)
- Social support often underestimated
- Need to develop a common European approach to social services for given rare diseases
- Specific administrative tasks for European reference networks to support patient mobility for cross-border care, addressing the reimbursement issue

5. Capacity to pool patients

The critical mass of patients is a condition for increasing scientific and medical knowledge on the disease. The identification of unknown aetiologies will help the management of complex and rare

disease situations, on condition that enough patients can be enrolled in clinical and physiological trials.

6. General expectations:

- Development of best practices, standards and guidelines for diagnosis, treatment and care of rare diseases at international level
- Dissemination of European reference diagnostic and therapeutic protocols will ensure equity at EU level by reducing the impact of the "post code lottery" and will increase trust in local services
- Provision of expert opinion, confirmation of diagnostic and therapeutic options

7. Participation in research activities at European and international level:

- Linking excellence of care with excellence of research, where the patients are and where the multidisciplinary expertise on the disease is
- Multi-centre clinical studies and facilitation of partnership with pharmaceutical companies
- Shared databases, shared biological resources (DNA, RNA, tissue, cells), registries (harmonisation of procedures), international epidemiological surveillance, pharmaco-vigilance
- Participation in EU-funded research projects

8. Perform education, information and communication outreach activities with the public and primary health care professionals (to improve referrals & follow up).

9. Perform training activities for health professionals, including staff exchanges, meetings and conferences to exchange best practices, to harmonise processes and to disseminate standards & guidelines.

10. Perform activities to empower patients at different levels - information, education, training - to build patients' and families' capacities to manage the medical & social aspects of their rare disease, to enhance their autonomy, increase their compliance, and help improve their quality of life.

11. Collaborate with patient organisations at different levels:

- Patient organisations' contribution to the management and evaluation of networks
- Facilitate the creation of patient groups
- Improve links and exchanges between professionals (care & research) and patients
- More broad links between European reference networks, research networks and patient organisations

12. A general agreement is that European reference networks should be:

- Initially evaluated and accredited at EU level via an agreed set of criteria (minimum set of standardised criteria and objectives + additional ones)
- Regularly assessed on common indicators with soft values and hard values

There is a need to develop methods and tools for European reference networks to perform regular self-evaluation.

13. Economic and management aspects of European reference networks

- Reference networks are perceived to be cost-effective
- They need proper funding for their specific European & international activities
- They need long term sustainable public funding
- They should be encouraged to share good governance practice (organisation, leadership, regulation, steering committee) and coordination practice between them
- They should be able to disclose their procedures and their outcomes

14. Importance of flexibility when selecting types of centres belonging to the networks and flexibility in relation to the geographic coverage of the networks.

- No obligation for a network to have centres in all Member States. Density of centres depends on the population size. European reference networks could play an active role in the accreditation of centres of expertise
- Patient agreement to travel should be confirmed, detailed and responded to
- Different suggestions were made on the structure of the networks, with "leading centres" and "associated centres", and possible "sub-national networks" with "centres of competence".
- Different centres could be grouped within a European network
- Excellent contribution of new Member States to European reference networks

Patients' comments

Overall positive comment: the European reference networks will highlight differences between healthcare systems (benchmarking) and will pressurise governments to reduce the inequalities of access to care and quality of care for rare disease patients.

Identified risks:

- The creation of networks may generate disproportionate bureaucracy for accreditation and evaluation mechanisms.
- Adaptation and sustainability of mechanisms for expenditures and reimbursement will have to be agreed at EU level.
- Political commitment of Member States to financially support centres of expertise. This will need political willingness in pursuit of pan-European equity

DEBATE

Dr Ségolène Aymé, France, insisted on the need to adapt the concept to the reality in each Member State. Thus the best approach would be to define standards and patients' needs and to suggest what services can be provided locally or at a distance. However it does not seem realistic to define regional, national and European networks and different kinds of organisations and structures at the outset. No model will fit all health care systems; instead a framework could serve as a basis for each Member State

to decide on its own organisation. In this way, nobody would own the network. This flexible approach was seconded by Manuel Posada, Spain and Prof Deybach, France and Yann Le Cam.

Prof Deybach regretted the lack of coordination between DG SANCO and the 7th Research Framework: both are able to fund reference networks, for different purposes, but getting support from one does not necessarily translate into support from the other. It is key for reference networks to conduct research projects in parallel with producing treatment guidelines and providing expert advice to other health care professionals. So DG Research and DG SANCO should coordinate their activities.

