OrphanPlatform

Contract n°: **LSSM-CT-2004-503246**

Project acronym **: OrphanPlatform**

Instrument: **Specific Support Action**

Project title: **A European Platform of Integrated Information Services for the coordination of rare disease research in Europe, with various stakeholders from research, SMEs and patient organisations and the coordination of early clinical trials**

Thematic priority: LSH-2002-2.1.1-12.

Final activity report

Period covered: from 1 April 2004 to 30 June 2006

Date of preparation: 10 July 2006

Start date of project: 1 April 2004

Duration: 2 years + 3 months

Project coordinator: **Ségolène AYME**

Organisation name **INSERM**

Draft 1

Final activity report

Project objectives

The project aimed at developing information tools to address in a comprehensive and integrated approach the set of factors that currently affects research on rare diseases and its coordination.
The specific objectives were: (1) to develop an information service, freely accessible on Internet, dedicated to research activities in the field of rare diseases and orphan medicinal products, including a database of research projects, funded at MS level and at the EU level, and a database of collections and research networks. (2) to develop services aiming at speeding up the enrolment of patients in clinical research. (3) to develop a database of research projects with development potential, to help scientists and Industry establish the necessary partnerships. (4) to organise a workshop with all stakeholders to discuss known bottlenecks and find solutions.
The project aimed at establishing the platform of services in 11 European countries in the pilot phase in order to propose an extension to the 25 European countries in 2006.
Ultimately, the goal is to convert scientific developments in the field of rare diseases into diagnostic tools and therapies as quickly as possible.
Two websites were supposed to be launched to support these activities: www.orphanplatform.org to serve as a management tool between partners; and www.orphanXchange.org to serve as a tool to facilitate partnership betweens researchers and Industry. All the collected information on on-going research activities and all the new services developed during the course of this contract would be available on the Orphanet website at www.orpha.net

Contractors involved

This project was based on input from the following (1) an EU funded information network: Orphanet (www.orpha.net) (2) A European platform of Patients organization, Science and Industry (EPPOSI) which actively supports partnering activities. (3) two umbrella organizations of patient support groups (Eurordis and VSOP) involved in supporting research and regulatory activities. (4) three umbrella organisations of Industry: Emerging Biopharmaceutical Enterprises (EFPIA), EuropaBio, LEEM. (5) 11 Academic institutions (INSERM (France), University College of Cork (Ireland), Istituto Casa Sollievo Della Soffenza (Italy), Universita Pompeu Fabra (Spain), Victoria University of Manchester (UK), Katholieke Universiteit Leuven (Belgium), Academic Medical Center Amsterdam (Netherlands), University of Turku (Finland), Instituo de Genetica Medica Jacinto Magalhaes (Portugal), Medizinische Hochschule Hannover (Germany), Medical University of Vienna (Austria) VU Medical Center (Netherland).

Coordinators contact details

The project was coordinated by:
Dr Ségolène Aymé
INSERM SC11 – 102 rue Didot – 75014 Paris – France
Tel : +33 1 56 53 81 37
Fax : +33 1 56 53 81 38
ayme@orpha.net
www.orpha.net

Project execution

1- Sub-project "Directory of research activities in Europe in the field of rare diseases"

The first sub project was to extend the Orphanet directory of services in order to provide accurate information on on-going research activities at the Member states level and at the EU level, in a format easy to use for researchers, clinicians, Industry, patients, administrative bodies and any decision-maker.

This specific objective was composed of two subprojects: (1) the extension of the Orphanet database to accommodate this new type of information and (2) the collection of data in the 11 participating countries.

All the informatics developments were performed during the first months. The database was ready for data injection by September 04 at the address www.orpha.net in 6 languages (English, French, German, Italian, Portuguese, Spanish)

The lists of research funding agencies and the sources to identify research projects in the Orphanet partner countries have been established. Collection of projects published on the DG SanCo and the DG Research websites was performed by the coordinating team and specific information sent to corresponding country partners. All the national agencies were contacted to obtain lists of funded research projects. The ones in relation with rare diseases were selected and the researchers approached to give more details on their project and to give consent for the publication on the Orphanet website, using a standard questionnaire translated in all necessary languages. This questionnaire was available as a PDF document but also on-line.

The directory of research activities in Europe was filled in as scheduled. During the first year, over 500 research projects have been entered into the Orphanet database: 131 clinical trials, 115 registries, 125 networks and 138 research projects. At the end of the contract, the data collection includes 392 clinical trials, 204 registries, 283 networks and 3,349 research projects. The total amount of collected data is 4,238 where the contract was expecting 4,000. The details by type of data and by country are accessible on the orphanplatform website for the partners and on request to the coordinator for the community at large.

