orphanet

2013 Activity Report

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For any questions or comments, please contact us: *contact.orphanet@inserm.fr*

1. Overview

1.1. Objective

Orphanet endeavours to provide the community at large with a comprehensive set of information on rare diseases and orphan drugs in order to contribute to the improvement of the diagnosis, care and treatment of patients with rare diseases.

1.2. 2013 activities

Orphanet is a reference portal for information on rare diseases and orphan drugs.

The site gives access to:
- An inventory of diseases classified according to existing published expert classifications. Each disease is indexed with ICD10, OMIM, MeSH, SNOMED CT, UMLS, MedRA and its 'identity card' includes the relevant prevalence class, age of onset class, mode of inheritance and associated genes.

- An encyclopaedia covering more than 4500 rare diseases, written by science writers and reviewed by world-renowned experts. Abstracts are produced in English and are then translated into French, German, Italian, Portuguese, Spanish, Dutch, Polish, Slovak, Greek and Finnish. For some selected diseases, emergency guidelines and articles for general public are produced and translated.

- An inventory of review articles on rare diseases and of clinical guidelines.

- An inventory of orphan drugs and of drugs intended for rare diseases, at all stages of development, from orphan designation to market authorisation.

- A directory of expert resources in the 37 partner countries, validated by national experts and providing information on: specialised expert centres and centres of expertise, medical laboratories, research projects, clinical trials, registries, networks, technological platforms and patient organisations.

A range of other services:
- A support-to-diagnosis tool (search by signs and symptoms).

- A newsletter in English covering both scientific and political news. This newsletter is also published in French and in Italian.

- Thematic studies and reports on overarching subjects: the "Orphanet Report Series", published as PDF documents.

- Quality articles published by other journals or learned societies. More than 990 articles have been published, with the permission of authors and editors, comprising national and international clinical guidelines produced by learned societies that are not published in peer-reviewed journals but available as reports.

Orphanet is currently the most comprehensive site in terms of referenced documents and also the only project that establishes a link between diseases, the textual information existing concerning them and the appropriate services for patients, researchers and healthcare professionals. Moreover, Orphanet website content (and data) is robust as it is expert validated, updated continuously and quality controlled. These unique features make Orphanet the reference website dedicated to rare diseases as it allows the different stakeholders, and in particular health professionals and researchers, to keep up with constantly evolving RD knowledge.

1.3. Main achievements of 2013

- The Orphanet rare diseases ontology (ORDO) produced in collaboration with the EBI is now available on Bioportal (http://bioportal.bioontology.org/ontologies/ORDO). It represents a powerful research tool.

- The international website and the database have been translated into Dutch and since June 2013 all the information is accessible to users in Dutch.

- The encyclopaedia of rare diseases has been expanded and updated. As of 31 December 2013, some abstracts are available in Finnish, Polish, Greek and Slovak in addition to English, French, German, Italian, Spanish, Portuguese and Dutch. Emergency guidelines are available in Polish in addition to English, French, German, Italian, Spanish and Portuguese.

- A new collection of texts in the Orphanet Encyclopedia has been established. It is devoted to the disabilities associated with each rare disease and is addressed to the professionals in the field of disability as well as to the patients and their families.

- The directory of expert centres, medical laboratories, clinical trials, research projects, networks, registries and patient organisations has been expanded and updated.

- A new Orphanet Report Series was created about the European infrastructures useful to rare diseases.

- The list of rare diseases (in English and French) has been published as an Orphanet Report Series for more effective communication but also for easy retrieval of the Orpha codes by clinicians and coders.

- Most of the Orphanet Report Series have been updated (List of Rare Diseases, Prevalence of Rare Diseases, Lists of Orphan Drugs, Orphanet Activity Reports, and Satisfaction Surveys).

- An Orphanet mobile application was released for iPhone, iPad and Android, including the list of rare diseases, textual information and list of expert centres.

- The Orphanet Activity report 2012 has been translated into French, Italian and Spanish.

- The Orphanet Standard Operating Procedures, according to which Orphanet national teams agree to work, have been posted on the website.

