EUROPEAN COMMISSION
DIRECTORATE GENERAL HEALTH AND CONSUMER PROTECTION

Orphan Medicinal Products to the service of patients affected by rare disorders
PARD 1

A project conducted by

EURORDIS
European Organization for Rare Disorders

Under the

Programme of Community Action on Rare Diseases

Contract n° SI2.288939 (2000CVG4-811)

Final Activity Report
March 2002

The Annexes to the Final Activity Report are provided in a separate document also dated March 2002 under the same reference.

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I - Executive Summary

Around 5000 rare diseases affect daily the life of 20 million people in the European Union. Due to the very low prevalence of these disorders, the organisation, networking and strengthening of patient organisations at national level and even more at European level is extremely challenging. It is estimated that over 1000 local or national patient organisations exist in the European Union. The vast majority of these organisations are isolated, with very reduced membership for most rare disorders, extremely limited resources hence limited access to information, best practices and knowledge on treatments, new therapies, research, etc.

A European partnership is therefore essential to reach a critical mass of patients, experience, resources, and knowledge. In the context of the implementation of the EU Regulation on Orphan Medicinal Products (OMPs), it was considered that creating and animating a European trans-national network would be a critical factor to put OMPs to the service of patients affected by rare diseases. To this end, the project was structured to achieve four core objectives:

1. to strengthen existing national alliances and to develop new national alliances in European countries, around the theme "Orphan Medicinal Products"
2. to strengthen collaboration at European level among patient organisations
3. to develop partnerships among all alliances
4. to develop European recommendations and national action plans.

The project was conducted from October 2000 to December 2001 and was structured in four phases, built upon a range of European co-ordination meetings and workshops and National workshops. Across the four phases, these workshops involved over 200 distinct persons, among which:

- 75% representing patient organisations,
- 11% representing pharmaceutical industry,
- 10% representing universities, government or international agencies
- 4% representing national health systems.

Through this approach each national alliance was able for the first time to put in common, in a structured and co-ordinated way, their experience and best practices. This led to the development and dissemination of recommendations for both European and National authorities and of national action plans aiming at co-ordinating the implementation of these recommendations and strengthening activities of national organisations.

Benefited directly from the experience of existing national alliances, four new national organisations were set up in Germany, in The Netherlands, in Portugal and in Belgium.

It is estimated that 500 associations were put in contact or touched by communication on the results of this project. This directly resulted in enhanced exchanges and links between patient groups.

The development of a partnership between patients/industry and competent authorities is also one of the most promising achievement of this project. As reported by the European Agency for the Evaluation of Medicinal Products in its press release of February 27th, 2002 “this project has achieved a common understanding among patients groups for rare diseases in Europe and established a platform for addressing issues regarding orphan medicinal products”.

II - Organisations and people involved in the project

This section lists the main people and partners involved in the project.[1]

A Steering Committee was in charge of taking important decisions through the project. Coaches helped and advised existing or potential national alliances, liaising with a national coordinator that had been appointed in each of them.

The list of all participants to the workshops is attached in the Annexes section.
Across the four phases, the workshops involved over 200 distinct persons, among which:

- 75% representing patient organisations,
- 11% representing pharmaceutical industry,
- 10% representing universities, government or international agencies
- 4% representing national health systems.

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[1] For further information on this project, please contact Claire MARICHAL.

Coaches

- Terkel ANDERSEN, also coach for Denmark, Germany and Sweden
- Christel NOURISSIER: coach for France, Italy, Portugal and Spain
- Françoise SALAMA: coach for France, Italy, Portugal and Spain
- Carol YOUNGS: coach for Belgium, The Netherlands and the United Kingdom
- Hawa DRAMÉ: Eurordis Therapeutic Development Officer

Consultants

- Maylis ROQUES DE BORDA, Gemini Consulting
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III - Development, progress and impact of the project

This project developed around the theme "Orphan Medicinal Products to the service of patients affected by rare disorders" is the first part of a long-term project initiated by Eurordis in the framework of the Programme of Community Action on Rare Diseases – 2000/2003, which objective is to create and animate a European trans-national network on rare disorders, linking patient associations, isolated patients, groups of associations, health care professionals and international organisations around structuring and motivating themes.

The aim of this section is to detail the progress of the project and explain, if any, the discrepancies between what had been expected and what was actually performed.

This project was particularly challenging due to the situation of patient organisations on rare disorders in Europe which can be summarised as follows:

- a large number of organisations disseminated across Europe, most of them being isolated
- a very small number of patients per disease
- very limited resources for each organisation, hence limited access to information, best practices and knowledge on treatments, new therapies, research, etc. .

All documents collected during the project have been grouped in the Annexes section of this report.

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1. Kick-off meeting in Brussels

As planned, the kick-off meeting took place on October 20th, 2000 in Brussels and gathered the 7 National Alliances and the 3 potential alliances.

Date : October 20th, 2000

Location : Brussels

Chaired by : Terkel Andersen (Project Manager)

Trainer : Maylis Roques de Borda (Gemini Consulting)

21 participants : 1 coordinator per national alliance (7) Denmark, Germany, Italy, France, Spain, Sweden, UK, 1 coordinator per potential national alliance (3) Belgium, The Netherlands, Portugal, Board members of Eurordis, Executive Director of Eurordis, Eurordis coaches

The Coordinators of existing National Alliances had been requested to send before the meeting a synthesis paper of the actions undertaken in their Alliance the past year and a SWOT (Strengths, Weaknesses, Opportunities, Threats) paper, giving a picture of their alliance today. An example of a SWOT paper was given to the coordinators beforehand to guide them in the designing of their own SWOT. These papers were distributed during the meeting to all coordinators to develop knowledge between National Alliances and share experiences.

After gathering the expectations of this project from each participant, the first part of the agenda was devoted to presentations of the current situation and to clearly define the objectives and expectations to carry out this project. Then a training session was developed using a role play with the Metaplan tool (see Methodology section) during the brainstorming session. Several questions were prepared to be developed during the future national workshops. One of them was chosen as an example for brainstorming. All the ten coordinators participated to the

brainstorming. Then a methodology was given to organise the 2-day national workshop. A questions and answers session followed that training. The last part of the meeting was devoted to emphasising the different commitments of each National alliance to reach the objectives of the project and more particularly the production of recommendations at national and European level.

Some coaches were designated during the meeting to cover 3-4 national alliances all along the project.
A list of actions and a timetable were set up during the meeting to prepare a two-day workshop in January/February 2001.
Minutes of the kick-off meeting were sent to all participants together with a list of actions for National Alliances, a timetable for the phase II of the project and Travel Expenses Form for Eurordis to reimburse travelling expenses during the project.

Conclusion: This kick-off meeting put on board each alliance involved and had them fully motivated for this ambitious project. It helped reach three objectives of the four initially set:

- Explanation and common understanding of the methodology of the project,
- Training to prepare national workshops and
- Direct personal exchanges enabling the alliances, whether existing or potential, to get to know each other and build further a common understanding of the theme of the project.

As to the objective of making an inventory of existing associations on rare diseases in Europe and isolated families per pathology, it was agreed at the kick-off meeting that it could not be interpreted in its broader sense as an exhaustive inventory of all patient organisations on rare diseases in Europe.
While this inventory is a project in itself, and could be carried out in the future, it was not considered as a realistic goal at this early stage. It was also noted that this goal was not a milestone to reach the overall objective to create and animate a European trans-national network on rare diseases around the key theme of orphan medicinal products. Rather, the participants considered as essential, in order to reach the objective of this project, to use the strong base of information already available, i.e. the membership base of Eurordis, the membership base of the national alliances and the DG-SANCO-supported Webserver Orphanet. The compilation of these lists is available in the Annexes section and its analysis is described as part of the results achieved (V-7: “to share best practices and knowledge").

