



# National Strategies & Action for Rare Diseases in Europe



Paris, 18th November 2008

## Opening Comments

**Roselyne BACHELOT-NARQUIN**

**French Minister for Health, Youth and Sports**

### **I. Values**

Cooperation and solidarity are two of the key values on which the EU is based. They are also the basic values of the series of events dedicated to rare diseases organised under the French presidency of the EU. The participants are numerous and diverse because we share common concerns. The issue of rare diseases impacted 30 million EU citizens. This event reflects a will to build solidarity in Europe when it comes to health.

### **II. Knowledge**

Skills and know-how in the rare disease area are highly specialised. There is much scope for cooperation here. France was the first EU country to implement a national plan against rare diseases, and this is widely acknowledged. The research skills of our experts and the ability of our health service to mobilise are exemplary. Such examples prove the importance of sharing and coordinating this experience.

### **III. Rare Disease Plan**

The rare disease plan for 2005-2008 led to breakthroughs for patients. Research on rare diseases has benefited from significant additional funding, which enabled the development of 200 clinical and basic research projects. The rare disease centres deal with 18 rare diseases. We are fighting to reduce the isolation of patients and their relatives. The standard of healthcare has greatly improved with the development of national diagnostic and healthcare programmes.

### **IV. Synergy**

The most important feature of the plan was the synergy it generated between public authorities, associations, scientists and the public. We will be sharing the lessons learned from this plan with our European partners. Building a Europe of health does not mean opposing national systems or

defining one as an absolute model, but rather benefiting from the experience of all countries. Rare diseases are best fought on a European scale. The EU Commission has defined five priorities for European cooperation: to improve knowledge and cooperation, strengthen research, implement and develop reference networks, pool expertise, and encourage regional cooperation. Common principles will lead to efficient and effective policies. France supports a European advisory committee on rare diseases, partnerships between public and private sectors, and national plans to relay European policy at a local level. Each EU country will be implementing a rare disease plan between now and 2011. France has already launched one.

## **EU Commission Proposals**

**Nick FAHY**

**Head of the Health Information Unit at Directorate-General for Health and Consumer Protection (DG SANCO), European Commission**

### **I. Origin**

We only bring together the ideas and the work of the 500 million people in the EU. The involvement of different partners goes back a long way, as do the research priorities. This is a clear recognition of the potential added value of addressing rare diseases at EU level. It is a classic area where more can be achieved together than individually. It is also a testament to the involvement of many people and organisations. We have not just supported cooperation between member states but also adapted our frameworks at EU level. We have worked with the Rare Diseases Task Force, and also gave an opportunity for public consultation at EU level. There was a huge response to the latter. We also carried out an impact assessment process for all the proposals. There is enormous potential for gains in efficiency and effectiveness at EU level.

### **II. Priorities**

The first priority is improving the visibility and recognition of rare diseases. It is about making these diseases real, giving a reference point for doctors to recognise diseases. This is an example of how working together can improve such visibility. The second priority is supporting policies on rare diseases in member states and developing cooperation at EU level in terms of practical tools.

### **III. Rationale**

Why should we do this? There are barriers to recognising these different conditions. This is not to underestimate the difficulties involved in identifying diseases. However, there must be better resources available to health professionals. We want to enable people to access resources even if they are only available in a member state. We will contribute to the formal classification of disease and continue to support the development of more information frameworks at EU level. A condition does not exist until it is recognised, and neither do support services.

#### **IV. National Plans**

The Commission has no power to decide what member states should do in this area. We have proposed a Council recommendation, inviting states to set out national and regional action plans in order to implement the ideas and approach set out in the communication. We will provide practical guidance to countries as to how that can be done, but it ultimately up to the member states. The treaties are very clear about where binding decisions can be taken at EU level and where collective agreement has to be sought. This area is one of the latter. Medical professionals are difficult to coerce.

The Council agreed to the political commitment of all member states to implement screening for breast, cervical and colorectal cancer. Enormous progress has been made in implementing this, even though the directive was not binding. Therefore, we are convinced that the recommendation will have a major impact. It is not just about the actions about member states. We hope to be able to work together and use the national plans as a framework for coordination. We will introduce a mechanism for designating and recognising centres of expertise at European level and recommend their inclusion within the national plans.

#### **V. Limits**

The health service of member states represent a basic commitment to care for people. We can help them in terms of expertise and research. However, in the end it comes down to how much member states are willing to put into it. The range of we can propose is limited. We will try to strengthen R&D incentives, and support member states toward a common understanding of the usefulness of these products.

#### **VI. Next Stage**

The rare disease programme is part of a wider campaign to make healthcare more relevant for patients across the EU. The directive on cross-border healthcare broadens the options open to those seeking healthcare in other states, qualifies health and safety rules, and proposes key areas of cooperation. We are launching initiatives on patient safety and quality in healthcare. We plan to establish a partnership for action against cancer next year. We also raise awareness concerning communicable diseases. The aim is to provide healthcare that is as closely adapted as possible through all these different aspects.

We need to show how relevant the EU is to people's lives. How does this action on rare diseases fit into this perspective? We will now start discussing the proposal for a Council recommendation on rare diseases with member states. Next year we will use health and research tools available at European level to start taking actions on the areas listed in the communication. These actions will be based around the three priorities of identifying rare diseases, supporting member states, and reinforcing cooperation at European level.

#### **VII. Conclusion**

These proposals are based on the work of many varied groups over many years. We look forward to working with them over the coming years to turn their potential into reality for the citizens of the EU.