- The Orphanet nomenclature has been included in several national health information systems; working groups and collaborations were set up in France, Germany, Belgium and Latvia. Collaborations are planned with Greece and Hungary.

- The Orpha codes have been added to the German modification of the ICD-10 (ICD-10-GM) in order to be able to code all RD within this German coding system.

- The Orphanet online registration tool was launched in order to allow health professionals, patient organisations and researchers to submit or update their information related to rare diseases in Orphanet.

2. The Orphanet Consortium

2.1. The Orphanet Europe Joint Action

Orphanet is mentioned in the documents of the European Commission on Rare diseases ("Rare diseases: Europe's challenge" 11 November 2008 and "Recommendations of the Council on Rare Diseases" - 8 June 2009) as the source of current information on rare diseases in the European Union and also as a strategic element of any national plan/strategy on rare diseases that each Member State is encouraged to develop by the end of 2013. In 2011, the Orphanet Europe Joint Action was launched, an instrument that combines funding from the European Commission with each of the participating Member States, as well as from Switzerland, a collaborating partner. The Joint Action began on the 1st of April. The overriding aim of the Joint Action is to improve and adapt the presence of Orphanet in each participating country.

To ensure optimal governance of the Joint Action and efficient management of the workflow, and also to reflect the new involvement of the health authorities of the Member States, Orphanet governance is organised by three different boards:

- The **Management Board** composed of country coordinators;
- The **Steering Committee** composed of representatives from the funding agencies/health authorities contributing to the funding of the core project (diseases database, encyclopaedia, database structure, infrastructures, and coordination of activities);
- The **International Advisory Board** composed of international experts.

These boards discuss the evolution of the project in scope and depth; ensure its coherence, its evolution in relation to technological developments and to the needs of its end-users, as well as its sustainability.

On 7 June 2013, the Joint Action Orphanet Annual Partners' Meeting was held in France. Future funding instruments for Orphanet were discussed with the European committee representatives. As of last year, several options were analysed and it was decided to prolong the Orphanet Europe Joint Action until December 2014, further funding still remains a pending issue at the European level.

2.2. Expansion of the consortium

Since its creation, the quality of the data has built a reputation and Orphanet has grown as a European consortium, gradually expanding into 35 neighbouring countries to the East and the South. In 2011, Orphanet went further west to include Canada. In 2012, the consortium expanded towards Australasia with the joining of Western Australia. In 2013, discussions went on with other countries but the lack of resources at a central level to support the coordination, training and quality control workload generated by new partners prevents the expansion of the network until an economic model is found.

2.3. List of partners and scope of their activity

2.3.1. Coordinating team

The coordination of the consortium is managed by the coordinating team, Orphanet France, located in Service Unit 14 of INSERM (the French National Institute of Health and Medical Research). INSERM has been the coordinator of the Orphanet consortium since 2001.

The coordinating team is responsible for the coordination of consortium activities, the hardware and software aspects of the project, the database of rare diseases and the production of the encyclopaedia, as well as the quality control of the directory of resources in the participating countries.

The coordinating team is also in charge of updating the database in regards to medicinal products in development, from the designation stage to their marketing authorisation and their availability in each country.

2.3.2. PARTNERS

The establishment of a Directory of Resources can only be achieved by the consolidation of data collected at the country level. The identification of expert resources requires a very good knowledge of the national research and health care institutions and their organisation. All national coordinators are located in high-profile institutions which can provide a suitable environment for the information scientists to work, in terms of documentation, secretarial facilities and access to the network.

The partners are responsible for collecting, validating and submitting data on clinical trials, medical laboratories, expert centres, research projects, registries and patient organisations.

Translations of the Orphanet content in the national language are also managed by the national teams when they have a sufficient budget. Currently Belgium, Germany, Italy, Spain and Portugal are undertaking the translation of the entire website's content into their national language, while the Polish, Finnish, Slovak and Greek teams are translating the encyclopaedia.

Management of the national website/entry point to the Orphanet portal is also carried out by every national team in their national language.