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2. National Workshops in seven Member States

Time frame : January/February 2001 – as planned

7 Member states : Denmark, France, Germany, Italy, Spain, Sweden, UK

Duration : two-day workshops

85 Participants across 7 countries

Objectives : To develop two-day workshops and brainstorming sessions on Orphan Medicinal Products. To explore the situation at national level, review the availability of Orphan Medicinal Products, Research, etc, make recommendations and start designing an action plan.

Methodology : Preparation of national workshops in coordination with Eurordis - objectives, agenda, list of participants, logistics aspects for 10 participants, common reporting – invitation of pharmaceutical industries representatives to participate in the discussion. After these two-day workshops, all national alliances have written a report giving their recommendations and plan of action according to guidelines sent previously to them.

Coaching : Steering committee meetings were organised. The first one, on December 8th, 2000 in order to review all the agendas of workshops prepared by National Alliances. At the end of that steering committee meeting, we drafted a sample agenda to help those alliances having difficulties to make one and asked each of them to draft a new agenda for December 21st 2000. The purpose of having a good agenda was to help national alliances to really prepare as much as possible their workshops so that the brainstorming days can bring good and valuable recommendations at the end. We sent together with the minutes of the steering committee meeting some guidelines regarding questions to be discussed during the workshop, for them to choose among.

On the basis of a second draft agenda, Eurordis coached coordinators of national alliances one by one, discussed the agenda, gave new suggestions in order for them to finalise it. We also prepared a presentation on the project « Orphan Medicinal Products to the service of patients affected by rare disorders » to be used as a common basis by each national alliance, at the beginning of the workshop.

Conclusion *:* All the workshops were developed in the 7 member states as scheduled. The expected outcome was reached in that needs and problems were identified and recommendations were reported through synthesis papers.
We received very positive feedback from all of them. A final version of the Report Guidelines was sent to all coordinators which they could follow during the preparation of their reports. National reports were submitted by February 28th, 2001.

3. Analysis of the reports

After the workshops, we asked coordinators to send us freely their first feedback, giving us a rate for this workshop from 1 (not successful) to 5 (very successful). The rates were very high and were quoted between 5 and 4.

The liveliness of the recommendations shows that great motivation and creativity were developed within national alliances in a good team spirit.

The excellent quality of the reports, following the same methodology and guidelines, gave a solid basis for a European analysis.

We organised a second steering committee meeting on March 20th, 2001 in London to review the reports and feedback of 6 national alliances, analyse furthermore the findings of each alliance and prepare the European workshop scheduled on June 7th and 8th, 2001.

4. Intermediate report and amendment to the agreement

A request was sent to the Mr A. Cluzeau, European Commission, on April 2nd, 2001 to get an additional clause to the present contract, asking to extend the duration by 2 months in order to organise the European Workshop in June instead of April as written in the initial contract. We received amendment N°1 to the agreement which modified the new address of Eurordis and the duration of the project to 14 months.

An intermediate report was sent in June 2001 to the European Commission which described Phase I, Phase II and the preparation of Phase III of our plan of action together with an intermediate finance report.

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5. European Workshop – Phase III

Time frame : Two days : June 7th/ 8th, 2001

Location : Brussels

Agenda : See agenda enclosed

56 Participants from 10 member states : Belgium, Denmark, France, Germany, Italy, The Netherlands, Portugal, Spain, Sweden, UK. Three to five representatives per member state, Gemini Consulting representatives, board of Directors of Eurordis and staff .

Guests for roundtable : European Commission (Emer Cooke, Luca Martinelli), EMEA/COMP (Patrick Le Courtois, Yann Le Cam), Pharmaceutical Industries and Biotechnologies (Bernard d'Auvergne from OTL, Catarina Edfjall from Actelion Pharmaceuticals Ltd, Adriaan Fruitjtier from Micromet, William Gunnarsson from Orphan Europe, Eric Tambuyzer from Genzyme)

Objectives : To develop 2-day workshop, set up a common understanding at European level, identify the needs and problems in Europe, share best practices and create synergies in Europe, make recommendations.

Day 1 : European network of patients through National Alliances of patients
was focussed on the reporting of each national alliance about their key findings both at national and European level. The 3 potential alliances have reported on progress of building an alliance in their country. By the end of the day, some key issues were identified, through a recommendations synthesis and explanation by Gemini Consulting representative on how we came to these important findings. We selected and prioritised the recommendations that we wanted to discuss with the Stakeholders the next day.

Day 2 : Partnership between patients and stakeholders
The second day, we started with a video from NORD, the American Organization on Rare Disorders « out of the Darkness » About some history back to 1983 , the lobbying action of patients groups to make the Orphan Drug act adopted.

Then representatives of Directorate General Enterprise and Directorate Health and Consumer Protection (DG SANCO) as well as patient representatives and Vice Chair of the EMEA/COMP presented the Orphan Medicinal Product Regulation impact.

At this point, Terkel Andersen, Project Manager, presented to the Eurordis guests the recommendations which had been selected and prioritised the day before.

The roundtable was chaired by Andrea Rappagliosi representing EBE group (Emerging Biotechnologies in Europe). He introduced each participant who presented their Companies or their institutional bodies. Then the debate was open. Several good questions came up from patients representatives. We have assisted to the start of a real partnership between patients representatives and the present stakeholders.

In the afternoon, the Project Manager made a synthesis of this workshop. He started to select some of the recommendations which had arisen during the two days and could be delivered to the EU towards the end of the project.

Conclusion: the major achievement of this session was that the various countries realised that they were facing the same type of difficulties, which enabled them to list common recommendations at European level, in particular:

- Key recommendation 1: to make an inventory of orphan medicinal products, make them available to patients in all member states and develop a European database
- Key recommendation 2: to provide information about new drugs, new methods of treatment, clinical trials equally in all countries
- Key recommendation 3: to list the molecules abandoned by pharmaceutical industry before development and possibly withdraw the products developed for common diseases but efficient for rare disorders
- Key recommendation 4: to develop epidemiological studies and a database on rare disorders
- Key recommendation 5: to develop specific clinical trial methodology and "Fast-track" process.

6. National Workshops – Phase IV

Time frame : September/October 2001

10 Member states : Belgium, Denmark, France, Germany, Italy, The Netherlands, Portugal, Spain, Sweden, UK

Duration : one day workshop

122 Participants across 10 countries

Objectives : To develop one day workshop, to report the results of the European workshop in Brussels, to comment the draft preparatory report and to design an action plan of recommendations at national level.

Methodology : Based on discussions of Brussels, preparation of national workshops in co-ordination with Eurordis - agenda, list of participants, logistics aspects for 10 participants, invitation of pharmaceutical industry representatives to participate in the discussion..

A steering committee on September 3rd, 2001 reviewed the agendas of the 7 national alliances and 3 potential ones. The national alliances were advised to develop the agenda as follows :

- **For the existing alliances :**
  - Morning
    - Report from European Workshop to all participants
    - Review and comments of Draft Preparatory Report
  - Afternoon
    - Prioritise your national recommendations (from last National Workshop), select no more than 2 or 3 recommendations (allocate only 30/60 minutes)
    - Develop action plan for these recommendations in your country (allocate 2 or 3 hours)

- **For the new alliances:**
  - Morning
    - Constitution of your national alliance, SWOT analysis (Where are we today ?)
    - First actions (one or two) you want to develop in your country.
  - Afternoon
    - Objectives of PARD I – Plan of action – Expectations
    - Report from European Workshop to all participants. Presentation of selected European recommendations
    - Review and comments of Draft Preparatory Report

Conclusion: Action plans were developed around recommendations. Key recommendations at national level are summarised in Paragraph 11 of this report.