## **Communication on Rare Diseases**

### **I. Recommendations**

**Terkel ANDERSEN, President of EURORDIS**

#### **1. Rare Disease March**

The annual Rare Disease Day march in Paris symbolises what we are doing here. It shows that people with rare diseases and their families are prepared to invest everything they can in achieving more, not only for them themselves but others who will follow. The communication on rare diseases was adopted a week ago. This is a turning-point, and a cause for congratulating the French for their commitment. Thanks to the French presidency, the EU health ministers will debate the draft recommendations. We need to act quickly if national plans are to be adopted by 2011.

#### **2. Cornerstone**

A cornerstone of these recommendations is that a priority is given to defining national plans for rare diseases. There is also the need to establish centres of reference and expertise in each country. Ségolène Aymé will now talk about this. She developed Orphanet, a fantastic reference not only for physicians but also for patients.

### **II. Priorities**

**Dr Ségolène AYMÉ, Coordinator of the DG SANCO Rare Diseases Task Force, Director of ORPHANET**

#### **1. Process**

Many things have happened within the member states. We should remember that we are in a process. There is a time dimension. Concepts need time to mature, and nothing can happen overnight. The US established the Office of Rare Diseases in 1993, and Denmark took similar measures around that time. Reference centres were set up at regional level in Sweden, as well as the Agrenska Centre. France opened the Orphan Drugs Office in 1995, in 1996 Orphanet and in 1997 EURORDIS. Rare diseases were already part of Italian public health policy.

#### **2. Initiatives**

Rare diseases are only identified as a public health issue in some countries. There were many outstanding initiatives in the UK together with patient associations. The Netherlands set up a steering committee in 2001, and Italy established reference centres in 2002. The Germans and the Spaniards tried successfully to finance the establishment of research networks in 2003 in order to force cooperation within the arena of rare diseases. France implemented its national plan in 2004. Then seven member states set up initiatives for joint funds through the AIRNET project. Romania and Portugal defined their own plans in 2007, followed by Bulgaria in 2008. Orphanet is present in 38 neighbouring countries today.

### **3. Needs**

Teams need funds to set up networks, and databases need to be shared. It is difficult to do, but it is mandatory. The concepts behind clinical trials need to be rethought. Experts are as rare as the diseases. Non-specialised doctors must be able to refer their patients to specialists in other centres. Expertise must be shared as widely as possible. Recommendations for clinical practice must also be developed, which is extremely difficult. We should be able to offer relevant information for diagnostic and healthcare purposes. This can only be done via guidelines, targeted by disease. Drafting guidelines is extremely difficult, so some countries should be considered adapting existing ones. A database is necessary to show doctors where the experts are.

Regarding patient organisations, nothing can be done in a given country without feedback from the people involved. The recognition of orphan drugs requires intervention by each member state, because the constraints imposed by regulations and markets are very heavy. Dedicated national funds need to be implemented. Regarding training, there have been many initiatives to raise awareness of rare diseases among professionals. They need to be able to access information resources, because they cannot be trained in all rare diseases. No state, no matter how large, can have expertise in every sector. Specimens have to be sent to specialised labs in different countries. Therefore, actions should be coordinated, and funds must be allocated.

### **4. Examples**

All countries should become involved in pooling resources. The expert centres should be developed, and there should be an added value at the European level. We should rely both on national and regional centres. The Orphan Drug Committee was established in Belgium. There is a French national drugs fund. Hungary also has a committee for treating rare diseases. Ireland, Holland and Poland also have platforms for debating orphan drugs etc.

### **5. Unfair Access**

Initiatives are needed to support patients. Not all countries are involved in such programmes. EURORDIS is a strong driver of this trend, but we do not yet have adequate patient organisations in every country. France and Sweden both have national information systems accessible to patients and professionals. However, it cannot be said that this tendency is universal.

### **6. French Plan**

Orphanet is a tool of national policy. More than 5,000 research projects are underway. There are 900 clinical trials, 400 registries, and 3,300 expert clinics in Europe.

France is the only country with a national plan, but other countries have at least adopted national action frameworks. The French plan was concerned with defining reimbursement of healthcare, because there are specificities linked to rare diseases. It also looked at developing national protocols for each disease. Two-hour training programmes were introduced for doctors. No significant progress was made on screening, but testing services have developed thanks to the concept of reference labs. 132 reference centres were approved and funded, and complementary competency centres were established in the regions. Significant efforts were made to fund orphan drugs and increase supply.

Progress has also been made in proving research facilities. The Rare Disease Platform holds over 200 meetings annually, with the aim of contributing to the definition of a European policy. There is a collective wish to share experience. Each member state should adapt the policies to their own health networks. Hopefully, results should be seen in two or three years.

### **III. Questions and Answers**

#### **From the floor**

What is the difference between a competence centre and a reference centre?

#### **Dr Ségolène AYMÉ**

This is a French concept. The reference centre has national competence, while the other has regional competence. It is a question of collaboration, because they have to share good clinical practices and expertise. Applicability to other countries will depend on their size. It is not always easy to translate this kind of system to other countries. France is the only European country with a centralised system, and this is not easily transferable. Some countries do not have the resources for the kind of expertise found in a resource centre.

#### **From the floor**

I am responsible for the research centre in Paris. We have what are called pilot units. What are the linkages between those pilot units and the reference centres?

#### **Dr Ségolène AYMÉ**

The rare disease centre in France does not include the cancer initiatives, because cancer has its own programme. The pilot units are experimental units. We are in charge of building a network so as to secure recognition for rare cancers, for example, as well as rare diseases. There is political will to provide a reference centre for cancer, because it has very specific procedures.

#### **François GOLFIER, head of the center on trophoblastic diseases**

We are increasingly seeing a feeling of guilt in patients as to how expensive their treatments are. There is a need to take the resources of patients into account. We should quantify the value of consultations.

#### **Nadia BELMATOUG, reference center on lysosomal diseases**

This was an excellent presentation and I agree about solutions being tailored to national systems. However, what would be the European indicators of progress?