2.3.3. LIST OF ORPHANET PARTNER INSTITUTIONS

Armenia: Center of Medical genetics and Primary Health of Armenia
Austria: Gesundheit Österreich GmbH
Medical University of Vienna
Australia : Office of Population Health Genomics Department of Health, Government of Western Australia
Belgium: Federal Public Service Health, Food Chain Safety and Environment
Institute of Public Health, WIV-ISP
Bulgaria: Bulgarian Association for Promotion of Education and Science
Canada: CIHR Institute of Genetics
Czech Republic: 2nd Faculty of Medicine, Charles University in Prague
Croatia: Zagreb University
Cyprus: Archibishop Makarios II Hospital
Denmark: University Hospital of Aarhus
Estonia: University of Tartu
France: National Institute of Health and Medical Research
Germany: Hannover Medical School
Greece: Institute of Child Health Athens
Finland: The Family Federation of Finland (Väestöliitto) & Rinnekoti
Hungary: National Institute for Health Development
Ireland: National Centre for Medical Genetics
Israel: Meir Medical Center, Kfar Saba
Italy: Bambino Gesù Hospital, Rome
Lebanon: Saint Joseph Beirut University
Lithuania: Vilnius University Hospital, Centre for Medical Genetics
Latvia: Centre for Disease Prevention and Control

Luxembourg: Ministry of Health of Luxembourg
Morocco: Department of Medical Genetics, National Institute of Hygiene in Morocco
The Netherlands: University Hospital Leiden, Leiden University Medical Center
Norway: Department for Rehabilitation and RD, Norwegian Directorate of Health
Poland: The Children's Memorial Health Institute
Portugal: Institute of Molecular and Cell Biology, IBMC
Romania: Medical University of Pharmacy « Gregory T. Popa »
Serbia: Institute of Molecular Genetics and Genetic Engineering-Belgrade University
Sweden: Karolinska Institute
Slovenia: University Medical Centre Ljubljana
Slovakia: Children's University Hospital in Bratislava
Spain: Centre for Biomedical Network Research on Rare Diseases
                     Ministry of Health and Social Policy
Switzerland: CMU, Institute of Medical Genetics
Turkey: Department of Human and Medical Genetics, University of Istanbul
United Kingdom: The University of Manchester

Fig.1 The Orphanet consortium in 2013

3. Orphanet: products and services

Entries in the Orphanet diseases database correspond to rare diseases, rare forms of common diseases, or, in some particular cases, non-rare diseases considered to be orphan because their diagnosis or management remains particularly difficult or they are very often requested of Orphanet.

The updating of the scientific content of the database is based on a literature watch of international journals that helps to identify new syndromes, genes or treatments, update classifications of diseases, and is the basis for the production of various texts (encyclopaedia, recommendations ...). All texts are produced in collaboration with internationally recognised experts, learned societies and patient organisations.

All the teams that make up the Orphanet consortium are responsible for the collection, validation and submission of data on clinical trials, medical laboratories, expert centres, research projects, registries and patient organisations. To publish data which are relevant and accurate (complete, valid, consistent with other data from the database), a validation and quality control is performed by the coordinating team, and regular updates are performed with other country teams via an intranet.

Also, additional services and new collaborations are developed regularly to resolve the issue of information dispersion and to address specific needs of the different stakeholders.

3.1. The Orphanet website

The Orphanet website provides a user-friendly homepage with ergonomics that have been designed to provide easier access to the numerous services offered by Orphanet and to enhance usability, with specific emphasis on improving accessibility for visually impaired users. Indeed, the typeface is magnified and information is organised in easy-to-spot blocks that allow users to more readily navigate the site. The disease search function is in the center of the homepage, while the tabs for Orphanet's other principal resources are organised into a table of contents. The popular Orphanet Report Series, which address relevant rare disease and orphan drug topics, are highlighted in a specific area. Finally, OrphaNews, the newsletter produced jointly by Orphanet and by the European Union Committee of Experts on Rare diseases (EUCERD) joint action, is easily identified near the top right of the homepage.