Dr Lara Fregonese commented on cost-effectiveness studies: it takes time before they can conclude in terms of decreased morbidity over ten years or improved life expectancy and quality of life. In the meantime we need to argue in favour of these networks and their appropriate funding using arguments other than putative cost efficiency, such as solidarity with rare disease patients. Centres that participate in research networks or European reference networks are not necessarily designated as centres of expertise at a national level, and this is OK because they function well and are already playing an active role within the networks.

Alan Summerside, United Kingdom, approved the idea of developing and sharing standards, however he expressed his concern that this might have only minimal effect and lead to only minimal improvement in the quality of care. He suggested that some kind of formal structure would be useful to legitimatise the comparisons and evaluations of quality of care that the networks will carry out in the future.

Birthe Holm, Denmark, concluded the discussion by balancing the reservation expressed by participants over increased bureaucracy and paperwork, with the necessity of structuring the networks at a basic level, in order for them to be able to get funding and to be accountable to their funders. Incentives are a very powerful tool for change, and that is why a key aspect of the policy for European reference networks should be their funding, both from European budgets and national ones.

Finally, Yann Le Cam emphasized the need to link the activities of reference networks with the activities of research networks: these networks should not be considered as separate entities.

DISCUSSION BASED ON THE PROPOSALS TO THE HIGH LEVEL GROUP

Dr Edmund Jessop, National Commissioning Group, United Kingdom

I have been asked to present to you the thinking on assessing outcomes of European Reference Centres as developed in the High Level working Group on Health Services and Medical Care.

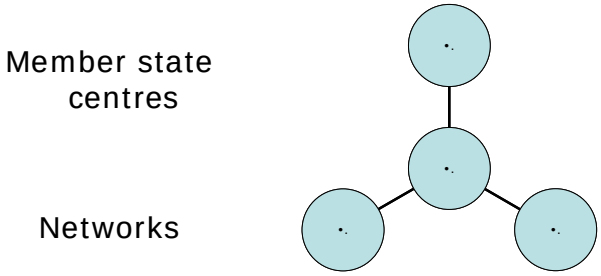
I wanted to start by making a point about evaluating outcomes. People who evaluate health care systems rather than individual treatments are in the habit of distinguishing the structures that we need to set up, the processes we will use to generate the outcomes that we seek: structures, processes, outcomes.

The reality is that it is much easier to describe a structure, to describe a process than to document properly the actual effects and outcomes that these structures and processes have achieved. Therefore most of the proposals seen so far describe much more the structures and the processes.

A network consists of nodes and the links between them. This session is focused not on the nodes because Member States are extremely resistant to any outside interference with what goes on inside their nodes.

For this session, the focus of the High Level Group is on the links between the nodes.

Just to draw your attention to some features: all nodes are equal. We are not in a model where imaging would be performed in one node, and laboratory analyses in another node. Secondly communication is between nodes and a central node, not between peripheral nodes. This model has implications that must be considered before being applied.



The plan is to have a few networks and to evaluate them. And this will take time. The distinction between treatment and research particularly in rare diseases is slightly artificial, but funding for research comes from a different source than the funding for these networks. These networks are funded as an information activity, because at the moment the EU has no competence over health services.

Proposed criteria discussed at the High Level Group

- Setting up the network
- Quality of care: how continuous compliance with the membership criteria is assured within the network. Just because people meet the criteria when they join does not mean they continue to meet these criteria
- Sharing knowledge: both between nodes within the network, and also when professionals move from centre to centre within the network/staff exchange

- Finance: both funding to set up the network, and funding if patients have to move as a last resort
- Administrative matters: language regime of the network
- Legal issues: who owns the data in the network? Even within England, which is one country of United Kingdom with Scotland, Wales and Northern Ireland running their own services, we cannot share data between hospitals, so strong are the data protection laws or people believe they are strong. Liability is also an issue: if I send a request to another centre, what gives me the guarantee the advice coming back will be good advice?

Different networks have different goals, therefore their evaluation will vary:

The network of rare bleeding disorders

- The primary task is to acquire more information about the nature of the disease, about which very little is known.

The network of cystic fibrosis

- The primary task is to translate and disseminate knowledge, but the knowledge is there.

The network of porphyria

- EQA[3] for laboratory diagnosis
- Agreed quality of care
- Evidence for drug use

The network Alpha 1 antitrypsine deficiency

- Establish common standards of care
- Early diagnosis

The network of dysmorphology

- Raise standards of diagnosis
- Best practice for care

What patients want

- Correct diagnosis…

…quickly

- Correct treatment

The question is whether we shall demonstrate that the network will help people get the proper diagnosis sooner. This question will probably be quite challenging. The same for correct treatment. Other frequently mentioned outcomes are longer survival and prosperity; these outcomes might be more difficult to assess, but they are not impossible to assess. And when you have them, you have a much more powerful argument. When clinical teams realise they are not achieving the best outcomes, they do not continue, they accept they are not good enough and they move the patients to other departments. Outcome data are very powerful if you can achieve them.