#### **Dr Frits LEKKERKERKER**

I noticed that you said in your presentation that the only plan with results was the French one. I tend to agree. However, what is your definition of a national plan with results?

**Dr Ségolène AYMÉ**

An action plan would be to implement a mechanism so that all stakeholders negotiate a solution. Different countries face different problems. Expertise is one of the fundamental concepts applying to all countries. The difficulties depend on available funding. Rare diseases are treated in level three centres in England, for example. Other countries do not have that kind of expertise. Therefore, we should define objectives and see how we can meet them. This will depend on the system.

**Luc BOLAND, Lou Foundation**

I would like to emphasise three topics. First of all, the families of patients have to become more involved in care. Secondly, experts in rare diseases cannot access the same level of funding as other groups. There is a lack of trust between associations and doctors. I think doctors do not want to recommend associations to patients.

**From the floor**

Germany is far behind France in this area. However, being a federal country, it may help create a model for the federal European situation. Recommendations and targets are laudable, but a textbook approach should be avoided. Both the member state ministries and the associations would like to be given meaningful information regarding closer cooperation. Failure to do so might jeopardise the effort to implement national plans.

**Christiane KARAKOGLU, AFPCA vice-president**

I am the vice president of an association against atrophic polychondritis, one of the rarest autoimmune diseases. I have this disease myself. The utmost priority is to be recognised. I used to be a neurologist, but my disease prevents me from doing that now. People have to know what we have to deal with. Only 10% of French GPs use Orphanet. That is not good enough. It is also good that GPs have two hours to learn about rare diseases, but that is not enough. We should be able to ask our GPs or specialists to engage in training in rare diseases. We have to get together and create this momentum.

You mentioned that 80% of rare diseases were genetic. Are you talking about monogenic or multigenic? Over 80% of children have non-communicable genetic diseases. Why not finance research into rare autoimmune diseases at the European level? There are increasing numbers of cases in Europe.

**Terkel ANDERSEN**

I wanted to draw attention to the point about linkages. It is important that we not only create national systems but also consider maximising resources throughout Europe.

**Dr Ségolène AYMÉ**

It is true that there are differences between member states. We have to take into account the fact that these diseases are rare, but we must also consider the other aspects. Autoimmune diseases are prevalent among rare diseases. You are right that we need targeted actions.

**Dominique ACKER, French Ministry of Health**

I have a question for Dr Ségolène Aymé and one for Nick Fahey. What do you think about telemedicine?

**Nick FAHY**

The Commission has just drafted a communication about this. We see an economy of scale in this area. It is no longer a matter of technology. The central message around telemedicine is that it is a real possibility in the area of rare diseases. Health systems have to try and integrate it. I would also like to answer two other questions. I agree with your definition of a programme. A recommendation is the list of questions to be dealt with by the roundtable. We hope member states will fund those recommendations and discuss them at national level. We have to recognise commonalities and well as specificities, and combine them.

Mr Sarkozy said that health is not something to be dealt with during periods of economic growth, but involves society as a whole. Health is about solidarity. The more solidarity you need, the more important it is to grant funding. It is not as if we spend more on our health system than the rest of the world. The US spends 50% more on average. It is important to highlight the notion of solidarity.

## **Session One: Sharing Experiences Between Member States**

### **I. Lessons from the Netherlands**

**Dr Frits LEKKERKERKER, Chair of the Dutch Steering Committee on Orphan Drugs**

#### **1. Recommendations**

It all started with the recommendations of the Advisory Council on Health Research in 1998. The first was to make an inventory of and coordinate all ongoing initiatives on orphan products and diseases. The second was to stimulate R&D and create research budgets. The third was to prioritise 25-30 rare disorders for research at European level.

#### **2. Steering Committee**

Our steering committee started in 2001. Its mission was to encourage R&D in orphan drugs, and to improve the situation for patients, particularly in the field of information. We reviewed our activities in 2004, and invited representatives of health insurance companies to join. We realised that doctors and pharmacists need more information. We held workshops from 2005 to 2008 on orphan products, and also focused on stimulating research in universities and companies. We are now making a new plan for the coming three years. There is no official national plan in the Netherlands. The steering committee has its own strategic plan, devised between all the actors.

### **3. Priorities**

The priorities for the next three years are as follows. The first is to encourage the development of orphan products. The second is to stimulate top level patient care in the context of diagnostics and research initiatives, and to ensure proper academic standards for students. The third is to improve access to information for patients, and the availability of orphan products.

### **4. National and European Roles**

We provide information; we conduct workshops in the area of orphan diseases and products. We have encouraged and secured additional funding for research. We have also constantly driven the national debate and increased awareness. Regarding the European level, we take part in the European network and in European initiatives.

### **5. Lessons**

One of the positive lessons that we learned is that our multidisciplinary nature enables us to learn from each other and work to remove barriers. New rules are proposed and accepted, such as that about reimbursement. We are also an information point and coordinator for the different actors.

However, responsibility for orphan products and diseases are split up between different government departments. We have a mission, but we do not have a mandate. Our budget is limited, but the terms of reference are very board. We are responsible for everything. It should be possible to move some of these responsibilities to other stakeholders.

### **6. Plan**

The goal is to delegate certain tasks. However, the problem is that not all actors are willing to take responsibility. We are discussing this with them, and new activities may be developed from these discussions.

## **II. The Italian Experience**

**Dr Domenica TARUSCIO, Director of the national Center at the High Institute of Health, Italy**

### **1. Plans**

Rare diseases have been a priority topic in Italy since 1998. There has been no overarching national plan, but a series of plans with specific objectives. Each has tried to establish a multidisciplinary approach at regional and national level. There has been an emphasis since the first plan on establishing centres for the diagnosis and treatment of rare diseases. A national registry of rare diseases was established, and a national research programme.