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7. Phase V: Reports from National Alliances and writing of final activity report

The final phase lasted from November 2001 to March 2002. Recommendations were collected from the countries, the final report was written by Eurordis and part of the dissemination of the results took place (see section VII).

IV - Concise description of the methodology used

The methodology was based on workshops spread in 4 phases and alternating exchanges at European and national level as explained in section 3.

The ultimate goal was for alliances to propose realistic action plans. They were helped by the steering committee in charge of advising coordinators at national level on the agendas and methodology of the workshops.

The project methodology was dovetailed to help achieve three major objectives:

1. Help alliances understand where they stood at the beginning of the project

Before the first meeting, existing alliances were asked to give a picture of their situation by describing their actions in the previous year and performing a SWOT (strengths/weaknesses/opportunities/threats) analysis. New alliances performed this exercise during phase IV.

2. Create conditions for exchange...

The first workshop held in Brussels gathering the steering committee and the national coordinators intended to help everybody get to know each other and initiate a regular communication between these two groups that was to be pursued throughout the project.

The workshops at national level enabled another type of exchange between patient organisations, as well as between alliances and other actors such as the representatives of government, pharmaceutical industry, research and health professionals. Through these meetings knowledge was developed and experience shared.

3. ...while ensuring consistency from one country to the other

The methodology explained during the Brussels European workshop of October 2000 at the beginning of the project and carried out throughout the project around the Metaplan[2] and brainstorming exercises had a double objective:

- to guide the alliances by showing them the various steps of the project, which tools were adequate, who should be invited, which subjects could be tackled and what was expected from them
- to ensure consistency from one country to another through the use of the same tools, particularly keeping in mind the reporting stage.

[2] tool to organise concrete ideas into more general conclusions leading to recommendations.

V - Description of the results achieved

Objectives of the project were:

1) to strengthen existing national alliances
2) to strengthen collaboration at European level among patient organisations on rare disorders
3) to develop new national alliances in European countries, around the theme "Orphan Medicinal Products"
4) to develop partnerships among all alliances
but also at a broader level:
5) to link patient groups across pathologies and borders
6) to give families and patients a voice at both national and European level.
7) to share best practices and knowledge
8) to create synergies in Europe around the theme : "Orphan Medicinal Products"
9) to identify and report needs
and most of all,
10) to produce recommendations at European level
11) to produce recommendations at national level
12) to generate concrete actions in the field both at national and European level

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1. To strengthen existing national alliances

The organisation of meetings at national level between patient organisations, representatives of the national health system, pharmaceutical industry and scientists had various benefits:

- For the national alliances on rare disorders, the first step towards strengthening was the analysis of their current situation. Its objective was to create the basis for decisions as to the actions to be developed in the coming years.

- The workshops, through their European dimension, attracted new patient organisations to national alliances and, through the collaboration they generated, strengthened existing relationships between members. For instance a working group on orphan drugs was created within the French Alliance. Its members representing various patient associations meet regularly and initiated a National Forum on Orphan Drugs on June 1st, 2001. It was the first time that 150 representatives of patient organisations, industry, policy makers and regulators met on the theme of orphan drugs. The media coverage was also very good which strengthened the awareness of rare disorders in France.

- Patients suffering from rare disorders and patient organisations themselves are very isolated. This project gave them some specific training on how medicinal products are generated and helped them build a network by meeting for the first time important actors in this area.

- For most rare disorders, therapies are still considered as distant objectives. Patient organisations understood that they have to play a role in encouraging the development of orphan drugs and making them available to patients. After the national forum on orphan drugs organised in France, a think tank on abandoned molecules started working at the SNIP (national association of pharmaceutical manufacturers) with representatives of national and international pharmaceutical industries, start-up industries and patient

organisations. The purpose is to facilitate the transfer of existing molecules not commercialised by the major companies but of great benefit for rare diseases.

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2. To strengthen collaboration at European level among patient organisations on rare disorders

Thanks to the project, each national alliance was able for the first time to put in common, in a structured and co-ordinated way, their experience and best practices. This led to the development and dissemination of recommendations for both European and National authorities and to national action plans aiming at co-ordinating the implementation of recommendations and strengthening activities of national organisations.
Some initiatives taken by national alliances contributed to break the isolation of patients affected by very rare diseases by being accessible to individuals and not only to organised groups of patients. The UK Alliance on rare diseases has several years experience in linking isolated patients based on the practice of Contact a Family. This experience has been a stimulus to other alliances. For instance, by accepting membership from isolated patients, Rare Disorders Belgium is able to locate patients affected by very rare disorders, put those who shared the same pathology in contact and help them build an organisation.
In France, Alliance Maladies Rares organises regular seminars for isolated patients in order to help them break isolation by working together and being trained to accessing sources of information such as the Internet for instance.

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3. To develop new national alliances in European countries around the theme "Orphan Medicinal Products"

The project directly helped to develop and structure 4 new alliances in Germany, Belgium, The Netherlands and Portugal.

In **Germany**, there was no alliance when the PARD 1 project was submitted to the European Commission. Soon after that, the German alliance was created within BAGH (umbrella organisation of people with disabilities and chronic diseases), thus benefiting from the 30 year experience of their mother organisation. At the kick-off meeting of PARD 1, the representatives of the various national alliances had the opportunity to meet the German representative for the first time.

In **Belgium**, the objective to create a new national alliance was reached during phase III of the project.

- A motivated group of volunteers helped Eurordis to organise an awareness day at the European Parliament in Brussels on October 19th, 2000. They sent a representative of their organisation at the kick-off meeting in Brussels, to become the co-ordinator of PARD 1 for Belgium.
- Soon after the beginning of this project, the potential National Alliance on Rare Disorders « Rare Disorders Belgium » organised an information day in Brussels on January 12th, 2001 and gathered representatives of about 35 patient associations from the different regions of Belgium.

- Following that meeting, the statutes of « Rare Disorders Belgium » were published in « Moniteur Belge » in February 2001. A General Assembly was called on March 17th, 2001 to adopt the text and officially launch the Alliance.

In The **Netherlands**, instead of building a new organisation from scratch, the new national alliance on rare diseases was built as a working group involving representatives of two strong existing alliances of patient organisations (most of which representing rare disorders).

- The creation of a structure for orphan diseases and orphan drugs was a strong recommendation from the Minister of Public Health, in 1998. The first official meeting of the Steering Committee Orphan Drugs in The Netherlands built and funded by the government for 4 years took place on April 6th, 2001. This steering committee gathers 2 representatives of each of the following groups: Industries, Scientists, Researchers, Pharmaceutical Industries and Patient organisations (one from CG-Raad and one from VSOP).
- The creation of this steering committee encouraged the two above-mentioned alliances of patient organisations: CG-Raad and VSOP, to create a working group gathering members from both organisations. This working group representing patients suffering from rare disorders benefits from the combined strengths of both well-established organisations.
- The preparation of the working group started in the summer 2001. In October 2001 the group organised its first meeting and in January 2002 it obtained financial support from the abovementioned steering committee. A working plan was written to decide what to do specifically with the funds, i.e. to organise another national workshop, an electronic newsletter and promotion.
- Its first initiative was to organise a survey about rare disorders. A questionnaire was sent to 70 patient organisations and 300 individual patients with rare diseases not covered by any patient group. Some interviews were held in 6 groups presenting different diagnoses (muscular dystrophy, children with metabolic diseases, etc....). Its results helped make a brochure for people with rare diseases published in March 2002 and feed a website, and will also be extremely useful for further policy making.
- The secretary of this working group on rare disorders was at the kick-off meeting of the PARD 1 project in October 2000 and operated as the national coordinator in The Netherlands throughout the project.