[3] External Quality Assurance

THE FRENCH NATIONAL AUTHORITY FOR HEALTH (HAS) APPROACH

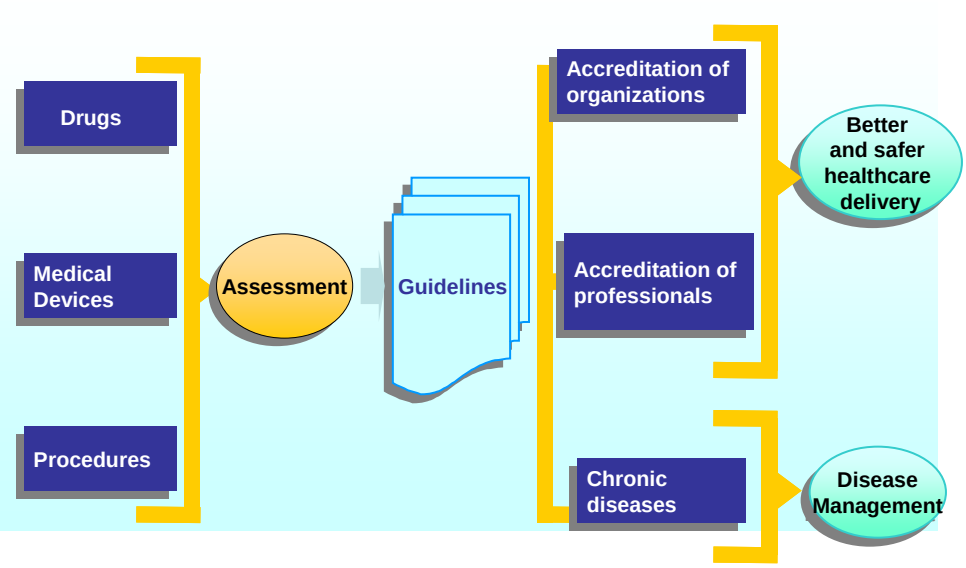
Dr Marie Claude Hittinger, HAS, France

Dr Marie Claude Hittinger, HAS, France

The missions of the Haute Autorité de Santé are:

- To advise decision-makers on pricing policies and reimbursement of health technologies (both products and procedures)
- To produce guidelines for health care professionals
- To perform accreditation of both health care organisations and health professionals
- To develop disease management approaches for chronic conditions
- To provide information for professionals, patients and general public

Overview of the HAS assessment activities



According to the national plan on rare diseases 2005-2008, dedicated health care centres can be designated as “centres of expertise”:

- 132 centres of expertise received designation
- designation is granted for 5 years by decision of the Ministry of Health based upon the recommendation of a National Approval Committee
- Assessment of centres of expertise by the HAS provides the methodological support for the evaluation process

The assessment is performed by the centre itself (self-assessment) and by outside experts (peer reviewed). The objectives of the centres of expertise when they apply for designation are as follows:

- Activity (number of patients)
- Second expert advice for establishing the diagnosis or confirming it
- Production of good practice guidelines
- Structure and coordination of both sanitary and medical and social networks
- Information and training of both health care professionals and patients, their families and caregivers
- Research and epidemiological follow up

The exercise consists in evaluating to what extent centres were able to reach their initial goals.

For example, to evaluate their efforts at better informing different audiences:

- Mission: Information and training of both health care professionals and patients, their families and caregivers
- Two criteria:
  - information and training for health care professionals (number of training sessions, publications, congresses etc.)
  - formalised relationship with patient organisations

There is no prioritisation of criteria. The assessment analyses gaps between planned activities and achieved outcomes. It produces an action plan for improvement. The aim is to measure the dynamics created by the centre of expertise in its field.

It is a three-stage process: self-assessment after three years, then peer-reviewed assessment after five years, and then an HAS report sent to the Ministry of Health for a decision.

The next steps are:

- Self-assessment by the first 34 centres: Q3 2007
- Peer review: November 2009

Documents can be downloaded from: ***www.has-sante.fr***

In conclusion:

French National Plan for Rare Diseases

- centres designated for 5 years
- renewal of designation based upon an assessment process

First practical implementation will start in autumn 2007.