### **2. Criteria**

The Ministry of Health promulgated a decree in 2001 for a national network aimed at prevention, diagnosis and treatment of rare diseases, and the exemption of patients from the cost of treatment. The constitution was changed in 2002, so that regions had to share the responsibility of organising

the survey and treatment network. We learned from this the importance of legislative instruments in implementing the framework.

We are in principle in line with the EU task force's suggestions as to objective criteria for centres. Therefore, our centres have to operate according to clinical protocols, collaborating with each other, with local services and family doctors. We also need inter-regional coordinating centres.

### **3. Lessons**

Selective criteria must be used to identify centres for diagnosis and treatment. A multidisciplinary approach must be promoted, as well as communication between centres and local health services. Integrating health and social services is a challenge. However, a bigger challenge is implementing a comprehensive framework, keeping in mind the different stakeholders involved.

### **4. Results**

Each region has identified coordinating centres. National registries have been established and dedicated funds are available. 36 of the 46 authorised orphan drugs are available. The Consulta has presented to the ministry a list of needs and priorities to be included in the national plan. We are monitoring the success of diagnoses and care programmes, as this data will be useful for future planning. Funding research programmes will lead to discovery of new drugs while patient quality of life studies are ongoing.

### **5. Lessons**

Rare diseases should be approached with a comprehensive, integrated strategy. The regional networks are collaborating very well. It is not a fixed model. The regions are continually improving, comparing their performance with other regions and optimising resources. There is engagement with patients at several levels. The Consulta is the main instrument for this, but there are other associations which promote the process. There are measures for supporting research at national and international level. The Italian Drug Agency issues calls for research, and the Ministry of Health is calling for clinical studies.

### **6. Challenges**

It is difficult to coordinate different stakeholders with different levels of autonomy. A critical point is ensuring access to care and services in all 21 regions. Funds need to be available for initiatives, and these initiatives need to be monitored.

## **III. Bulgaria**

**Pr Rumen STEFANOV, Director of Information Center for Rare Diseases and Orphan Drugs, Bulgaria**

### **1. National Plan**

The information centre began work in 2004, with a campaign for a national plan which did not succeed. A new campaign in 2006 had strong support from the EU and Bulgarian patient associations, and this one succeeded. The final version is not very different from the first draft.

The plan was officially adopted at the beginning of September with a budget allocation of around €1 million. There are nine priorities from epidemiological surveys to genetic services, including new tests. New attention is being paid to research and training. We consider collaboration with member states to be very important.

## **2. Needs**

Support from the medical community is assured; public support is crucial to ensure common understanding. The communication issued by Brussels is very important for ensuring that new member states take the issue seriously. We also lost a lot of time by underestimating the need for political goodwill.

## **3. The Future**

We are very optimistic about the establishment of a national diagnosis and treatment network. There are still problems we cannot solve. There is a significant issue with the availability of registered orphan drugs owing to the size of the population. There is little money available for orphan drugs owing to low GDP. There are also problems with the transparency of reimbursement procedures, and with integrating social with medical services.

## **IV. Portugal**

### **José ROBALO, Deputy Director General of Health, Portugal**

#### **1. National Programme**

The national programme was approved by the minister six days ago. The main goals are to improve the national response to patients and to improve healthcare. There are three main issues in the programme: intervention, training, and collating and analysing data. It is vital to improve research and access to medicine, and to ensure transnational cooperation. Our budget for 2008 is small, but we intend to coordinate the programme over the next month.

#### **2. Preparation**

The first draft was prepared by a working group and launched in November 2007. The programme was open for public consultation until 31 January 2008, and over 100 submissions were received. Three workshops were held with healthcare professionals, the drug industry and patient associations. The final programme incorporates all the input from the stakeholders. The 2008 and 2009 budgets were prepared. The programme was adopted by the minister one month after the final draft was prepared.

## **V. Questions and Answers**

### **Karen BLUM, Novartis**

Congratulations on the national plans. Can the panellists give some feedback on how far the voice of industry was heard? They are a source of expertise and could provide a lot of input. The

industry was included in the workshops in Portugal. Has this been the case in other countries, and if so, was the input considered worthwhile and valuable?

**A speaker, French plateletary hepatology center, Bordeaux,**

We talked this morning about the creation of European networks. I agree that it was very fruitful to build a national network in France. There are many large-scale programmes at European level, but not all countries are funding them. Italy did not finance the ERA project this year, for example. Would it be possible to finance further networks for European collaboration?

**From the floor**

I am the coordinator of the reference centre for contagious diseases. Fritz Lekkerkerker said that your budget was €500,000 per year. What kind of support can we expect from the steering committee? We have submitted an application for a new orphan drug to the EMEA. Could you provide support to this kind of work?

**A speaker, Germany**

I like the emerging emphasis on the participation of patient organisations in programmes, initiatives and forums. However, it seems unclear how that should work if there are no patient organisations, as in the case of the very rare diseases. How do we ensure that such patients share their experiences with social and medical services? It is a doctor's responsibility to inform the patient of the existence of disease-specific groups. The doctors could learn about the patient groups and their scope.

**Frits LEKKERKERKER**

Both large enterprises and SMEs are included in the Dutch steering committee. Regarding licensing, there are brilliant initiatives in the academic domain, but they need the help of small companies to develop them, and the companies need help to get orphan designation. Money is still needed to fund trials, and most of it should come from the EMEA. Support in obtaining orphan designation is an important priority in the Netherlands.

The ERA project should involve coordinating centres in different locations in Europe. The Netherlands recently contributed €1 million to ERA. Regarding patient organisations, umbrella organisations are also important. There should be a way of funding organisations for patients with very rare diseases.