In **Portugal**, the objective to create a new national alliance was reached at phase IV of the project.

- In February 2000, Eurordis met at a conference on Rare Diseases in Sevilla a representative of Associação nacional de Fibrose Quistica (ANFQ), a member organisation in Portugal. After that, the Spanish National Alliance supported them in the long process towards the building of a national alliance on rare disorders.

- A representative of the potential Portuguese alliance was among us at the kick-off meeting in October 2000. Three members of patient associations came to the European Workshop to report on their activities.

- Until the European Workshop in June 2001, very little progress was made due to the fact that there exist very few patient organisations on rare disorders in Portugal (1st estimate: 10 associations) and that only a few persons were concerned by this project.

- During the Phase IV workshop of October 19th, 2001, the invited associations decided unanimously to constitute the “Aliança Portuguesa de Doenças Raras – PARD", according to the Portuguese Law and under the principles, objectives and mission of Eurordis. By-laws were approved on that same occasion. Until the official procedure is completed, the group working on this new alliance project can be reached at ANFQ.

4. To develop partnerships among all alliances

Due to limited resources, lack of European experience and a very large number of national organisations, national alliances had neither experience nor possibility to build effective partnership, if by partnership we mean concrete collaboration which could be evaluated.

During the PARD 1 project, the seminar organised in Brussels in June 2001 was a very good occasion for a large scope of members from all national alliances to meet. They realised that, what they had in common was stronger than their differences as to diseases, cultures, languages and social systems. The needs they had identified were very close and the actions they had proposed were very similar. This is the first step and an essential basis of a long-term partnership.
Further partnerships between national alliances are envisaged in the framework of the Programme of Community Action on Rare Diseases, through the PARD 2: "New communication technologies (website) to the service of the rare disorders network and sharing of good practices in different help services to patients, already existing in Europe (hot line)" and PARD 3: "Pan-European network for patients information on rare diseases and orphan drugs " projects, for instance around the organisation of a European Day on Rare Disorders.
Some very concrete actions can also be mentioned. The Danish alliance who had organised a European conference on rare disorders in Copenhagen in 2001 is sharing its experience with the French alliance who will organise the next one in 2003 in Paris. As to the Spanish alliance, it worked closely with the Portuguese associations to help them build an alliance.

5. To link patient groups across pathologies and borders

For very rare disorders affecting very few children, such as rare chromosome disorders, identification is very recent and linking families across borders is the only way to break isolation.
The Brussels meetings of Phase 1 and Phase 3 were occasions for the participants to meet and exchange contact names, either because they realised that they were part of patient organisations covering similar pathologies, or because they could give each other useful contact names.

For instance Christel Nourissier, member of Prader Willi France met, within the Portuguese umbrella organisation, parents of children with the Prader Willi syndrome who needed information about the disorder.
It was also the occasion for the representatives of various diseases to realise that some of their daily problems are shared by other families. For instance, many parents are facing a difficult situation when their child reaches the age of 18 as their diseases are often considered as children's pathologies and structures do not exist to give them further assistance once they reach adulthood.

6. To give families and patients a voice at both national and European level.

The organisation of meetings at European Union level had two positive effects. On the one hand, it gave the European Union the opportunity to hear the voice of patients and, on the other hand, it increased the understanding among patients of the European Union policy on rare diseases and related European Union proceedings, thanks to face-to-face contacts.

Representatives of patient organisations attended the first EMEA Workshop on Orphan Medicinal Products entitled “Understanding how the system works and paving the way forward” that took place on March 21st, 2001 in London.
Portugal found an additional way to publicise the programme of Community action on rare disorders: the name of the new alliance that is being built there will be "Aliança Portuguesa de Doenças Raras – PARD".
Altogether it can be estimated that about 500 patient organisations have been reached or have heard about this programme of Community action during the PARD 1 project.

7. To share best practices and knowledge

Beyond the sharing of a common understanding and a common terminology across Europe, one of the achievements of this project was to gain better understanding on prevalence and knowledge of rare diseases and patient organisations across Europe. The following key findings emerged during the project.

One of the findings of PARD 1 has been to provide key figures about the patient organisations on rare diseases in the EU. By patient organisations we mean organisations where patients and families represent a majority in the governing board or general assembly.

- It can reasonably be estimated that in the 15 member states there exists a minimum of 400 associations and a maximum of 1100 associations. Among those, the associations being members of Eurordis and the national rare disease alliances forming the pan-European network of Eurordis amount to 430 associations. Those associations represent over 900 different diseases among the 1100 rare and very rare diseases affecting patients in EU. This leaves aside the 4000 extremely rare diseases or sub-class of diseases. It can also be estimated that those associations represent a total number of 4.3 million minimum to 10 million maximum patients affected by one of those 900 rare diseases out of the 20 million persons estimated to be affected by a rare disease. Still, those figures have to be considered very cautiously as very first estimations, but do provide a base. More specifically, it can also be estimated than 500 patient associations have participated, or have been exposed at least through the dissemination of information, to the work achieved through PARD 1.

- Those estimations are based on the collection of the lists of patient associations on rare diseases through the national alliances, on the membership base of Eurordis (see Annexes section), on the figures provided by the partners of PARD 1 during the Phase 1, and on the DG SANCO-supported Website Orphanet.

Based on those data the following facts emerge:

- **The most significant rare diseases.** Over 5000 rare diseases exist. The current contents of DG SANCO’s supported Webserver Orphanet are: 3523 rare diseases and synonyms listed and about 1150 rare diseases well documented, which are the rare diseases ranging from rare to very rare but not the extremely rare. Those 1150 can be considered as the most significant rare diseases at the European level. The population affected by rare disorders in the European Union is considered to be 5% minimum (28 million patients) to 8% maximum (30 million patients).

- **The estimated minimum number of associations on rare diseases in the EU**. Currently, among Eurordis members, 203 patient associations are members of Eurordis in 12 EU member states, including 10 national rare diseases alliances in which the same and other patient associations participate. Because of this overlap, we cannot simply sum them up in order to obtain an estimate at the European level. However this can be estimated by comparing the number of rare diseases associations involved in the national

alliances with the population of each country. For the following five member states the respective figures are: Germany (79 associations; 81.1 million inhabitants), France (93 associations; 58 million), Italy (27 associations; 57.8 million), Spain (39 associations, 39.1 million), Denmark (30 associations; 5.2 million). The average number of patient's associations forming the national alliances is about 50 associations. For those five countries (representing two third of the EU population), the total is 268 associations for a population of 241 million which is equivalent to 1.1 association for 1 million habitants. Therefrom we can estimate that for the current 377 million EU population there should exist a strict minimum of 400 patients associations on rare diseases in the EU.

- **The estimated maximum number of associations on rare diseases in the EU**. For some of the EU member states we have an estimation of the maximum total number of rare diseases associations in the country: France (150 associations for 58 million inhabitants), The Netherlands (70 associations for 15.2 million inhabitants), Belgium (50 associations for 10.1 million inhabitants), Portugal (10 associations for 9.8 million inhabitants), Italy (160 associations for 57.8 million inhabitants).. For those four countries (representing one quarter of EU population), the total is 260 associations for 93.1 million inhabitants, which is equivalent to 2.7 associations for I million inhabitants. Therefrom we can estimate that for the current 377 million EU population there should be a maximum of 1100 patient associations on rare diseases in the EU. Not surprisingly, there seems to be more associations per million inhabitants in the northern half of EU than in the southern half.