The next step is now to extend these services to all European countries with the support of an other contract. In addition to the current country partners, we have identified possible new partners in the following countries so far: Bulgaria, Cyprus, Czech Republic, Croatia, Denmark, Estonia, Greece, Hungary, Latvia, Lebanon, Morocco, Norway, Poland, Romania, Serbia, Slovakia, Slovenia, Sweden, Switzerland, Tunisia and Turkey.

2- Subproject "Development of a registration service for patients willing to participate in clinical research"

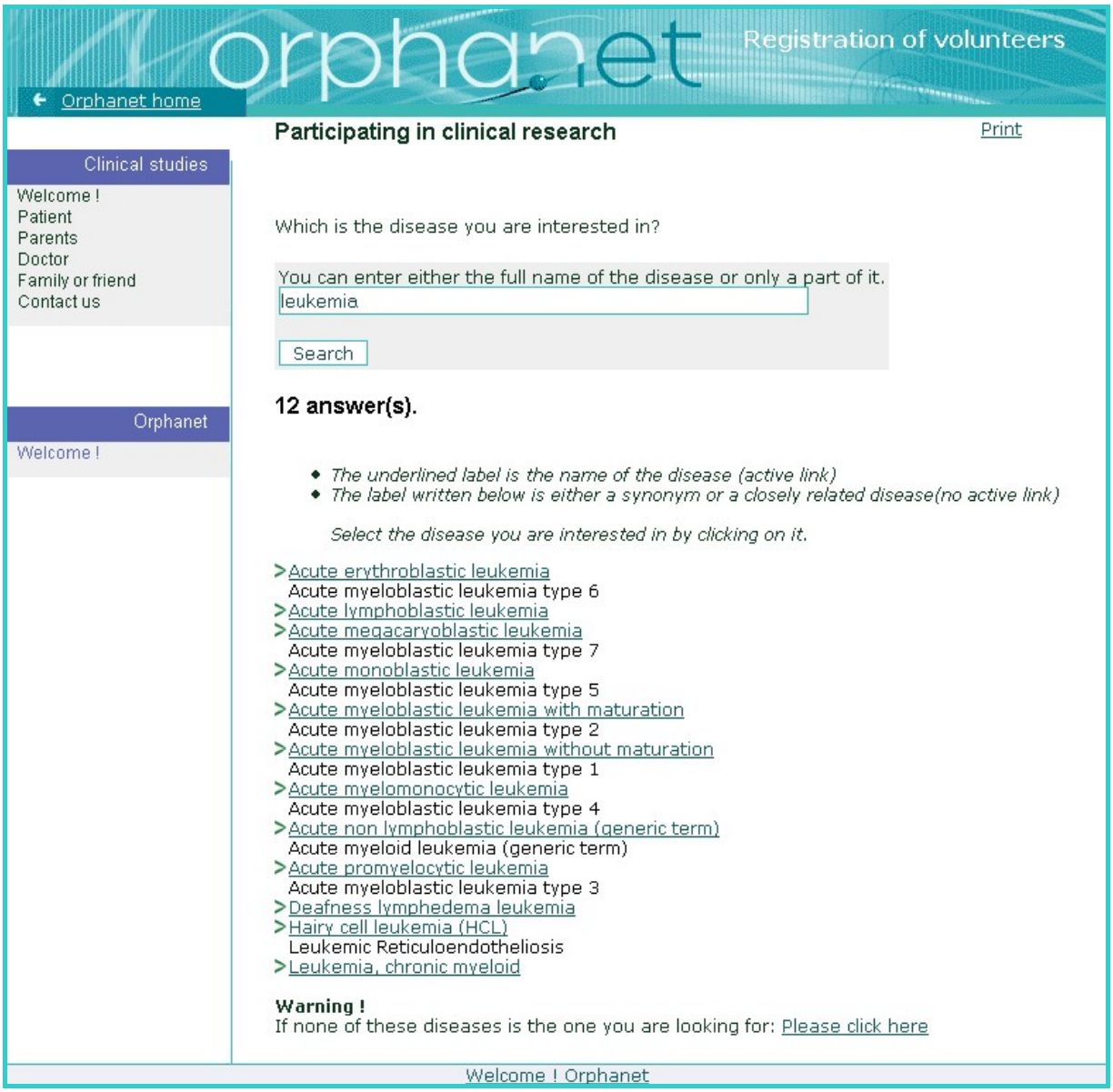
The second subproject was to develop a new facility to allow patients to find out whether there is a clinical research project on their disease, which they could participate in.
This facility has been developed according to plans with the following principles:

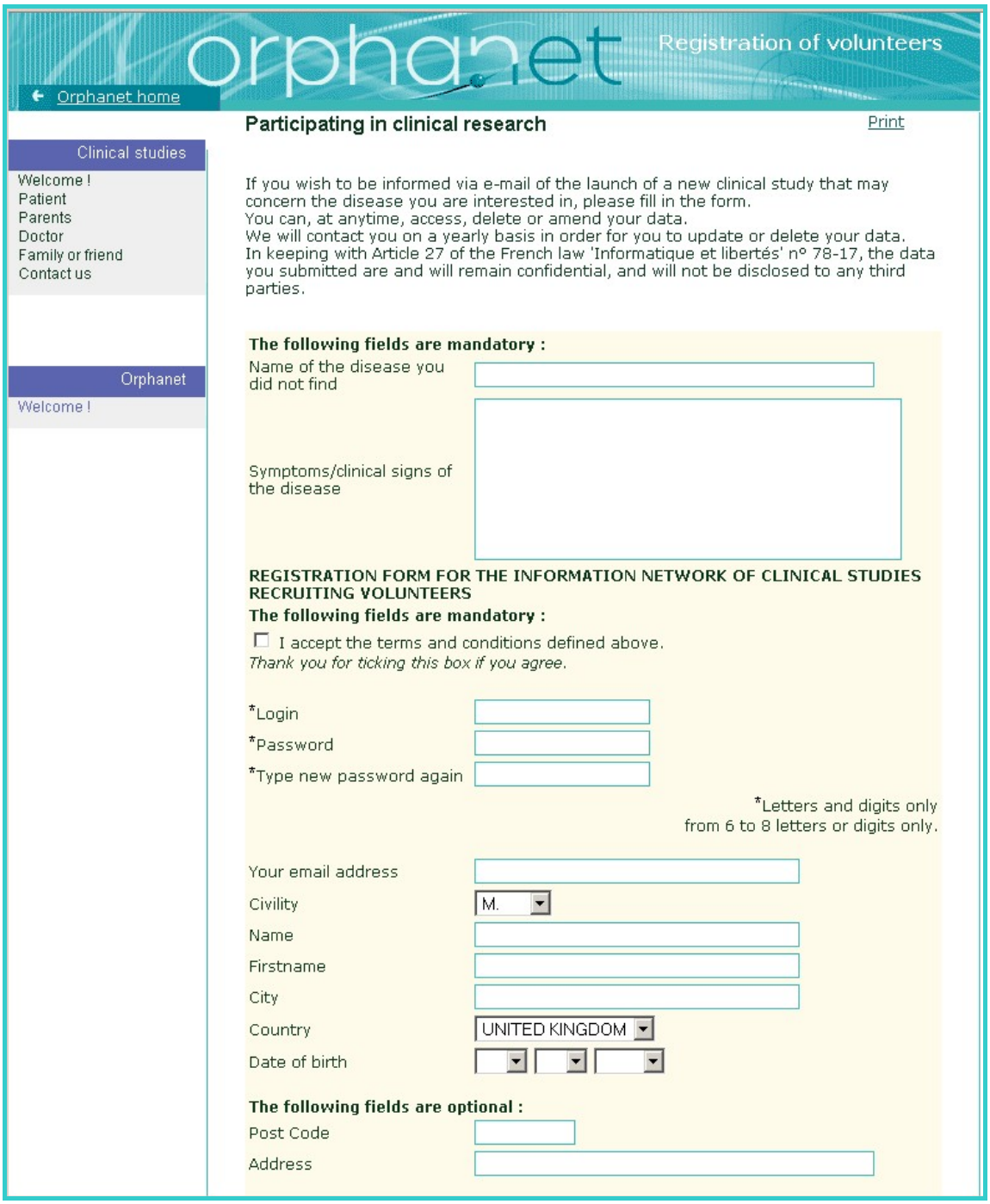
Only patients can register, or parents and legal representatives of a person suffering from a rare disease; family and doctors can pass on information to patients (an information letter is available and may be downloaded from the website).
It is be an **opt-in** service

- Patients can access the list of clinical trials regarding their disease. If there is no on-going trial, the patient can decide to leave his contact details in order to be informed about any new project.
- If there is an on-going trial, the patient can access the protocol to check whether he seems eligible. He is advised to discuss with his physician about the possibility to apply for enrolment.
- The patients who leave their contact details can access, modify or suppress their data at any moment.
- They will be systematically asked to re-confirm their willingness to remain in the database, once a year.