In response to Manuel Posada, Marie Claude Hittinger explained that it is more of a qualitative and pragmatic approach than a quantitative one, and the criteria are proposed by the centres themselves at the time of their designation. Numbers of scientific publications are not necessarily the chosen criteria.

To clarify the composition of the Comité National Consultatif de Labellisation (CNCL), the committee that designates the French centres, Dr Ségolène Aymé explained that the CNCL is composed of six health care professionals working in rare diseases, plus three representatives of patient organisations, plus five representatives of national agencies involved in rare diseases, representatives of deans of schools of medicine, of universities and of social security.

About outcome evaluation, Yann Le Cam asked how to evaluate networks and centres themselves, not health care systems as a whole. Dr Edmund Jessop replied that it will be very difficult to dissect out whether the effect is a result of the network or the centre. However the network activity will be funded by the EU, and if people cannot show that what EU is paying for is achieved, then the EU will find something else to do with the money.

Teresa Coelho, Portugal, mentioned the difficulty of organising selection and evaluation committees in small countries where everybody knows everybody. Independence is particularly difficult to achieve in this context.

Prof Olaf Riess, asked a provocative question: whether France had considered announcing in advance that 20% of designated centres will not have their status renewed. Dr Ségolène Aymé replied that this was more or less planned: of the 132 centres of expertise already designated, some designations will not be renewed and other new centres will be designated. The figure is in the region of 10-20%.

Terkel Andersen, Denmark, asked whether patient organisations participate in these assessments. Another question was whether any centres are evaluating changes in quality of life. In response, Marie-Claude Hittinger explained that HAS encourages centres to invite patient representatives to join the working groups that perform self-assessment. However, this is not mandatory. The external evaluation is peer–reviewed, with an on-site visit. These experts can also meet with patient organisations, but this is also not mandatory. As for quality of life, some parameters can be monitored: impact on employment, on mobility capability, on care support needs. Though it is difficult to measure how much may be attributed to the interventions made.

Martin Dorazil, European Commission DG SANCO, confirmed that the EC will ask for quality management and quality assessment reports from the leaders of reference networks. It will be a bottom up approach, rather

than imposing a model from the top. The experience of the pilot projects that are in progress, together with that of pre-existing networks, will inform this process.

Prof Josep Torrent I Farnell, Barcelona, asked what budget had been allocated to centres of expertise, and what process was used to allocate these funds. In response, Dr Ségolène Aymé reported that 100 million euros have been allocated for five years, 2003-2008. A report has just appeared in Orphanews: the funds were used to create positions for 140 full time hospital practitioners, 102 nurses, 115 secretaries, 67 psychologists, 60 clinical research medical assistants, 34 laboratory technicians, 30 social workers, 25 physiotherapists, 16 genetic counsellors, 14 engineers, 12 speech therapists, 11 clinical study technicians, 9 dieticians, 3 orthoptists, 3 midwifes, 3 administrators, and 1 chiropodist, for a total of 645 positions.

Antoni Montserrat, European Commission DG Health and Consumers' Protection – Health Information Unit

The Commission has a strong interest in doing something really solid in the domain of rare diseases.

Proposal for a Commission Communication to the European Parliament and the Council on a European action on rare diseases (including genetic diseases)

The concept of rare diseases

The concept of "rare disease" (RD) emerged in 1978 with the publication of an article (Holzman NA. Rare diseases, common problems: recognition and management. Pediatrics, 1978; 62(6): 1056-1060) stating that rare diseases, though diverse, have common problems of being recognised by physicians and problems of being effectively managed as knowledge about each is very limited and little clinical research in the field exists.

Legal basis for the developments of Public Health Policy

A Community action programme on RD, including genetic diseases, was adopted for the period of 1 January 1999 to 31 December 2003 with the aim of ensuring a high level of health protection in relation to RD. As the 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 EU Public Health Programme 2003-2008. According to the DG SANCO 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.

Future legal basis for the developments of health indicators in the EU Public Health Policy

In 2007 the Commission plans to adopt a new Health Strategy. This will be an ambitious project and one of DG SANCO's top priorities for the coming year. It aims to:

- Set a clear strategic framework which covers the broad range of work done within DG SANCO, as well as in other parts of the Commission, and includes some new initiatives
- Set broad objectives for a 10 year timeframe, with a 5 year mid-term review
- Enable the closest possible cooperation with Member States to improve health in Europe in the decade to come
- Focus on key health issues, on mainstreaming health in all policies, and on global health issues, address key challenges such as pandemics and other threats, demographic change, new technologies, health inequalities, chronic disease burden, globalisation, patient and health professional mobility etc.
- Need of a Commission Communication in the field of rare diseases
    - DG SANCO will elaborate during 2007/2008 a proposal for a **Commission Communication on the European Health Information and Knowledge System:**

- Summarising the principles basing the EU health information and knowledge system,
- The responsibilities of the different actors in this field, the role of DG SANCO,
- The national and EU responsibilities on the mechanisms for collecting data (health surveys, hospital information, etc.),
- The interoperability of different systems of health indicators, the cooperation with other actors (Eurostat, ECDC, OCDE),
- The role of the consultative structures,
- A code of good practices on health information,
- Obligations that the European Commission should assume with respect to the Member States in the field of health information.