- **The estimated number of patients associations on rare diseases involved in Eurordis and in the national rare diseases alliances forming the network of Eurordis.** In addition to the 5 alliances mentioned above totalling 268 associations, we can add : United Kingdom (200 patient groups, not all incorporated as associations, but half of them are legal entities according to Contact a Family), Belgium (at least 15 patient associations involved in Rare Disorders Belgium; and 50 patients associations participated in their first information day on Phase 1 of the project), The Netherlands (at least 20 patient associations involved in the rare diseases alliance of VSOP), Sweden (at least 10 associations in Sällsynta Diagnoser), Portugal (all 10 existing associations in Portugal are members), the 10 alliances amount to 423 associations. On the top of it we can also add the associations which are members of Eurordis in EU member states where there is no alliance: Ireland, 6 associations including umbrella association, and Greece, 1 association. The total is 430 associations.

- The only country where a national alliance has estimated the number of diseases and patients represented with a rigorous methodology that allows reliable estimation and possible control is France. The French Rare Disease Alliance is requesting from each of its member associations to provide a list of rare diseases covered by the association. For 93 current member associations, the French Alliance represents over 900 different diseases. Most associations are representing only one disease such as Cystic Fibrosis, Prader Willi Syndrome, Tuberous Sclerosis, etc. But a large number of associations are themselves representing clusters of diseases such as AFM (over 75 neuro-muscular diseases), VML (over 40 lysosomal diseases), APPT (over 45 small size syndromes), etc. The similar situation applies to UK, Germany, Denmark, Spain, to all EU member states, which is quite obvious when we look at the lists attached. The number of patients represented has been calculated by the French Alliance by using the prevalence figures provided both by the patients associations and by Orphanet. Their estimation are very conservative in order to avoid any criticism of over estimation: for the 93 associations, representing over 900 diseases, the total minimum number of patients represented is 1 million. If we extrapolate from this base to all EU, it can be estimated that the minimum 400 associations/maximum 1000 associations represents over 900 rare diseases for a total number of patients minimum 4.3 million/ maximum 10 million. Still, those figures have to be considered very cautiously as very first estimations, but they do provide a base.

8. To create synergies in Europe around the theme "Orphan Medicinal Products"

This project strengthened synergies between patient organisations and other actors around the theme of Orphan Medicinal products.

Thanks to these contacts with patient organisations, industry representatives are progressively becoming aware of increasing opportunities in the area of rare disorders:

- the recent progress in fundamental research, particularly in genetics, enabling new therapies (gene and cellular therapies)
- the fact that rare disorders are useful models for understanding the course of more common diseases and for improving methodologies of clinical trials.
- the European Regulation on Orphan Drugs and its benefits: 10 year exclusivity, protocol assistance, fee reduction and other incentives.

9. To identify and report needs

The Phase II workshops met their objective to analyse the situation in each country and identify the most important and urgent needs. Although access to diagnosis and treatment is very unequal across Europe, the reports show surprising similarities in various areas as to:

- a limited access to information on rare disorders and innovative drugs
- insufficient structures
- an inadequate level of cooperation at both national and European level.

These common needs gave the basis and rationale for European and national recommendations in order to effectively ensure the development of research, the production and marketing of orphan medicinal products and the access of patients to these OMP.

10. To produce recommendations at European level

This paragraph lists the recommendations that originated from the first national workshops (phase II of the project) and were discussed during the second European workshop (phase III).

I - Orphan medicinal products

1. Improve access to information

- Create a register of medicinal products used for rare disorders available to patients in all member states including those:
    - benefiting from pre-marketing access in member states,
    - with Marketing Authorisation in the EU,
    - with Marketing Authorisation in only one or several member states,

  in order to establish a map of availability of Orphan Medicinal Products in Europe and reduce disparities of access

- create a European database and provide information about new orphan drugs, new methods of treatment, ongoing and closed clinical trials, equally in all countries

2. Develop research and clinical trials

- Promote alternative methodology of clinical trials adapted to the specificity of rare disorders and encourage transparency for patient organisations to be informed and involved in the setting-up of clinical protocols
- Encourage pharmaceutical industry to revive abandoned molecules and assess their potential for treating rare disorders with experts
- Encourage pharmaceutical industry to ask for extended marketing authorisation for drugs developed for other diseases

3. Encourage the implementation of national incentives following the OMP Regulation

4. Speed up Marketing Authorisation of new molecules

- The COMP (Committee for Orphan Medicinal Products) needs to involve experts, both scientists and patients, on rare disorders in the evaluation process.
- The time period before Marketing Authorisation (often more than 120 days) should be reduced and Fast Track Marketing Authorisation Procedure encouraged.

5. Reduce the lapse of time between European Marketing Authorisation and actual availability to the patients in all member states and monitor that information

6. Reinforce the monitoring of side effects and set up follow-up records

7. Establish an indicative price range at European level at the marketing authorisation stage of orphan medicinal products for the various member states.

8. Maintain and amplify fee reductions on protocol assistance and on marketing authorisation and post-marketing authorisation.

II - Structures

1. Strengthen the network of National Alliances on rare disorders as well as encourage the creation of new ones and the benchmarking of best methods of work in order to continue to spread information all across Europe on the OMP-legislation.

2. Develop the network of DNA and tissue banks to encourage research

3. **Establish centres of excellence for care and treatment of rare disorders at national and/or European level (for very rare disorders),**

4. **Create a task force at European Commission level comprising representatives of DG SANCO, DG Enterprise, DG Research, EMEA/COMP and possibly of the pharmaceutical industry and of patient organisations to reinforce the European policy on rare disorders and increase consistency.**

5. **Organise regular conferences with multiple actors, giving an in-depth look at fundamental and clinical research, epidemiological and clinical studies to inform pharmaceutical industries about new opportunities offered by rare disorders. Health care authorities and research institutes should also be invited to participate.**

6. **Provide additional resources from the European Commission to the EMEA in order to have appropriate staffing at EMEA, financing of COMP activities and OMP transparency activities.**

III - Best practices

1. **Build up health care guidelines on different pathologies from screening and diagnosis to treatment**

2. **Organise the training of physicians and families on the state of the art for persons affected by rare disorders**

IV - Epidemiology and course of rare disorders

1. **Improve knowledge of the causes and the course of rare disorders with research studies of patients all over Europe**

2. **Co-ordinate pan-European epidemiological studies along with compared quality of life and life expectancy studies**

11. To produce recommendations at national level

This paragraph summarises the recommendations issued by the national alliances in their reports. To facilitate reading, these recommendations have been grouped by subject and refer to the country reports that can be found in the Annexes section.

I - Information and cooperation

1. Develop help lines and websites (France, Germany, Spain, UK)

The idea is to offer by all possible means information to patients and family members about the pathology, treatment, evolution, psychological considerations, put them in contact with other persons affected with the same disease or direct them to the corresponding association, if there is one.
On line access to the European data banks listing all the drugs on the market has already started in the UK. Such an evolution faces reservation in some Member States: Eurordis could try and get rid of them.

2. Working together (Denmark, France, Germany, Italy, The Netherlands, Spain, Sweden)

Strengthen co-operation between health professionals and patient organisations.
Groups gathering representatives of the various actors on the subject of orphan drugs (patients associations, health professionals, government agencies, industry…) are necessary.
Among the aims of this type of groups:

- developing innovative therapies
- singling out obstacles to the swift availability of medication for patients
- reviving molecules abandoned by pharmaceutical industry before development
- and more broadly, improving the situation of patients.