The service to allow patients to register as volunteers for participating in clinical trials was launched in French and English on January 2005 and in German, Spanish, Portuguese and Italian six month later. It had received an approval (n° 820077) from the C.N.I.L (National Committee on Informatics and Liberty) in France as the personal data are stored in France.

The search for a disease is as in Orphanet. A list of diseases corresponding to the search is proposed. The patient may choose the disease he/she is interested in. If the patient does not find in the proposed list the corresponding disease, he/she can describe the disease (symptoms/clinical signs) and register.





The launch of this registration service was advertised in OrphaNews France (the Orphanet newsletter in French) and in OrphaNews Europe (the newsletter of the rare diseases task force in English). Since March 2005, new clinical studies entered in the Orphanet Database are listed in OrphaNews with a link to the registration service. This initiative has resulted in a great increase in the number of patients registering to the service.

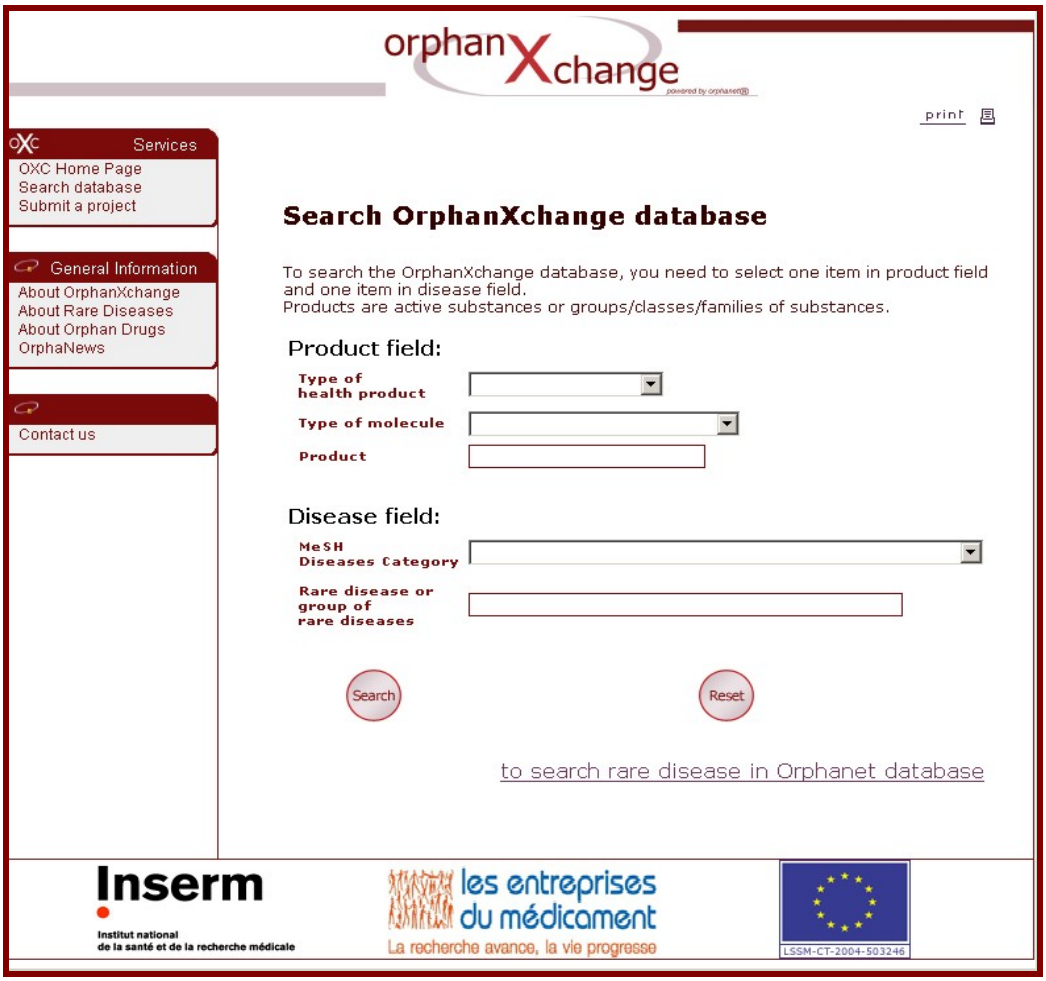
The service to allow patients to register as volunteers has registered 457 patients during the first year and 1356 patients during the second year. They are suffering from 700 distinct diseases. These patients are from 50 countries. During the second year, 123 patients out of the 1,813 registered patients have been contacted to be informed that a new recruiting clinical trial was starting for their disease.