Ongoing DG SANCO priorities on rare diseases

- EU Projects identifying rare diseases and assessing prevalence
- EU Projects supporting cooperation between rare diseases organisations
- EU Projects creating networks of action for rare diseases
- European Conferences on Rare Diseases
- The European Commission Task Force on Rare Diseases
- EU action to improve classification and codification of rare diseases in the next ICD-11 (International Classification of Diseases)
- Contribute to the Orphan drugs strategy
- Contribute to the European Community Framework Programme (FP7)
- Pilot reference networks (centres of reference) for rare diseases
- A proposal for a Communication and a proposal for a Council Recommendation on rare diseases

DG SANCO priorities on rare diseases

Pilot reference networks (centres of reference) for rare diseases

- DG SANCO has established the High Level Group on Health Services and Medical Care as a means of taking forward the recommendations made by the reflection process on patient mobility. One of the Working Groups of this High Level Group refers to reference networks (centres of reference).
- In 2006 the Rare Diseases Task Force Working Group on centres of reference submitted a report 'Contribution to policy shaping: For a European collaboration on health services and medical care in the field of rare diseases' updating the information about centres of reference in Europe. The report details the use of the concept of centres of reference in Europe as well as the respective functions.

The suggested criteria to be fulfilled by the European centres of reference are:

- Sufficient activity and capacity to provide relevant services and maintain quality of the services provided
- 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
- Demonstration of a multi-disciplinary approach;
- High level of expertise and experience documented through publications, grants or honorific positions, teaching and training activities
- Strong contribution to research
- Involvement in epidemiological surveillance, such as registries
- Close links and collaboration with other expert centres at national and international level and capacity to network
- Close links and collaboration with patient organisations where they exist.
- Appropriate arrangements for referrals of patients from other Member States established within a framework
- Appropriate capacities to diagnose, to follow-up and manage patients with evidence of good outcomes so far as applicable.

European Conferences on Rare Diseases

- Luxembourg 2005 : http://ec.europa.eu/health/ph_threats/non_com/ev_pre2005_en.htm
- Lisbon 2007 : http://www.rare-diseases.eu
- Poland 2009
- The Netherlands 2011

The European Commission Task Force on Rare Diseases

To better emphasize the importance of and action in the field of rare diseases, the European Commission set up an advisory structure: the Task Force on Rare Diseases (RDTF).

- The main objectives of the Task Force on Rare Diseases are to identify morbidity and mortality indicators for rare diseases, set up a common framework in the field of public health for rare diseases, and to produce an electronic newsletter
- Single structure in the EU to monitor Rare Diseases Health Policy
- Plus COMP (Committee for Orphan Medicinal Products) and WG on Reference Centres
- The Task Force is assisted by a Scientific Secretariat which was set up to contribute to the development of public health action in the field of rare diseases
- The RDTF publishes a monthly electronic newsletter on the EC's Rare Diseases actions: **ORPHANews Europe**: **http://www.orpha.net/actor/EuropaNews/2006/060316.html**

A proposal for a Communication and a proposal for a Council Recommendation on rare diseases

- There is probably no other area in public health in which 27 national approaches could be considered to be so inefficient and ineffective as with rare diseases. The reduced number of patients for these diseases and the need to mobilise resources could be only efficient if done in a coordinated European way.
- This initiative is one proposal in the AMP 2007.
- Article 152 provides for the adoption by qualified majority by the Council of Recommendations, on the basis of Commission proposals, for the purposes set out in that article.
- These Recommendations are the only legislative tool provided for in Article 152 on public health except for the few areas where measures or incentive measures may be adopted (see Article 152.4).

Recommendations are without legal force but are negotiated and voted on according to the appropriate procedure. Recommendations differ from regulations, directives and decisions, in that they are not binding for Member States. Though without legal force, they do have a political weight. The Recommendation is an instrument of indirect action aiming at preparation of legislation in Member States, differing from the Directive only by the absence of obligatory power.