**Pr Rumen STEFANOV**

The question of industrial participation is an important one. We incorporated representatives from the National Alliance for Rare Diseases in the working group. It turned out that the industry was not willing to openly declare an interest in supporting such an initiative. The European Pharmaceutical Enterprises could consider setting up a working group or a statement that might be used by member states as their official position regarding the industry. My experience is that individual pharmaceutical companies are unwilling to cooperate in policy formation.

Regarding ERA, it took us more time to prepare the financial annexes to the programme than the programme itself. It was difficult to define how much of the national budget would go to each

activity. The ERA should look at the national bodies responsible for research and request that specific diseases are made a priority.

**José ROBALO**

We held a workshop for the industry in the National Institute of Medicines, which is responsible for regulating the industry. Regarding the participation of patient associations, the Health Ministry has a directorate on civil participation which handles all interaction with patients' associations.

**Dr Domenica TARUSCIO**

Industry representatives are usually invited to participate in our annual meetings. We contributed €2 million to E-RARE. Resources are very limited, but I am still urging our Ministry of Health to find resources to contribute. This is a great opportunity to stimulate research. I agree that umbrella organisations at EU level can be useful.

**Dr Ségolène AYMÉ**

I would like to comment on greater industrial involvement in defining future actions. We tried to have industrial representatives included at task force level in our committee, and this was rejected by the European Commission. They have had bad experiences in the past with policies surrounding tobacco etc. Rare diseases are very different, and all stakeholders should take part. I think there should be no problem in having industrial participation in formulating action plans.

**Terkel ANDERSEN**

Rare diseases are a focus of all national alliances when they meet under the auspices of EURORDIS. EURORDIS is taking measures to ensure that the Internet can be used to coordinate discussions. 12 key words came up at this discussion. One was tailor-made. The solutions must be adapted to individual member states. The second was the European vision of ensuring collaboration and integrating that into the national plans. The third is to establish a baseline for identifying good centres. The fourth concerned clear and measurable objectives. That was very clear in what Ségolène said. The fifth is to define indicators for measuring development and progress.

The sixth is to establish a network of centres of excellence. EURORDIS has defined common principles for these centres. The seventh is training of medical professionals to ensure they refer patients to the right centres and patient organisations. The eighth is coordination on national and EU level. The next is multidisciplinary. Evaluation is essential for wrapping up the work of the Commission. Then we come to funding. Funding is closely linked to sustainability. Last but not least is patient involvement at all stages to make the best of our expertise.

## **Session Two: Towards an EU Council Recommendation on Rare Diseases National Action Plans**

### **I. Introduction**

**Dr Alexandra FOURCADE, Medical councillor for Hospital and Care Offer, France**

This event is a culmination of the various research efforts on orphan drugs and rare diseases. The community of stakeholders, beginning with the patients' associations, have been the engine and these national and European partners. There are also the funding partners, whether public or private. This event is a step towards a more operational phase. We have an opportunity to elaborate common strategies. We will look first of all at the Europlan project and how it can complement the work of the Commission. Hopefully we can develop a toolbox accessible to all member states where all our knowledge can be pooled.

A national action plan should have concrete and measurable objectives. You need to evaluate them according to what has been achieved and what needs to be achieved. Therefore, we are looking at more the practical side of how to achieve the European Commission's recommendations.

### **II. Europlan**

**Dr Domenica TARUSCIO, Director of the national Center for Rare diseases at the Institute of Health, Italy**

#### **1. Definition**

Europlan is a three-year project, funded by DG SANCO. It officially began in April 2008. The main goal is to give recommendations on how to define a national plan for rare diseases. The priority areas have already been well-defined. We have to collect additional information and establish the various steps toward building a plan.

#### **2. Objectives**

The specific objectives are as follows. The first is to collect additional information. We are describing member state initiatives, and analysing the best cases to use as examples. We need to elaborate indicators for the evaluation of the impact of national plans. Finally, we will specify recommendations for developing strategic plans, mainly in the area of methodological guidance.

#### **3. Work Packages**

EURORDIS will organise several conferences throughout Europe to present the recommendations of the Commission. The coordination for the work packages is based in Italy. The fourth will gather information on existing initiatives. The fifth will elaborate indicators for evaluating the impact of the initial plans. The sixth, led by Sweden, will conduct case studies of successful experiences. The Netherlands will draft the core recommendations in conjunction with experts globally. This will include methodological guidance on implementing national plans.

#### **4. Partners**

The application now involves 25 partners. EURORDIS and the US Office of Rare Diseases are also involved. Many of the stakeholders are now involved in Europlan, including researchers and patients' groups. Other countries have been invited to join. Collaboration is needed in order to learn from other experiences. The Commission allows other partners, who were not part of the initial agreement, to join.

#### **5. Questionnaire**

We are collecting information via a questionnaire on national plans. It is a tool for gathering information on various countries' priorities.

#### **6. Aims**

We want to reach consensus on what is required in national plans, and also to facilitate the elaboration of national plans.

### **III. Activities**

**Dr Annalisa TRAMA, Researcher at the National Center for Rare Diseases, Italy**

#### **1. Aims**

These activities are related to work package four, which describes the activities of the different countries in the areas already identified in the Commission's communication. The process is about identifying the needs of different countries. Information will be gathered through questionnaires, and the information will be used to refine priorities.

#### **2. Questionnaire**

The questionnaire provides information on each country's involvement and activities, but also identifies needs. It has already been sent to the Europlan partners, and they have been asked to identify the different stakeholders and to secure information from them.

#### **3. Respondents**

Healthcare professionals and patients have been involved, but healthcare planners and policymakers also responded.