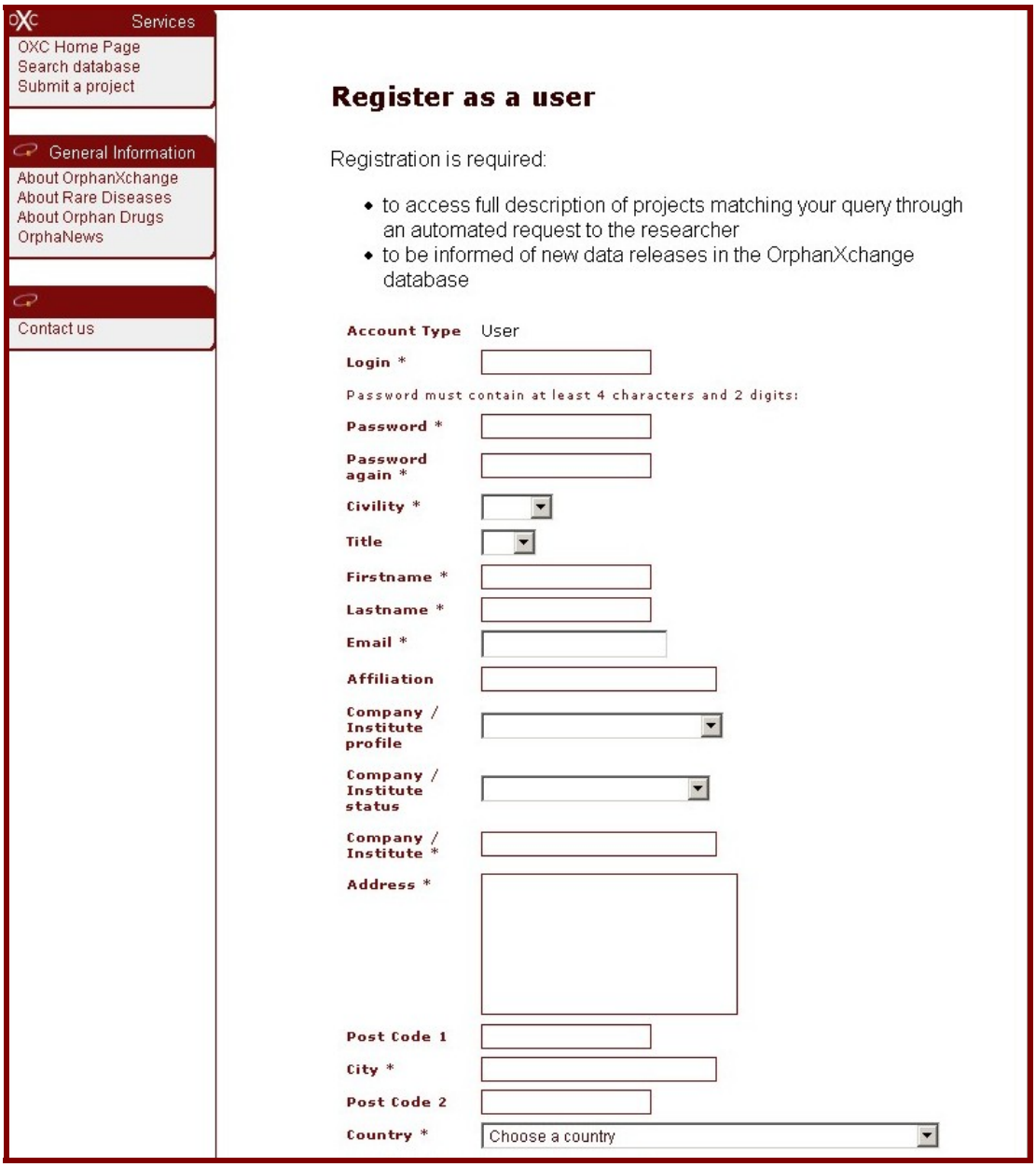
3- Subproject: "Establishment of a directory of academic research projects seeking industrial partnership"

The third sub project was to identify, among all the research projects listed in the database, the research projects which reach a stage at which they can be carried out by an industrial company or form the basis for a start-up company, and be developed into a commercial product or technics. These projects were be made accessible and visible on the OrphanXchange website, a separate website from Orphanet but with functional links. The two projects would share part of the Orphanet database but the front ends would be different. The necessity to have a separate website came from the fact that the OrphanXchange website had to be password protected when the Orphanet website is fully accessible without any registration.