Content of the Communication (Chapters' Headlines. See the presentation of Toni Montserrat in the annexed documents for more information)

- Common definition of rare diseases in the EU
- Necessity of national plans for rare diseases in the EU Member States
- European guidelines for the elaboration of the national plans for rare diseases
- Common databases and medical protocol for the identification of genetic rare diseases
- Common approach for a better codification and classification of rare diseases in the process of revision of the International Classification of Diseases
- Creation of the EU Forum on Rare Diseases: The EU Forum on Rare Diseases will accomplish the tasks now still performed by the EU Task Force on Rare Diseases
- The European Conference on Rare Diseases: The Conference should follow the model of the last ones (Luxembourg 2005 and Lisbon 2007) organised with the support of the Public Health Programme. The conference should be organised by the EU Forum on Rare Diseases with the specific budget to be fixed in the EU Budget during the coming years for the activities of the EU Forum.
- Common approach to the support of patient organisations
- Creation of the EU Rare Diseases Portal as a part of the EU Health Portal and as a common tool for rare diseases identification
- Creation of networks of action for rare diseases supported by the Public Health Programme
- A solid benchmarking could be established with successful EU Public Health Programme ongoing projects, having World relevance in the area [EUROCAT (Surveillance of congenital anomalies in Europe), ENERCA (European Network for Rare Congenital Anaemias, EU Rare Forms of Dementia Project or EAIS (European Autism Information

System)] or EU FP6 ongoing projects [EUROWILSON, RBDD (Rare Bleeding Disorders Database) or EUROSCA].

- Better integration of the EU rare diseases public health action with other rare diseases policies (research, orphan drugs, advanced therapies, etc.)
- A procedure for the creation and recognition of EU networks of reference for rare diseases
- Certification of laboratories that perform gene testing
- Networking of Bio Banks in the EU
- Data protection: a special attention has to be drawn to the EC Data Protection Directive.
- Training of rare diseases researchers and professionals
- Intensifying Therapeutic Research, toward a Public–Private Partnership
- A systematic report on the situation of rare diseases in the EU
- A monitoring for the future: On the basis of the work of DG SANCO and the advice from the European Forum on Rare Diseases, the creation of a European Office on Rare Diseases could be considered as an appropriate way of action

Timelines

- June 2007: Scoping Paper to the Commissioner's Cabinet
- July 2007: First Draft in consultation with Rare Diseases Task Force
- September 2007: Final Draft
- September 2007: Process of public consultation starts
- Health Impact Assessment Starts
- 1st Semester 2008: Under the priorities of the Slovenian Presidency
- Discussion on the Council and the European Parliament (???)
- 2nd Semester 2008: Approval under French Presidency (????)

DG SANCO priorities on rare diseases Web site

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

Terkel	**Andersen**	Eurordis	EU
Prof Generoso	**Andria**	Napoli University	Italy
Dr Ségolène	**Aymé**	Rare Disease Task Force / Orphanet	EU
Dr Martin	**Benes**	State Institute for Drug Control SUKL	Czech Rep.
Marcelle	**Bousbaci**	Alliance Maladies Rares	France
Dr Pierre	**Chauvin**	Inserm	France
Teresa	**Coelho**	Hospital Geral Santo António	Portugal
Paula	**Costa**	Rarissimas	Portugal
Jane	**Cox**	National Health Service	United Kingdom
Ana Rita	**Dagnino**	Haemophilia Association	Portugal
Michaela	**Damin**	Barth Syndrome Trust	United Kingdom
Dorica	**Dan**	Prader Willi Association	Romania
Marjolein	**de Booys**	St. Hoofd Hart En Vaten	Netherlands
Evanina	**de Morcillo**	DEBRA	Spain
Prof Jean Charles	**Deybach**	Louis Mourier Hospital	France
Martin	**Dorazil**	European Commission DG SANCO	EU
Christophe	**Duguet**	Association Française contre les Myopathies	France
Jean	**Elie**	Vaincre la Mucoviscidose	France
Prof Anders	**Fasth**	Göteborg University	Sweden
Dr François	**Faurisson**	Eurordis	EU
Dr Alexandra	**Fourcade**	Ministry of Health	France
Dr Laura	**Fregonese**	Patient Associations and AIR Registry	Netherlands
Marguerite	**Friconneau**	Association Française contre les Myopathies	France
Dr Marie-Noëlle	**Gaveau-Glantin**	Asso. Française Synd. Ehlers Danlos	France
Liz	**Gondoin-Goedert**	ALAN asbl	Luxembourg
Anja	**Helm**	Eurordis	EU
Muriel	**Hérasse**	Eurordis	EU
Dr Marie-Claude	**Hittinger**	Haute Autorité de Santé	France
Birthe	**Holm**	Rare Disorders Denmark	Denmark