In countries where they already exist, they have enabled many activities. Discussions can tackle various subjects such as research, health, social, legal and ethical issues.

3. Centres of excellence for diagnosis and treatment (France, Germany, Italy, Spain, Sweden, UK)

Establish centres of excellence aiming at diagnosis, care and treatment, that have adequate knowledge about all medicinal products for the diagnosis/group of diagnoses the centre is intended for.
Identify existing reference centres, create a committee of health professionals and associations to register them and create a system to coordinate all the reference centres.
To explore transition to adult services for those disorders where children now reach adulthood.

II – Diagnosis (France, Denmark, Germany)

Quality control for diagnosis is lacking in Europe. An independent body should be entrusted with the maintenance of quality and efficacy standards (authentication of analysis and interpretation of results), which is not the case right now.

For extremely rare disorders, a unique Centre of reference in Europe with its own budget should be sufficient.
Transferring academic research to public or private analysis laboratories has yet to be dealt with. After publishing their results and when running out of funds, researchers are not able to make diagnosis any longer.
Good practices in delivering a diagnosis to patients and families have to be part of medical studies , as present ways are not at all satisfactory.
Organise new born screening when a treatment exists.

III - Medical care (Belgium, France, Germany, The Netherlands, Spain, UK)

- Build up health care guidelines on different pathologies from screening and diagnosis to treatment.
  In many cases damage has already been caused because of wrong treatment. Most rare diseases are only treated for the symptoms and there is no consensus about the best treatment.
- Organise the training of physicians and families on how to take care of rare disorders, in some countries create a specialty in genetics.
- Identify direct and indirect costs of treatment through a national survey
- Enlarge codes
  Creating patients registers is expensive. This cannot be done for over 5000 disorders. It would not prove more efficient anyway than good extrapolations based on well targeted one-shot surveys. Epidemiological researchers know that a patient organisation brings together 10 to 20% of people affected with a disorder, that a survey conducted in active hospitals gathers data on 50% of patients.
  The best way to get reliable data on rare disorders would be to study the cost of medical acts and hospitalisation. This is not possible today, because specific codes do not exist.
  Target: ask the World Health Organisation to create an enlargement of codes (International Classification of Diseases), for a precise taxonomy of rare disorders.

IV - Access to medicinal products

1. Research (Denmark, France, Italy, The Netherlands, Spain)

Develop National Action Plans for research on Rare Diseases and improve research climate whenever the use of animals for research is questioned.
Involve pharmaceutical agencies in the process.

2. Adapt the methodology of clinical trials to the specificity of rare disorders - FastTrack and compassionate access (France, Germany, Italy, Spain)

Forming clinically homogeneous groups meeting protocol criteria is difficult.
Phase I can be carried out either on healthy people, or, even better in this case, on people suffering from rare disorders.
Phase II should test product efficiency, tolerance and secondary effects during an appropriate time.
Requests for marketing authorisation at the end of phase II should be allowed to speed up access to new drugs thanks to a fast track approval procedure for marketing authorisation and a European system of compassionate use for medicinal products meeting the following criteria:

- they have not yet been approved
- they may be available to individual or cohort of patients beyond the current conditional marketing approval procedure.

The monitoring of side effects should be reinforced and follow-up records should be set up.

The involvement of patient associations during the development of clinical protocols is essential. They play a key-role in preliminary information and in the transmission of results. Funds for information documents for patients and family doctors need to be found.

It is especially important to have a good understanding of the known progression of the disease. When using a new molecule, it actually helps differentiate its very effects from the symptoms of the disease. No time shall be lost and results shall be correctly interpreted.
Networking with methodologists will not only contribute to adapting clinical trials methodology to rare disorders, but also to training interested MDs and to informing them on those new methods as well.

3. Adoption and implementation of regulation in the countries where it has not already been done (Denmark, Germany, Italy, Portugal, Spain, UK)

Encourage countries who don't have incentives and funds to implement the European Regulation on Orphan Medicinal Products. This Regulation is focused on acting specific incentives and funds for:

- the research and development of orphan drugs
- the improvement of health care on rare disorders.

4. Improve the distribution of adequate treatment in hospitals, pharmacies (The Netherlands, Spain)

New treatment is being developed for a few rare diseases, like Gaucher, Pompe and Fabry. But still there remain a lot of problems in getting the medicine for all patients and for a good price.

5. Reimbursement (Germany, Italy, The Netherlands, Spain)

Request the Public Health System to finance orphan medicinal products (OMP) for chronic diseases.

6. Other obstacles (France, Sweden)

When prescribing for rare disorders drugs developed for regular pathologies, European physicians do so under their own responsibility. The cost for offering new directions for use when renewing a marketing authorisation is very high for the pharmaceutical industry, whereas in the USA, the Office of Orphan Products Development at the Health Department commands appropriations in excess of 10 million $ in subsidies to help its own companies in case of rare disorders.
When the medical industry wants to withdraw effective medicinal products from the market for economic reasons, it must be possible to keep these medicinal products available for the people who need them.

V Awareness (Belgium, Germany, Italy, The Netherlands, UK)

Maintain the use of media coverage, organise events such as awareness days and keep contact with official publications to raise awareness of rare disorders issues.

VI – Strengthening of alliances (Germany, Italy, Sweden)

Make sure that Alliances have the funds needed to do their work, that their structure is representative of their country and that, together with their patient organisation members, they are educated to become active and strong actors.

12. To generate concrete actions in the field both at national and European level

The final goal of this project was to generate concrete actions from the recommendations presented in this report.
Each alliance worked on an action plan according to their capacities and to their constraints. These action plans are exposed in the individual reports. Eurordis intends to have the alliances evaluate every year the actions they have carried out and identify new proposals for the following years so as to continue the action of this project over time.

Some actions have already been initiated since the beginning of this project. The following give an outline of European and national actions.

At European level

Based on the EMEA Workshop with Patient Organisations on March 2001 and on the EMEA Workshop with Industry on April 2001 followed by the European Workshop on Orphan Drugs in Brussels on June 2001 in the context of the Phase III of this project, to which participated representatives from the industry, the European Commission and the EMEA, the EMEA created the COMP Working Group of Interested Parties to further the transparency policy and information actions of EMEA on orphan drugs.
Two specific concrete actions are addressing the expressed needs from the patients in information:

- COMP Public Summary of Opinions for Orphan Medicinal Products Designated by EMEA started to be published in March 2002. This publication occurs at the time of the Decision by the Commission.
- The so-called Shared Database under development by EMEA to provide on-line information on the orphan drugs under development in the European Union, facilitate access to information on the clinical trials and monitor availability in each member state.

Also, along the various phases of the project the situation appeared very different from one country to the other. This is the reason why different partners: Eurordis, OTL Pharma and IBS-Mediscan, who met during the project decided to launch another initiative together: “EurordisCare, a European Study on Access to Care for Patients affected by rare diseases” to identify the ways and difficulties of access to care in different countries through the national alliances, on a few “model” diseases.