This subproject had two components: (1) the establishment of a website and of a database of research projects seeking partnership with Industry, (2) the collection of research projects to fill in the database. The website opened in June 2004. It is accessible at: www.orphanxchange.org
The research projects included in the database are coming from three sources: (1) a selection of projects of potential industrial interest listed in Orphanet; (2) potential orphan designations identified through mail surveys sent yearly to European clinicians; (3) projects collected by departments of technology transfer of research institutions.

The website is freely available. Registration is needed only to obtain detailed information and to be put in contact with the researcher.





OrphanXchange has received 1580 requests during the first year and 6,000 during the second year. About 70% of the requests are performed by registered users of which 50% comes from the private pharmaceutical sector, the major targeted public for the database.
The number of registered users was 130 at the end of the first year and 208 at the end of the second year (50% Pharma-Biotech-Venture Capital-Consulting, 36% Public research/Healthcare, 7% patient support groups, and 7% other). The number of registered visiting countries: **27** (Austria, Belgium, Brazil, Bulgaria, Canada, Czech Republic, Denmark, Estonia, Finland, France, Germany, India, Ireland, Italy, Japan, Latvia, Lithuania, Malta, Netherlands, Pakistan, Portugal, Romania, Spain, Sweden, Switzerland, Tunisia, United Kingdom, United States).
The visits by registered users have induced 51 contact requests accepted by the researcher for further discussion on a possible partnership.

4- Subproject "partnering workshop"

The fourth sub project was to organise a partnering workshop during the second year of the contract. There is a strong view that additional action needs to be taken to energise and expedite the development of therapies and suitable diagnostics for rare diseases. A workshop was needed to exchange views and explore options for facilitating the development of therapies and identify research projects in advanced stages. It was supposed to follow the scheme of previous partnering workshops organised by EPPOSI: Brussels (2000); Paris (2001), Rome (2002), The Hague (2003), Berlin (2004), but this one was supposed to focus on Orphanplatform main concepts: coordination of research activities and research funding in Europe; improvement of partnering activities; improvement of clinical trials in the field of rare diseases. The expected total number of participants was 100 to 150 of which 50 would be invited, the other ones having to register. The registration was planned to be free of charge for scientists and patients.
The workshop would be advertised by a mailing to the previous participants to EPPOSI workshops, by putting the information of the EPPOSI website, the Orphanet website and the EURORDIS website, and by putting the information in OrphaNews and in the EURORDIS newsletter.

The workshop took place in London on 25-27 October 2005. The total number of participants was 150, composed of a third of patients representatives, a third of Industry representatives and a third of researchers and health professionals. It was organised in collaboration with the FDA, the NIH, the EMEA and American and European patients organisations, and was co-sponsored by the British Department of Health as well as by Industry. The programme is available on-line at www.epposi.org.

The workshop was advertised by a mailing to the previous participants to EPPOSI workshops, by putting the information of the EPPOSI website, the Orphanet website and the EURORDIS website, and by putting the information in OrphaNews and in EURORDIS newsletter.
The EPPOSI workshops are problem-solving oriented workshops to identify bottlenecks and solutions at all stages of research and therapy development. They are also partnering workshop between patients, industry, researchers and venture capital.

A report of the workshop can be obtained from www.epposi.org.

Intention for use and impact

All the services developed through this action are freely accessible to all stake holders.

1- *Intention for use*

OrphanPlatform is particularly relevant in four areas:

1. The project addresses the needs of diseases specific research networks

Through bridging the upstream needs for data availability with the downstream issues faced by clinical researchers, the project contributes at building synergies with, and acting as a facilitator for other important research and development projects in the fields of rare disorders, genomic and post genomic, gene and cell therapies.

2. The project addresses the needs of EMEA and industry

The project is of course directly relevant to the activities of the Committee for Orphan Medicinal Products and of the Committee for Proprietary Medicinal Products, including its Scientific

Review Group to provide protocol assistance and its safety, efficacy and quality Working Parties. The project is also expected to have direct benefits for European industry and particularly to small and medium enterprises (SMEs), which account for 80% of OMP applications submitted to EMEA. The platform of services at the centre of the project is now providing these industry partners with cost-effective services and solutions that are not yet available. The platform is expected to steer innovation capacity for new therapies and to reduce the current competitiveness gap of EU industry versus US.

3. The project will benefit to paediatric drugs and cancer treatments development

This represents another major public health objective for the EU on which the European Commission envisages specific regulatory and research initiatives. 80% of rare diseases appear at an early age and are directly responsible for 25% of the mortality in childhood. Experience gathered in the US and in Europe also shows that around 40 % of Orphan Medicinal Products are new and innovative products for cancer and leukaemia treatment.