Tomas	**Honzik**	Patient representative	Czech Rep.
François	**Houÿez**	Eurordis	EU
Hanne	**Hove**	Clinic for Rare Handicap	Denmark
Jiri	**Hruda**	Huntington Disease Association	Czech Rep.
Helena	**Hülsmann**	Sigma Tau	Germany
Lene	**Jensen**	Rare Disorders Denmark	Denmark
Dr Edmund	**Jessop**	National Commissioning Group	United Kingdom
Dr Martin	**Johnson**	Thalidomide Trust	United Kingdom
Simone	**Keita**	Eurordis	EU
Anna	**Kole**	Orphanet / Inserm	EU
Dr Maryna	**Krenkova**	State Institute for Drug Control SUKL	Czech Rep.
Inge	**Kristensen**	CSH	Denmark
Dr Paolo	**Lanzi**	Alekos	Italy
Prof Joao	**Lavinha**	INSA	Portugal
Yann	**Le Cam**	Eurordis	EU
Dr Elisa	**Leao Teles**	Hopital de Sao Joao	Portugal
Mirjam	**Mann**	ACHSE	Germany
Marketa	**Mikulackova**	Patient representative	Czech Rep.
Toni	**Montserrat**	European Commission DG SANCO	EU
Christel	**Nourissier**	Prader Willi France	France
Prof Luis	**Nunes**	Dona Estefania hospital	Portugal
Dr Christian	**Nuttin**	Centre Hospitalier de Luxembourg	Luxembourg
Kasia	**Peala**	Eurordis	EU
Prof Flora	**Peyvandi**	University of Milan	Italy
Bianca	**Pizzera**	IPOPI	Italy
Dr Gabor	**Pogany**	Williams Syndrome Association	Hungary
Barbara	**Poli**	Aniridia Association	Italy
Dr Manuel	**Posada**	RD Research Institute Madrid	Spain
Dr Bernd	**Quadder**	Sarcoidosis Association	Germany
Alvaro	**Ramirez**	European Autism Information System	Spain
Prof Olaf	**Riess**	Tübingen University	Germany

Dr Maria Clara	**Sa Miranda**	Instituto de biologia Molecular e Cellular	Portugal
Rosa	**Sanchez de Vega**	Aniridia association - FEDER	Spain
Dr Janos	**Sandor**	Rare Disease Task Force	Hungary
Denisa	**Sevctkowa**	Coalition for Health	Czech Rep.
Mona	**Sjostrom**	Swedish Association of Rare Disorders	Sweden
Dott. Ssa Annarosa	**Soresina**	Brescia University	Italy
Alan	**Summerside**	Thalidomide Trust	United Kingdom
Dr Domenica	**Taruscio**	Istitute Superiore di Sanita	Italy
Prof Josep	**Torrent i Farnell**	COMP	Spain
Caroline	**van Heesewijk**	European 11Q network	Netherlands
Dr Sonia	**van Weely**	Dutch Steering Committee Orphan Drugs	Netherlands
Jeanet	**van Zoelen**	VSOP	Netherlands
Prof Joan Lluis	**Vives Corrons**	ENERCA	Spain
Bettina	**Vogel**	ALAN asbl	Luxembourg
Prof Thomas	**Wagner**	Goethe University Frankfort	Germany
Elizabeth	**Wallenius**	Swedish Association of Rare Disorders	Sweden
Ariane	**Weiman**	Eurordis	EU
Keith	**Williams**	Sigma Tau	United Kingdom
Melissa	**Winter**	Genetic Interest Group	United Kingdom
Lynne	**Zwink**	X Fragile Association	United Kingdom

CENTRES OF EXPERTISE & EUROPEAN REFERENCE NETWORK IN RAPSODY

Yann le Cam, chief Executive Officer, Eurordis

As a reminder, Yann Le Cam introduced the workshop objectives:

- To produce a new set of data, primarily based on patient needs & experiences, supporting proposals for public health policy and healthcare organisations for centres of expertise and European reference networks for rare diseases
- To facilitate dialogue
  - Between patient representatives, health care professionals and policy makers
  - Both at national and European levels

aiming at:

- Exchange of experience and perspectives
- Appropriation of concept
- Development of common vision and approaches across rare diseases and across Member States
- To promote policy on centres of expertise and European reference networks

In order to facilitate dialogue at the national level, a series of workshops were held:

Member State	Date	Lead contact person	Organisation	
Czech Rep.	2nd March	Maryna Krenkova	SUKL	21 PO, 12 HCP, 4 PM = 37
Denmark	26th March	Torben Grönnebaek	RDD	10 PO, 7 HCP, 2 PM = 19
France	29th March	Françoise Antonini	Alliance Maladies Rares	12 PO, 6 HCP, 7 PM, 1 Pharm = 26
Germany	19th March	Mirjam Mann	ACHSE	11 PO, 6 HCP, 5 PM = 20
Italy	24th March	Simona Bellagambi	UNIAMO	10 PO, 7 HCP, 1 PM = 18
Luxembourg	22nd March	Bettina Vogel	ALLAN asbl	2 PO, 8 HCP, 1 PM = 11
Spain	23rd March	Rosa Sanchez de Vega	FEDER	17 PO, 16 HCP, 4 PM = 37
Sweden	16th March	Elisabeth Wallenius	Swedish Alliance	11 PO, 10 HCP, 7 PM, = 28
Netherlands	11th April	Pauline Evers	VSOP	9 PO, 11 HCP, 2 PM = 22
United Kingdom	28th March	Alastair Kent & Melissa Winter	GIG	16 PO, 12 HCP, 1 PM = 29
Portugal	30th March	Ana Rita Dagnino	Ass. Haemophil Portugal	14 PO, 10 HCP, 1 PM = 25
				Total 272 participants

Preparation of the workshops

All workshops were based on same methodology:

- Same agenda
- Similar composition of participants: PO, HCP, PM
- Template report

A synthesis of the Rare Diseases Task Force report on centres of expertise (2nd Update) was sent to all organisers on 10th January, and a synthesis of the "Report of the work of the High Level Group on Health Services and Medical Care in 2006" and annexes was sent to all organisers on 31st January together with a presentation prepared by Martin Dorazil (DG SANCO) and validated by WG ERN.

Agenda of national workshops

The European political agenda and the state of the art today

1. The agenda: political orientations of the High Level Group on Health Services and Medical Care

- A synthesis by the national representative of the High Level Group on Health Services and Medical Care (HLGHSMC) to present the proposed concepts of the European reference networks of centres of expertise outlined in the 2005 report.
- Options for a procedure for identification and development of European reference networks outlined in the 2006 report

2. State of the art of existing centres of expertise for rare diseases in Europe today

- Key findings of the DG SANCO Rare Diseases Task Force report and rationale for establishing EU collaboration, by the national representative of the Task Force or the Orphanet contact
- Key figures and data, typology of specialist centres relevant to the national debate and comparison with other Member States.
- Recommendations of the Rare Diseases Task Force

Questions for debate

Question N° 1: Needs and expectations for national rare diseases centres of reference/expertise

- What are the expected benefits for patients?
- How does the concept of centres of expertise meet these requirements?
- How does the concept of centres of expertise apply to the national health care system?
- What criteria to use to identify/designate them? How is it done already or how would you like to do it?
- What cooperation between centres of expertise and other specialist care centres? Are national networks of centres of expertise the solution?
- How to ensure long term sustainable funding?
- What critical view do you have of the risks and benefits of the approach, expected advantages and potential risks?

Question N° 2: Proposals for the evaluation of national centres of reference/expertise in your country

- How would you measure if the centres of expertise actually respond to your expectations?
- How can we ensure that patients really benefit from them?

Question N° 3. Cooperation with other countries and recommendation for European reference networks

- How do you see your centres cooperating at the EU level?
- What role would European reference networks play?
- Which specific added value can you identify when networking your national centres of expertise at European level?
- On which criteria to identify/designate European reference networks?
- What would the specific expected benefits for patients be?

Steps for synthesis and dissemination of outcomes

- Synthesis 10 reports by Advisory group meeting (Paris): 11 June 2007
- Information to EU HLG WG ERN (Brussels): 14 June
- Information to DG SANCO RDTF (Luxembourg): 20 June
- Analysis first results EurordisCare survey (Paris): 29 June
- European Workshop (Prague): 12-13 July

- Report from European Workshop Prague September
- Dissemination CD-Rom to all 272 participants of national workshops, all 116 patient groups in EurordisCare Survey, EU HLG WG ERN & RDTF October
- Information to EU HLG WG ERN & RDTF & COMP October
- Additional national workshops organised on similar but adapted agenda (request from Hungary & Greece) October
- Analysis full results EurordisCare Survey October
- European Conference on Rare Diseases (Lisbon) 27-28 Nov

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