At national level

In **Denmark**, first meetings were organised with the National Board of Health, Hospital systems, Danish pharmaceutical agency. Such meetings will continue to take place on a regular basis.
In **France**, the French Rare Disorders Alliance organised the National Forum on Orphan Drugs on June 1st, 2001. It was the first time that 150 representatives of patient organisations, industry, policy makers and regulators met on the theme of orphan drugs. The media coverage was also very good. After this national conference on orphan drugs, a think tank on abandoned molecules started working at the SNIP (syndicate of pharmaceutical industries) with representatives of national and international pharmaceutical industries, start-up industries and patient organisations. Understanding pathology of rare disorders will permit the construction of cellular models from which computer programs can be designed to test archived molecules, using very high screening.
In **Spain** a proposal to support rare diseases research was voted on March 20th, 2002 and awarded a budget of nine and a half million euros. A National Rare Diseases Research

Institution will now be created to coordinate research and act as a reference centre. The media coverage has also helped to raise awareness of rare diseases in Spain.
The **Swedish** alliance obtained a state grant for disability organisations given to about 50 such organisations in Sweden, which was one of the objectives of their action plan.
The new alliances have also made significant progress. In **Belgium,** a website and a survey on the cost of treatment are in progress. The number of patient organisations members of the alliance is progressively increasing, particularly since a TV programme on RTBF, a national TV channel, improved the awareness of Rare Disorders Belgium. Phone calls are skyrocketing since then...
As to The **Netherlands**, a survey on rare disorders was conducted, leading to the publishing of a new brochure.

VI - Overall assessment of the results

Assessment of the project

This project "Orphan Medicinal Products to the service of patients affected by rare diseases" is the first project funded to Eurordis by the European Commission. This grant was approved as a result of the first call for proposal of the European Public Health Programme for Rare Diseases. At that time, in year 2000, three years after the creation of Eurordis, none of the patient associations or patient representatives in the steering committee had previous experience in submitting to, contracting with, managing a project funded by the European Commission in general or specifically by the DG SANCO. The project manager, the project coordinators and the coaches however had previous personal experience in managing programmes and all, in the course of the development and implementation of this project at Eurordis, have been advised initially by Paul Adamson Consultant and BJK Conseil, and assisted by Gemini Consulting and GPC. This in itself has been an important learning process.

At the final term of this project, overall, we can assess that the objectives and the methodology of the project were well defined and there were no major difficulties to implement them.
All the partners involved in the project have been real partners, enthusiastic, dedicated, productive, honest, collaborative. We all had a sense that this project was helpful for each of the partners involved, for Eurordis itself, for the network of national rare diseases alliances, for the interested parties involved and creating a common value useful for the European institutions as well as for the people directly affected by rare diseases.

What made the project more difficult to implement is that all the constituencies and partners involved in the project do not have the same level of knowledge and capacity. They are not at the same level of development and structure. This had an impact on each phase in the internal communication, in the ability to focus on the deliveries.

Coordination in itself is an essential key success factor. Overcoming the above difficulties was a time-consuming task all along the project and particularly at phases III and V. Initially we had underestimated the diversity of the tasks involved in that coordination and the time for the project coordinators, the project manager and for the coaches. This lack of anticipation was also true for the administration and accounting of the project and for reporting and communication. A proper administrative handling requires a rigorous method of work, time with the partners involved, time with the persons responsible for the upcoming expenses at each phase and for reporting them with adequate documentation, as well as some work with a chartered accountant, auditors and the Commission. Reporting requires time to handle the content of the report itself but also back and forth communication with all partners involved. Time to prepare and implement dissemination was underestimated. Also it was not well anticipated that, by nature, the major part of the dissemination work take place in the last stage of phase V, several months after the end of project itself.

The actual costs reported are well below the estimated budget of the project. It is important and useful to note that all phases and actions stated in the project have been implemented. The costs are below the total amount and below the headings for travel and accommodation, for room renting, for copying and translation. This reflects the great vigilance and sense of responsibility of Eurordis and of its partners as well as the capacity of the organisations involved to do more with less allocation of financial resources, using a lot of in-kind inputs and great talent to do cost-killing on every action. With the same total budget amount and to better

reflect the reality of the real costs of this project, it would have been fair and more adequate to allocate more resources for coordination and administration expenses at the European level of Eurordis and at the national level of the alliances.

Assessment of the results achieved compared with the initial objectives

Overall the results achieved reflect all the twelve objectives stated in the projects.
First of all, it must be recognised that this project, made possible by the grant received from the European Union and the funds from AFM, the French Neuromuscular Association, has sped up the collaborative process. Over the 14 months of the project, tremendous progress was made that would not have been possible otherwise.
This project has been a structuring one for the pan-European network of patient organisations on rare diseases and has greatly contributed to building their own capacity as well as creating a common sound ground for future works around orphan drugs to address patients needs.

This project :

- has raised understanding of the European regulation on orphan medicinal products, of the European policy on orphan drugs and rare diseases, and on the issues around them.
- has enabled appropriation of a common language and common concepts.
- has raised understanding and common goal across diseases and borders.
- has strengthened the activities of the existing alliances and has created new alliances from and around the issue of orphan drugs.
- has developed an operational partnership among all alliances on the issues around orphan drugs and has linked a large number of patients associations across diseases and borders.
- has helped identify all interested parties and stimulated interaction with them.
- has reinforced the perception of the patients associations and interested parties involved that orphan drug policy in Europe requires a comprehensive and articulated approach both at the community and at the national levels.
- has educated the leaders of the rare diseases patient associations to think and to act strategically.

It has enabled the patient associations involved to have a voice at national and European level based on an in-depth analysis and joint effort of works to express their needs and to produce recommendations at European and national levels, generating concrete actions as reflected in this report in Section V, paragraphs 10, 11 and 12.

VII - Plan of dissemination of the results

The dissemination of the results was made along the fives phases at national and European levels.

At the national level, the dissemination occurred on the initiative and under the control of the national alliances:

- Syntheses of the national workshops at phase 2 and phase 4 have been distributed to the members of the national alliances and all the interested parties involved in the workshops.
- Some alliances have disseminated the results at conferences and meetings at national level. Eurordis has not set up an exhaustive tracking of those local dissemination actions; it is no easy information to obtain because the actions vary a lot and all the information is in local languages. For instance, in France: Christel Nourissier presented these results to a National Forum on Orphan Drugs organised by the French Alliance on June 1st 2001 to which participated 150 persons (about 1/3 of association representatives, 1/3 of industry representatives, 1/3 of administration representatives, hospital clinicians and media -15 journalists-); several oral progress reports have been presented at the "Réunion d'Information des Membres –RIMES" which takes place every two months.

At the European level, the following actions have been undertaken by Eurordis:

- Articles in the Eurordis Newsletter N° 5 (12%), N° 6 (50%) and N°7 (50%) that are distributed to 400 people each.
- Those articles are also displayed on the Eurordis Website www.eurordis.org.
- The PARD 1 project has been presented twice to the COMP members at the EMEA, by Terkel Andersen: first on December 18th, 2000 to present the objective and the methodology and collect comments; a second time on February 26th, 2002 to present the findings, results and recommendations to COMP members, EMEA staff involved in orphan drugs and Commission DG Enterprise. A discussion followed on possible actions at the European and at the national level.

At the end of Phase V:

- The full final report, including the final activity, all annexes and the final financial report will be provided in English to the 10 national alliance partners involved in PARD 1.

- An article will be published in the Eurordis Newsletter N° 9 (50%) to disseminate final recommendations to all stakeholders: members of Eurordis, other patient associations, industry, medical experts, the European Commission, members of the European Parliament, WHO, FDA and NORD.

- A 4-page letter of information from the CEO will be sent on letterhead to the 205 Eurordis members, together with a copy of the final activity report.

- The final activity report will be sent with a cover letter to key interested parties including: DG Research and DG Enterprise of the European Commission, EMEA, COMP members, EFPIA, EBE, EUROPABIO, WHO, FDA, NORD, CORD, all industry sponsors who have submitted an application for orphan drugs, and five copies will be sent to each of the national alliance partners involved in the PARD 1 project.

- The final activity report will be translated into Spanish, Italian, German and French. The translated document will be sent –in printed and electronic format- in the relevant languages to all concerned alliances. The dissemination will be under the responsibility of the national alliances, as a special distribution to their members, in their newsletter/magazine or on their websites.