4. The project was an archetype of the need for action at European level

Not only the project could not be developed at the level of Member States acting independently, but non-integrated national actions are now adding to obstacles faced by clinical researchers and industry. The specificity of the small number of patients, scarce professional competences and fragmented resources are defining the relevance of this structuring project at the Community level.

2- *Dissemination of the knowledge*

2.1. Through websites

All the services developed and all the data collected are accessible from three websites:

- www.orphanplatform.org which access is restricted to partners. It provides all the documents produced during the contract time and detailed statistics by country partner.

- www.orpha.net which gives free access to the directory of research activities in Europe and to the service of registration for patients willing to participate in clinical trials

This website was accessed daily by 4,000 users at the beginning of the contract. In June 2006, the average number of users per day was 15,000.

An on-line survey was performed in March 06 to better know our customers and to assess their satisfaction. The questionnaire was systematically proposed to all visitors but they had the possibility to accept or refuse to complete it before accessing the website. The questionnaire was left until 1,000 were completed in each language.

The main results are the following:

	Francophones	Anglophones
Categories of users:		
Health professionals:	61.4 %	47.1 %
Patients and families:	29.8 %	19.8 %
Others	8.8 %	33.1 %
Ways to discover the website:		
Search engine	51.6 %	64.3 %
A doctor	7.6 %	2.8 %
A colleague	6.6 %	5.9 %
A hospital website	5.2 %	1.6 %
A patients organisation	2.2%	8.1 %
Other	26.8 %	17.3 %
Frequency of visits to Orphanet:		
First visit	49.3 %	76.8 %
Over twice a year	17.8 %	11.3 %
Over twice a month	22.7 %	8.1 %
Over twice a week	10.2 %	3.8 %
Type of information looked for:		
A specific disease	82.5 %	80.9 %
A patients organisation	10.2%	5.3 %
A clinical laboratory	11.8 %	8.2 %
A research project	10.5 %	10.9 %
A clinic	10.0 %	4.7 %
A clinical trial	8.1 %	8.8 %
Satisfaction with the information:		
Totally satisfied	73.6 %	64.9 %
Partially satisfied	25.6 %	31.2 %
Not satisfied	0.8 %	3.9 %

This survey shows that 10% of the Orphanet users are looking for information on on-going research activities in the field of rare diseases, which corresponds to 4,500 visits per month.

The registration service for patients

- www.orphanxchange.org which gives access to the directory of academic research projects seeking industrial partnership

The website http://www.orphanxchange.org was launched on June 15th, 2004. A press conference was held on the same day at the Plateforme Maladies Rares in the presence of Pierre Le Sourd, president of the French pharmaceutical companies association, Christian Brechot, Director of INSERM, Alain Fischer, Director of GIS Institut des Maladies Rares, Jacques Bernard, representative of the French rare diseases alliance, and Ségolène Aymé, director of Orphanet. The press release (see Appendix 4) has been translated into English by Orphanet and sent to EFPIA (EBE), EPPOSI, EuropaBio, Eurordis, European Commission, EMEA, FDA and to 20 Orphanet partners in Europe. The press release was then translated into 15 national languages and sent to the national media and national competent authorities by our partners.

In France,

- 3 Press Agency news releases - June 15th 2004 (AFP, APM et AEF)
- 1 News Brief in national daily newspaper (Le Parisien - June16th 2004)
- 5 articles in national medical/specialised journals (Le Quotidien du Médecin - June 17th 2004, Le généraliste and Impact Médecine - June 18th 2004, Le Concours Médical - June 30 2004, Scrip August 13th 2004)
- Newsletter Pharmaclient (June 2004)
- Bulletin International d'Information (June-July 2004)
- Yahoo News(June 15 2004)
- La Croix (June 16th 2004)
- Nouvel Obs.com (June 16th 2004)
- Samaritains Handicap France website (June 16th 2004)
- L'usine nouvelle Biotech Info (July 2004)
- ivs-info.com, Biotechs diffusion letter (July 7 2004)
- Destination santé.com (July 8 2004)

In the other European countries, newspapers reported about OrphanXchange in : Austria, Estonia, Finland, Hungary, Italy, Portugal, Spain, Switzerland, UK.

2.2. Through reports

The initial plan was to produce a report on research activities in Europe, based on the analysis of the data collected through out this project, and to publish it as a paper in a scientific journal. We now believe that it is a bit too soon as we need a more careful mapping of these projects before being in a position to say anything meaningful. We wish to postpone this publication by one year to have a better report.