### **IV. Questions and Answers**

**Andreas REIMANN, German Alliance for Rare Diseases**

How will the responses be weighted? The evaluation by a health ministry may be different in value that one from a single doctor. How do you ensure that the same organisation is not handing in multiple questionnaires?

**Dr Annalisa TRAMA**

Weighting is not really the issue. The main point is to understand how the different perspectives differ.

**From the floor**

There should be consensus within each of the stakeholders as well as between them. Each stakeholder is an organisation. Decision makers may have different opinions from patients. We have a consensus conference between all the members to discuss differences and arrive at a common viewpoint.

**Annalisa TRAMA**

This could be a useful methodology to take on board. We have to ensure that the starting point is as inclusive as possible. We will not achieve consensus through the questionnaires. We just want a description of the differences. Consensus will have to be reached at country level, and we would like to provide the methodology to enable this.

[French audio]

**From the floor**

The needs in different countries are very diverse. Can we reach a general consensus?

**Domenica TARUSCIO**

We have identified the priority areas, and these are common to all countries. The differences lie in the actions that are prioritised. Therefore, we have to have profiles that specify each country's social and health situation.

**Annalisa TRAMA**

Europlan will provide evidence of what works to ensure that others can take advantage of these examples.

**Christiane KARAKOGLU, AFPCA vice-president**

The objective for patient organisation is to establish national protocols for identifying and monitoring diseases. The patient will always struggle without a national therapeutic protocol. This could lead to permanent disabilities.

**Dr Alexandra FOURCADE**

National healthcare protocols still need to be defined. One or two protocols are produced annually for every 7000 diseases. Harmonising practices requires time. We can use protocols that have been established already in one country instead of waiting for new ones to be drafted. Each member state can adapt them to their contexts.

**Patrick DUPUY, Orfagen president**

An important stakeholder is missing from Europlan, the pharmaceutical industry. How do you intend to involve their national representatives?

**Dr Domenica TARUSCIO**

We will involve them in the discussion. We will decide with all partners how to involve more participants.

**From the floor**

It is difficult to see where the pharmaceutical industry fits into the questionnaire. It is about the treatment given to patients from the point of view of patients, policymakers and doctors. A more comprehensive process would probably include the views of the medical product industry as well as the pharmaceutical industry.

**Domenica TARUSCIO**

We will not reach consensus through the questionnaire. We have tried to be inclusive from the beginning. That is why everyone is welcome to our meetings and can provide feedback. Bear with us and follow the process as it evolves.

**From the floor**

The Commission suggests that the member states draft plans for 2011. This deadline is a challenge. How will you achieve any deliverables before 2011, and allow the member states to start working on their national plans?

**Dr Alexandra FOURCADE**

The Commission can help with that.

**Antoni MONTSERRAT, European Commission**

The 2011 date was not randomly chosen. We decided Europlan was to be implemented within three years. It will comprise guidelines for good practices, the content of plans, implementation etc. This should be a sound basis for the member states. We will be holding debates with stakeholders in the member states about the different aspects of the national plans. A very robust and practical policy will be defined. We might consider extending the deadline to 2012 or 2015.

## **V. Patient Associations**

### **Yann LE CAM, Chief Executive Officer of EURORDIS**

#### **1. Message**

We have a chance to build a comprehensive and long-term strategy to address patients' needs across Europe. What do we mean by integration? The Commission communication, Council recommendation and national action plans offer a chance for an integrated approach at European level. The Commission communication points to different parts of EU programmes, such as research or legislation. Each objective of future national strategies should be articulated with this EU policy in mind. The specific added value of rare diseases sets this strategy apart from other public health policies.

The Commission communication provides the opportunity to engage with priority areas such as research, diagnosis, care, information, support and treatment. Each of these should be common to every national plan. We want to see comprehensive research pathways.

#### **2. Sustainability**

It is a long-term commitment. The only possible approach is to have a common strategy across the range of rare diseases, with all parties, sharing infrastructure and tools. National centres are only a start. We need to concentrate on these few building blocks on which to build future national strategies.

#### **3. Key Priorities**

Research comes first. We need to identify the priorities for clinical, transnational and social research. This needs to be linked to the centres of expertise. We expect national plans to allocate resources for research. We need both resources across rare diseases and specific disease projects. We need both biomedical and social and public health research. We regret that PPPs have been taken out of the Commission communication. We need to utilise all these resources in order to achieve results. There needs to be long-term funding for essential infrastructure such as biobanks, registries and clinical research.

#### **4. Centres of Expertise**

This is the second building-block. Multidisciplinarity means that we need both medical and social skills. There must be coordination between hospital and home care. A long-term view is essential for sustainability. It is also essential to provide information networks in national plans, and ways of raising public awareness. A dedicated EU phone number would make a lot of sense in terms of accessing better care. A stronger national basis for Orphanet would mean a stronger European basis. Respite care is essential.

Common EU protocols on diagnosis, screening and care are essential. Fair and just access to orphan drugs across Europe needs to be provided.

## **5. Empowerment**

Empowerment of patient organisations is important. We can praise the work of patient advocates and representatives, but fail to support projects and build capacity. We need strong policy as part of national plans. This is not only linked to social policy but to public health and the generation of knowledge through research and clinical trials. National plans need to ensure that patients and patient representatives are involved at each step of policymaking.

## **6. Methodology**

Steering committees are needed at national level to ensure that decision making is quick and efficient. That should involve all interested parties. The plan should have a clear strategy. The base for this is provided by the Commission communication. The plan needs to be addressed to specific national contexts. The national plans should have common key priorities, and priority actions tailored to specific countries. Budgeting is the critical issue. Budgets should be earmarked for each priority area and, if possible, its specific measures. Finally, transparency and accountability are central. National strategies should be made public, and regular meetings of the national steering committees should be held so that stakeholders can monitor the implementation.