- The Final Report will be made available in the 5 languages on the Eurordis Website.

- Three conferences should provide a Forum for further dissemination of the recommendations through different perspectives:
    - The Eurordis European Awareness Conference on Rare Diseases, Barcelona, Spain, 14-15 June 2002.
    - The EPPOSI Third Workshop on Rare Diseases and Therapy development, Rome, Italy, 24-25 October 2002.
    - The EMEA Conference on Orphan Medicinal Products with all Interested Parties, London, UK, 2-3 December 2002 (tentative dates).

VIII - Final conclusions

On the implementation of the project and lessons to take forward

This project "Orphan Medicinal Products in the service of patients affected by rare diseases" is the first project funded to Eurordis by the European Commission, Programme of Public Health, and by AFM, the French Neuromuscular Association. Its implementation in itself has been an important learning process for Eurordis at large and for all the persons involved in the coordination and management.

At the final term of this project, overall, we can assess that results achieved compare well with the objectives and that the methodology of the project was appropriate.

All the partners involved in the project have been real partners, enthusiastic, dedicated, productive, honest, collaborative. These partners have learnt to work together. We all had a sense that this was a project helpful for each of the partners involved, for Eurordis itself, for the network of national rare diseases alliances, for the interested parties involved and creating a common value useful for the European institutions as well as for the people directly affected by rare diseases.

The major difficulties lay in three facts:

- real differences in the level of development and structure of the partners involved,
- coordination capabilities and resources as essential key success factors,
- the actual costs reported are well below the budget of the project and it would have been very helpful to allocate in the estimated budget fewer resources to travel, accommodation, room renting, translation, copying, dissemination and more resources to coordination and administration at the European and national levels.

Overall, we believe Eurordis has demonstrated its ability to carry out a European project. Also, we acknowledge that all the participants have gained specific experience in coordinating and managing such a pan-European project and administrating Commission grants. This is a strong experience on which to build for the next projects both at the stage of implementation and reporting as well as at the stage of developing, budgeting and planning those projects.

On the achievements beyond the scope of the project as of March 2002

Primarily, this project has been a structuring one for the pan-European network of patient organisations on rare diseases and has greatly contributed to building their own capacity as well as creating a common sound ground for future works around orphan drugs to address patients needs.

Secondly, some of the recommendations developed in the course of the project are already implemented or well advanced. These outstanding results are due to the processing of the project itself and how it has been led and managed: the other interested parties were involved

at each step, the elaboration of recommendations was inclusive and communication to key decision makers was monitored at critical steps. This approach allowed to bring positive changes during the project.
Key positive changes that can already be attributed totally or partly to the impact of this project include:

- The publication of COMP Public Summary of Opinions for Orphan Medicinal Product Designation by EMEA since March 2002.
- The so-called Shared Database under development by EMEA to provide on-line information on the orphan drugs under development in the EU, facilitate access to information on the clinical trials and monitor availability in each member state.
- The raising awareness on the need to recognise alternative methodologies and statistical approaches for clinical trials on rare diseases, and on the specific role of patient organisations in the development and evaluation of these trials.
- The creation of a working group in France between the patient associations and the manufacturer association to focus on the revival of abandoned molecules in France.
- The development studies by patient groups on access to care for patients affected by rare diseases such as the ongoing survey in The Netherlands, the Eurordis spot surveys across EU on newly marketed orphan drugs, the study in Spain conducted by FEDER and the Carlos III Institute.
- The emergence of institutional structures at the national level to coordinate policy efforts on orphan drugs and stimulate incentives such as in France, The Netherlands, Denmark, Spain.

Thirdly, Eurordis will continue to follow the implementation of the national action plans developed by the alliances in order to track the concrete actions to be derived from the recommendations presented in this report.

Fourthly, this project has been instrumental to identify and stimulate critical European projects and its partnership to increase the quality and access to information on orphan drugs in EU, to improve orphan drug development in EU, monitor the availability and access to orphan drugs in the member states. Those projects include:

- The submitted Eurordis project to the Commission for “Pan-European Network for Patient Information on rare Diseases and Orphan Drugs”.
- The submitted project to the Commission on the EuroBioBank project to coordinate the DNA and tissue banks on rare diseases in Europe initiated by Eurordis in partnership with major research centres in several EU member states.
- The future European Collaborative for Research and Clinical Trials on Rare Diseases, involving several scientific partners and Eurordis to study the feasibility and develop the action plan toward a pan-European co-ordinated efforts to better serve the development of orphan drugs in EU.
- The ongoing project to accelerate the transfer and access for patients in the EU to the orphan drugs marketed or designated in the USA, through proactive actions with industry, clinical centres and patient groups, thanks to a new collaboration between EMEA-COMP, FDA, Eurordis and US NORD.
- The ongoing project EurordisCare to evaluate access to care for patients with some rare diseases.

IX - List of annexes

N°	Type of document
	1) Copies of documents produced
	Kick off Meeting – Brussels, 20th October 2000
1	Agenda of the Kick off Meeting in Brussels, 20th October 2000
2	Synthesis papers of actions undertaken by each National Alliance the previous year
3	SWOT analysis sample given to coordinators to prepare the analysis of their alliance
4	SWOT analysis of each National Alliance
5	Methodology to organise the 2-day national workshops
6	Timetable of Phase II of the project
7	Minutes of the Kick-off Meeting – Brussels, 20th October 2000
8	Agenda and Minutes of the 1st Steering Committee Meting, 8th December 2000
	National Workshops in each country – January 2001
9	PARD 1 presentation
10	Proposed agenda to organise the workshops, created at the 1st Steering Committee Meeting
11	Guidelines given to National Alliances regarding questions to be discussed during the workshops
12	Agendas of each National Alliance
13	First report guidelines, defined in November 2000
14	Modified report guidelines, revised on 12th February 2001 and congratulation to coordinators
15	Reports of the workshops with recommendations and action plans of each National Alliance
16	Agenda and Minutes of the 2nd Steering Committee Meeting, London 20th March
17	Intermediate report sent to the European Commission in June 2001 on Phase I and II and the preparation of Phase III of the project
	European Workshop in Brussels, 7-8th June 2001
18	Agenda of the European workshop in Brussels, 7-8th June 2001
19	Synthesis of the recommendations given by the National Alliances (presentation)
20	Minutes of the Roundtable Session – European Workshop, Brussels, 8th June 2001
21	Conclusion of the European Workshop by Terkel Andersen (project leader)
22	Agenda and minutes of the 3rd Steering Committee Meeting, 3rd September 2001
	National workshops in each country, autumn 2001
23	Timetable of Phase IV of the project (2nd semester 2001)
24	Guidelines sent by Eurordis to organise the 2nd national workshops
25	Reports of the national workshops and feedback from each National Alliance

N°	Type of document
26	**2) List of the participants in the workshops**
	3) Dissemination of information
27	Eurordis Newsletter N°5 Autumn 2000
28	Eurordis Newsletter N°6 Winter 2001
29	Eurordis Newsletter N°7 Spring 2001
30	Eurordis Newsletter N°8 Autumn 2001
31	Dissemination of information on Eurordis website (www.eurordis.org)
32	Presentation to COMP and EMEA press release
	4) Rare diseases, prevalence and list of rare diseases
33	Definition of rare diseases on Orphanet's website (www.orpha.net)
34	Some of the rare diseases represented in Eurordis
35	List of rare diseases on Orphanet's website (www.orpha.net)
	5) List of patient organisations, either members of Eurordis or of National Alliances
36	Members of Eurordis
37	Members of some of the National Alliances