We also planned to publish a report of the workshop which took place in London on October 2005. This report was produced and sent to all participants, then put on the EPPOSI and Orphanet websites as PDF documents. The publication of this report was advertised in OrphaNews Europe which reaches 7,500 readers.
It is accessible at the following address:
http://www.epposi.org/05%2010%202527%20EPPOSI_London_Report.pdf

An editorial from Nature mentioned OrphanXchange as a tool to support the development of therapies for rare diseases under the title:
« Wanted: social entrepreneurs »
Nature. 2005 Apr 21;434(7036):941

2.3. Through conferences and lectures

The dissemination was also done through conferences and lectures:

- Ségolène Aymé : “Identifier de nouvelles indications de molécules déjà sur le marché: le projet orphanXchange”
Colloque du GIS Maladies Rares “Développer la thérapeutique des maladies rares: stratégies de recherche de molecules d’intérêt”, Paris , 7 juin 2004

- Ségolène Aymé : “OrphanPlatform: services for the development of orphan drugs”
EFPIA/EBE workshop on orphandrugs. Brussels, 11 June 2004

- Ségolène Aymé : “What epidemiological data are lacking in orphan drugs development and what are the possible solutions?”
International conference on pharmaco-epidemiology and therapeutic risk management
Bordeaux, 25 August 2004

- Ségolène Aymé : « Are orphan drugs priority medicines for Europe ?
Drug Information Association European meeting, Lisbon, 8 March 2005

Valerie Thibaudeau: « Increasing awareness of rare diseases in eastern Europe: the place of Orphanet » Conference on Rare Diseases, Plovdiv, Bulgarie, 27 May 2005

Segolene Ayme : « Orphanet : Centre de ressources européen pour les maladies rares »
Salon européen de la recherche et de l’innovation, Paris, 4 Juin 2005

Valérie Thibaudeau: "Les indications orphelines en 2005: résultats de l'enquête auprès des associations et des professionnels"
VIème Forum Interne, Paris, Paris, 13 June 2005

Valerie Thibaudeau: «Strengthening cooperation between academia and industry » European Conference on rare diseases, Luxembourg, 21-22 June 2005

Valerie Thibaudeau : « Strengthening cooperation between academia and industry » Spanish Human Genetic Society Congress, Valencia, Spain, 29 September 2005

Segolene Ayme : « Facilitating the development of orphan drugs : the OrphanXchange experience »
Sixth EPPOSI workshop on partnering for rare disease therapy development. London 25 October 2005

Segolene Ayme : « Rare Diseases action plans in Europe »
National Polish Conference on Rare Diseases, Warsaw, Poland, 16 December 05

Segolene Ayme : « European initiatives in the field of rare diseases »
Rare Diseases workshop of the Veneto region. Padua, 13 janvier 2006

Segolene Ayme : « European initiatives in the field of rare diseases »
Rare Diseases workshop of the Adige region. Trente, 16 janvier 2006

Segolene Ayme : « Les nouvelles thérapies en développement pour les maladies rares : heurs et malheurs »
3èmes assises de génétique humaine et médicale, Montpellier, 28 Janvier 2006

Segolene Ayme : « Les nouvelles technologies de l'information au service de la recherche clinique sur les maladies rares »
Colloque « Maladies rares : spécificités de la recherche clinique ». Université Claude Bernard-Lyon 1, 7 avril 2006

Segolene Ayme : « Orphanet project: Improving health through eHealth"
E-Health high level conference, Malaga, Spain 11 May 2006

Segolene Ayme : 'Interfacing patients and researchers: the Orphanet initiative"
International Clinical Trial Day, Brussels, 19 May 06

Valérie Thibaudeau: "The contribution of Orphanet in the field of Orphan drugs"
EUOrphan meeting, Pavia, Italy, 16 June 2006

Segolene Ayme : "Consultative structures on Health information through the Public Health Programme: the experience of the rare diseases task force"
Seminar on health information, monitoring and analysis, TAIEX, DG Enlargement, Brussels, 20 June 06

Segolene Ayme : "Information projects under Public Health Programme: the experience of Orphanet"
Seminar on health information, monitoring and analysis, TAIEX, DG Enlargement, Brussels, 20 June 06

Segolene Ayme : "Les médicaments orphelins: un choix de société"
Colloque du LEEM "Traiter les maladies rares : un espoir hier, une réalité aujourd'hui"
Paris, 26 Juin 06

Valérie Thibaudeau: "Favoriser le partenariat public - privé: orphanXchange"
Colloque du Leem: "traiter les maladies rares: un espoir hier, une réalité aujourd'hui", Paris, 26 June 2006

A leaflet describing all the products and services issued from this contract was printed and distributed at all the meetings where a lecture was given.