To help users navigate the website, a list of our principal services is proposed on the "Help" page. Services are categorised to accommodate different user profiles.
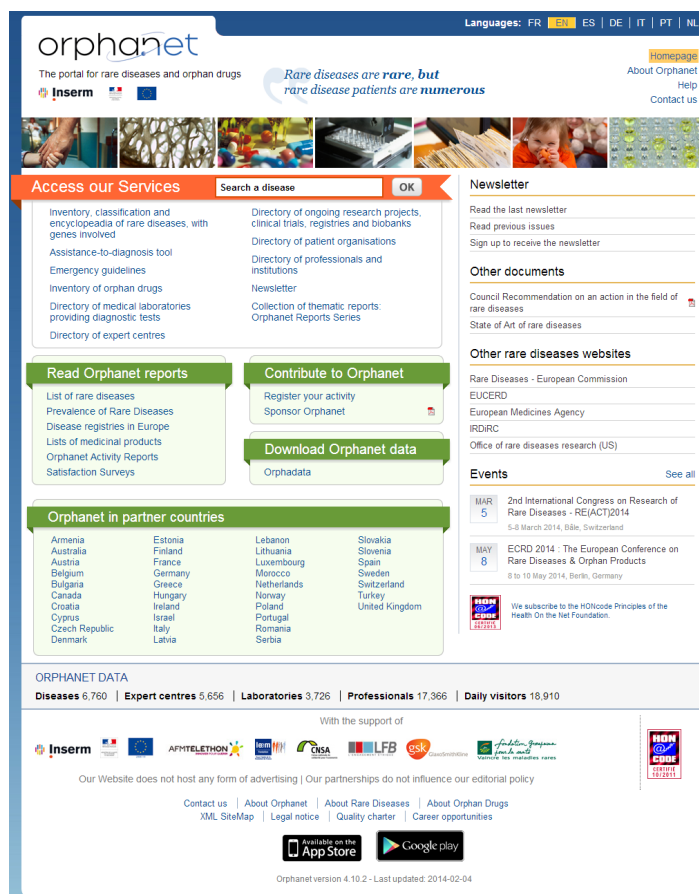

Fig.2 The Orphanet portal homepage in 2013

3.1.1. Indexation by search engines

According to Google, the prominence of the www.orpha.net site can be assessed by the number of results obtained by using the site name as a query, for which there are 3,130,000 responses.

Users mainly access the Orphanet website through search engines (83.6% of visits according to Google Analytics) and Google alone accounts for 95.1% of queries. Other sites generating traffic to Orphanet represent 8.6% of visits. The remaining visits are made via direct access (bookmarks, 7.8%).
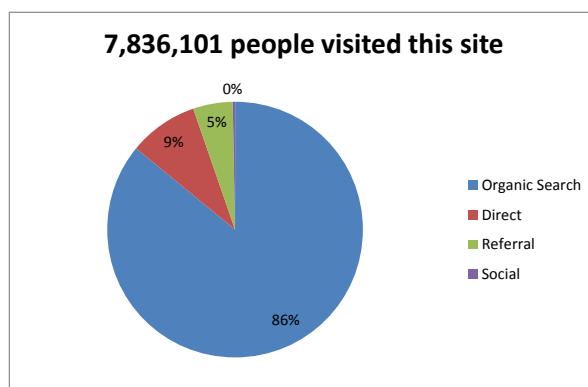

Fig. 3 Distribution of the traffic sources
(Source: Google Analytics, 1st of January 2013 to 31st of December 2013)

The wealth of information available on our site attracts a substantial number of visits due to a sizable corpus of keywords (rather than just certain predominant keywords). The keyword primarily used to access our site is simply "Orphanet" which represents 5.1% of visits. The indexation of our site is of the "long tail" type: more than 954,307 different keywords generate traffic to the site.

Since November 2009, Google Analytics allows users to trace visits made from mobile devices (smartphones, tablets). These visits represented 23% of all visits during 2013, i.e. 1,791, 223 visits. In 2012, it represented only 12% (525,769 visits).