## **7. Success Factors**

Success will involve not only involving patients and patient representatives, but all interested parties as well. The pharmaceutical industry must be involved, as it has a key role in implementing the national plans. We must involve not only healthcare professionals but those in charge of managing the healthcare provision, such as hospital directors. We need to keep a comprehensive and long-term approach in view.

## **VI. Evaluation and Monitoring of National Plans**

**Pr Luciano VITTOZI, Research Director, National Centre for Rare Diseases, Italy**

### **1. Rationale**

We have an opportunity to learn from each country's experiences to improve the national plans. However, evaluation and monitoring has always suffered from a lack of resources. Regular evaluation allows the system to adapt over time.

### **2. Guidelines**

The system must be simple. We should only be concerned with information that might have an impact on decision making.

### **3. Requirements**

Stakeholder interests must be identified, and bottlenecks in the process should be pointed out. We also need measurable objectives. The overall objective is to improve quality of life for patients. Therefore, we need to identify short-term metrics to enable us to adapt the plans. We need structured sets of indicators in order to measure the success of the plans. Attention should be paid

to how the indicators are used. We need to know the initial conditions against which we can measure the improvements we implement.

#### **4. Participation and Ownership**

These are important for improving the efficacy of a plan. Patient empowerment will be vital if we include them in the monitoring process.

#### **5. Current Situation**

The French plan makes comprehensive provisions for monitoring and evaluation. The Portuguese plan also makes some provisions for it. However, other plans do not, so there is still scope to promote this activity.

#### **6. Performance Indicators**

Patient centres should be the main focus for monitoring and evaluation. We also have to address sustainability because of lower health budgets.

### **VII. Preliminary Monitoring Results – France**

#### **Pr Gill TCHERNIA, Evaluation Committee, French High Council for Public Health**

##### **1. Centres**

The GIS provides funding for specific rare disease programmes in generics and therapeutic research. These schemes will need help in the long term. One of the main acts of the 2004 plan was to create an initial 34 reference centres, and 98 from 2005-2007. There are between 600 and 700 competence centres linked to those reference centres. Those networks have created clinical research programmes, primarily targeting rare diseases.

##### **2. Labelling**

The labelling system implemented by the CNCL is based on two major criteria, expertise and the role of patient organisations. Communications between the various levels is conducted mainly through Orphanet.

##### **3. Evaluation Committee**

It is not easy to reconcile all the stakeholders. An evaluation committee was created with nine members, assisted by a private consulting agency. We had our first meeting in April 2008, and will deliver the final report in March 2009. Our objective is to evaluate the various topics defined in the national plan. We want to maintain equality among patients with regard to access to diagnosis and medical care.

#### **4. Methodology**

We evaluate previous reports from the High Council, the health ministry and Orphanet. We meet with various stakeholders. We are also analysing the self-analysis reports compiled by the 35 reference centres in 2004. We also drafted an open questionnaire for the 98 centres. A national survey was performed on a sample of patients to get a feeling on whether care had improved as a result of the plan. This is important for discovering geographical discrepancies. We will draft a final report to be given to the health minister.

#### **5. Initial Reflections**

There is improved recognition of rare diseases among health professionals, and increased public awareness. Patient isolation has decreased. Practitioners began to be recognised by their peers.

#### **6. Main Points**

We have underlined the quality of clinical and fundamental research. There is close connection between patients and research. There are fewer boundaries between care of children and of adults where rare diseases are concerns. Quality of information has improved due to Orphanet and reference centres. We have also published a number of high-quality brochures. The links between patients and reference centres have also improved. Patient associations are now part of the scientific councils.

#### **7. Drawbacks**

Social care is insufficient. It is difficult to secure travel funding, for example. More home support is required. Regional discrepancies in quality of care need to be overcome. There are not enough epidemiological studies being performed. Follow-up on treatment is also insufficient. Ante-natal and pre-symptom screening has been neglected. Certain reference centres felt intimidated by complex questionnaires and the multiplicity of actors. Researchers and scientists do not want to be treated as administrators. There has also been a partial loss of funding. The financial impact of orphan drugs needs to be kept under control.

#### **8. Outside Europe**

Should efforts to build networks against rare diseases stop at the borders of Europe? We need to work with Southern countries by providing samples, for examples. Networks must be developed within the South and between South and North. Reference centres must be developed, and collaboration encouraged in teaching and research. The renewal of visas for patients or family of patients should be a constant concern for immigration officials.

### **VIII. Questions and Answers**

#### **Christiane KARAKOGLU, AFPCA vice-president**

You highlighted the fact that the ARH allocates funds to hospitals, and that the global budget is shrinking on a daily basis. Does this work against the everyday operation of national reference centres? Patients expect a lot from the reference centres. Will they have the logistic and financial

means to enable them to operate? Finally, Mr Le Cam emphasised that the research aspect of national plans should be clearly defined. There must be technical and financial assistance for patient organisations. This was not an aspect of the Commission's questionnaire.

### **Pr Gill TCHERNIA**

There must be a monitoring system to track how each year's budget is spent. Some the HIV/AIDS resources were channelled to other purposes, even though a lot of the breakthroughs came by this route. Some erosion is unavoidable.

### **Yann LE CAM**

Regarding the role of patient associations, resources are difficult to come by, and using them well is a heavy responsibility. Orphanet is there to ensure clear definition of research projects, but each member state needs to support this. We also need to identify where resources can be pooled. There is one area where we want to see the publication of negative results, and that is rare diseases. This principle has already been accepted in paediatrics, and it should be accepted for rare disease research in general.

It is good to involve patients' organisations in task forces and decision making. However, it is also a good idea to fund them for at least part of their activities. Patient advocacy is no good unless it is supported by an efficient network. Help lines, for example, give individual, personalised information, and it would be good to see a common toll-free number.