3.1.2. THE WEBSITE'S AUDIENCE

In 2013, around 20 million pages were viewed, thus on average around 54,000 pages viewed per day. This figure has increased by 61% in comparison to 2012 (12.2 million page views in 2012).

The Google Analytics tool does not include direct access to PDF documents. However, PDF documents are an important entry point and generate a consistent volume of visits: each month, 850,000 PDF documents are consulted on the Orphanet website. This represents more than 10,000,000 downloads in 2013, which is approximately the same amount as in 2012.

The users come from 211 countries. The top ten countries are: France, Italy, United States, Germany, Spain, Mexico, Brazil, Canada, Belgium and Switzerland .
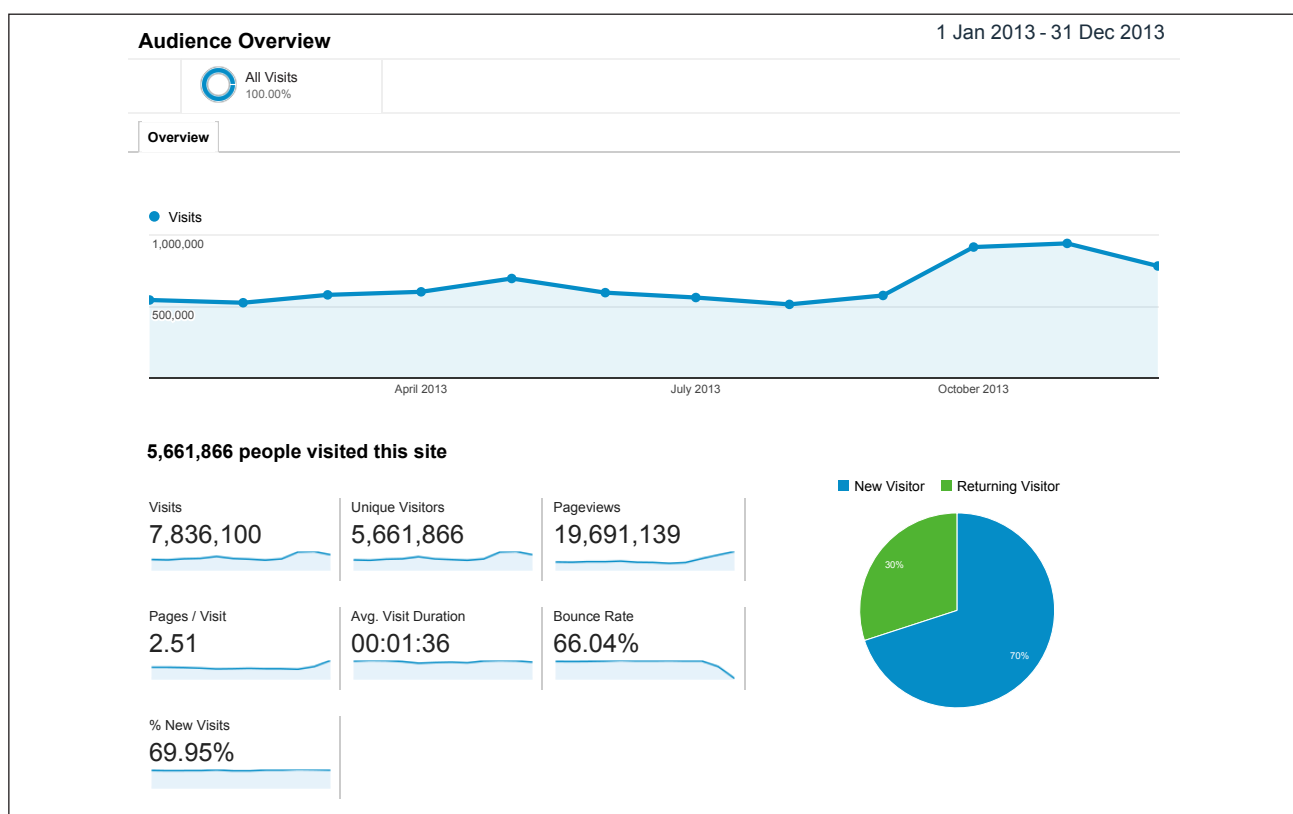
Fig.4 Orphanet website consultations in 2013