### **From the floor**

Could you not use the regions as a building block, for example by setting up pilot schemes for regional bodies?

### **Yann LE CAM**

Regional resources are useful in terms of accessibility, but healthcare plans are usually national. Competence centres are usually inter-regional, and are often not easily accessible to patients because of the need to combine expertise and healthcare in the same place.

### **From the floor, Denmark**

Would it be possible to use simple indicators inter-country indicators, such as delay in diagnosis and age of mortality?

### **Gill TCHERNIA**

Diseases that were unheard of 10 years ago can now be diagnosed. Genetic research has also linked many diseases to the same gene. Therefore, delay in diagnosis can be explained by that aspect as well.

The core set of indicators from our point of view would be linked to the objective of the plan. We could be in trouble if we spend time and resources on impact instead of what is really vital. We

need not restrict ourselves to indicators from academic research or the public health system. We can also seek help from companies and doctors in monitoring programmes.

**From the floor**

Increased expenditure on orphan drugs shows that research is finally bearing fruit. The ATU and fast track systems for orphan drugs in France may allow industries to increase profits, but also allow patients to access more efficient treatment. This might be implemented more widely in national plans.

**From the floor**

You need to mobilise players and resources in order to catch up. However, in the case of rare diseases you need to provide for a number of specificities. We should provide for the sustainability of the specific devices. Therefore, if the plan is stopped there are structures.

**Gill TCHERNIA**

A political commitment was given to a second plan in France, ensuring sustainability. I agree that things should be sustainable.

## **Panel of Policymakers**

### **I. Next Steps**

**Anthoni MONTSERRAT, Project Officer, Health Information Unit (DG SANCO)**

#### **1. Shared Competence**

The next two countries to assume the EU presidency are in a position to continue the momentum that has been established. The approval of the communication is only the first step. The next is to implement it. Part of the process is identifying the shared areas of competence between the EU and the member states.

#### **2. Parliament**

The Parliament will do at least two things in this process. One is to give a positive opinion. The second is to decide on the budget, along with the Council. This might be a good time for the Parliament to propose a budget for rare diseases.

#### **3. Advisory Committee**

This will hopefully be created in 2009. The intention is that all stakeholders will get involved, not only the member states but patient organisations, the industry etc. This will be able to issue recommendations on behalf of all the stakeholders at EU level.

#### **4. Financing**

€65 million were spent on research in Framework programme five (1996-2002). €240 million were spent in FP six (2002-2007). Total spending in this period rare disease projects was €320 million, but it could be better. The aim has been to create added value.

#### **5. Future Action**

Projects like Europlan, Orphanet, and the pilot reference networks must be developed. Patients are expecting the directive on cross-border healthcare to be approved. A comprehensive European reference network cannot succeed without it. The national networks need to be linked together in this way. The Commission wants the WHO to approve a world initiative on rare diseases, but it cannot do this. One of the next presidencies must do this.

## **II. Sweden**

**Olivia WIGZELL, Director of the Health Care Division at the Ministry of Health and Social Affairs, Sweden**

### **1. Commission Strategy**

Sweden fully approves of the Commission's assessment. Cooperation between EU programmes must be strengthened. Likewise, the cross-border directive is vital. E-health is also important, with Sweden hosting initiatives in this area.

### **2. Requirements**

Sweden created a commission on specialised care to decide which area is to be considered highly specialised. There is ongoing work in the area of orphan drugs. Budgeting structures are crucial for structuring both European and national approaches. Sweden and other countries can do a lot more in this area.

## **III. Czech Republic**

**Pr Milan MACEK, Chairman of the Department of Biology and Medical Genetics, Czech Republic**

### **1. Common Issues**

We need to identify common issues, and also to implement structures based on the cross-border initiative. You cannot establish reference centres for all the rare diseases in a small country, and you have to rely on centres in other countries. A lot of the centres have de facto existence, but do not have adequate funding.

### **2. Patient Needs**

The activities and funding of patient support groups are also very fragmented. There are more than 60 patient support groups in the Czech Republic, and there is little coordination among them. You need to communicate with patients and physicians in their national language. E-health is a priority. ECORN is a portal through which patients can consult specialists about their specific needs.

## **IV. Summary**

**Annie PODEUR, French Director for Hospitals and Care Offer**

The Orphanet portal needs continued funding. We can only hope that EU funding for R&D will continue, and we hope for coordinated action among different states. This will enable funding to be pooled between countries, and for smaller countries to optimise their efforts. We share the objective of establishing European reference networks. The 131 reference centres need to be federated. The Czech Republic was able to call on information which enabled you to avoid investing where others had already done so. European guidelines on good practices will save time and resources.

Finally, you rightly emphasise the need for international cooperation. We must ensure that our efforts are sustainable. Therefore, France supports the creation of a European rare disease fund. The allocation of resources requires each country to develop its own rare disease plan. The Commission could be a link between all the different initiatives. European guidelines should be a toolbox, adaptable to each country depending on its resources and objectives. Today's event proves that we share values, and that we need to pool the resources available to us.

## **Closing Remarks**

**Annie PODEUR**

**French Director For Hospitals and Care Offer**

Rare disease is an area where we really need to pool our resources. We have been able to share our experiences, our hopes and our pragmatic objectives, both as regards strategy and resource activation. There are at least four keys to success. We need to promote a global approach. This means not only integrating the scientific and medical approaches but also the support mechanisms for patients. The second factor is that the definition process needs to be developed with all the different partners, thus promoting synergies between all stakeholders. The third is national steering of the plans, with clearly identified financial resources. Finally, the success of any plan requires assessment indicators. Cooperation at European level will show its added value, because rare diseases are so many and diverse, and require so much funding that they require pooled resources.