(Source: Google Analytics, 1st January 2013 to 31st December 2013)

3.1.3. ORPHANET NATIONAL WEBSITES

In order for Orphanet to become an instrument in national plans or strategies for rare diseases, the international portal in six languages has evolved towards customised websites by each country in their national language(s). National websites dedicated to each partner country enable them to have an entry point in their national language(s). The national pages include information on national events, news and access to policy documents concerning rare diseases and orphan drugs. Beyond the scope of national information, these pages provide access to the international database in seven languages.

As of 31 December 2013, 37 national websites are online. Some of these national websites are published completely in their national language while for other countries, the layout of the national webpage is in English and the mandatory texts (General Information) are in their respective national language.

The global increase in the number of visits, all websites together, reflects the increased awareness of the existence of these national entry points by the users.

3.1.4. ADDITIONAL FUNCTIONALITIES IN 2013

Release of the Orphanet mobile application

Orphanet released its mobile application; it is available on iPhone, iPad and Android. The Orphanet application is freely downloadable on the Apple store and the Google Play Store.

The main goal of this application is not to reproduce the Orphanet website, but to give access without any

Internet connection to services that could be helpful, in 6 languages of the Orphanet website (English, French, German, Italian, Portuguese and Spanish).

The application gives access to:

- The list of rare diseases (Their abstracts, identity card and other resources information). Search can be performed by the name of the disease, a synonym or the Orpha number.

- The expert centres (clinics) tab allows you to search an expert centre by disease name, by centre name or by professional. The advanced search options allow you to search by country: you can specify if you are looking for a centre of expertise performing genetic counseling or medical management, and for adults or for children. The location of the centre is tagged on a map, giving you the possibility to find the best itinerary from where you are to the centre.

- The emergency guidelines can be searched by disease name, synonym or Orpha number. The list displayed is the list of diseases having an emergency guideline in at least one of the 7 languages of the Orphanet website.

Orphanet in Dutch

In June 2013, Orphanet extended its reach by launching its Dutch version. The translation of the site was one of the measures recommended by the Belgian Fund of Rare Diseases and Orphan Drugs (in 2011). The Belgian Scientific Institute of Public Health receives funding from the National Institute for Health and Disability Insurance (INAMI-RIZIV) for the translation of the Orphanet portal into the Dutch language (structural webpages, the lists with medical terms and scientific abstracts). The Dutch and Belgian Orphanet teams are working collaboratively to validate the translations. Not only does this provide additional endorsement, it also ensures that certain Dutch synonyms relevant for the Netherlands (but not for Belgium) are included in the database.

3.2. The Orphanet servers

From 2007 to 2012, the servers needed to run all the services that Orphanet offers were hosted by the DSI (Department of Information Systems) of INSERM. Growing demand (more than one million pages per month are viewed on the site www.orpha.net), along with the need to develop new services in an appropriate technical architecture, led to a complete re-organisation and the purchase of new software licences and more powerful servers.

The production servers were re-located to the largest civil data centre in France, the CINES (Centre Informatique National de l'Enseignement Supérieur). To ensure structural security, the development servers are located in an INSERM building close to the CINES and linked to it by a fiber optic connection. This allows an excellent connectivity between production servers, development servers and backup environments.

Many production environments are in place: back office, pre-production, preservation and development environments. This makes the Activity Recovery Plan (PRA) of the Orphanet website highly efficient.

Migration operations took place between March 2012 and September 2012. The migration of services happened without any interruption of access to the Orphanet website, with less than a week of inconvenience for all other services. We also secured the access to back-office tools used by the coordinating team in France and other teams internationally. To do this we set up VPN (Virtual Private Network) servers and deployed VPN clients to the teams in the 37 countries.

The year 2013 was achieved without any major trouble and with a high availability of the www.orpha.net website despite an increasing amount of visitors, especially in the last three months.
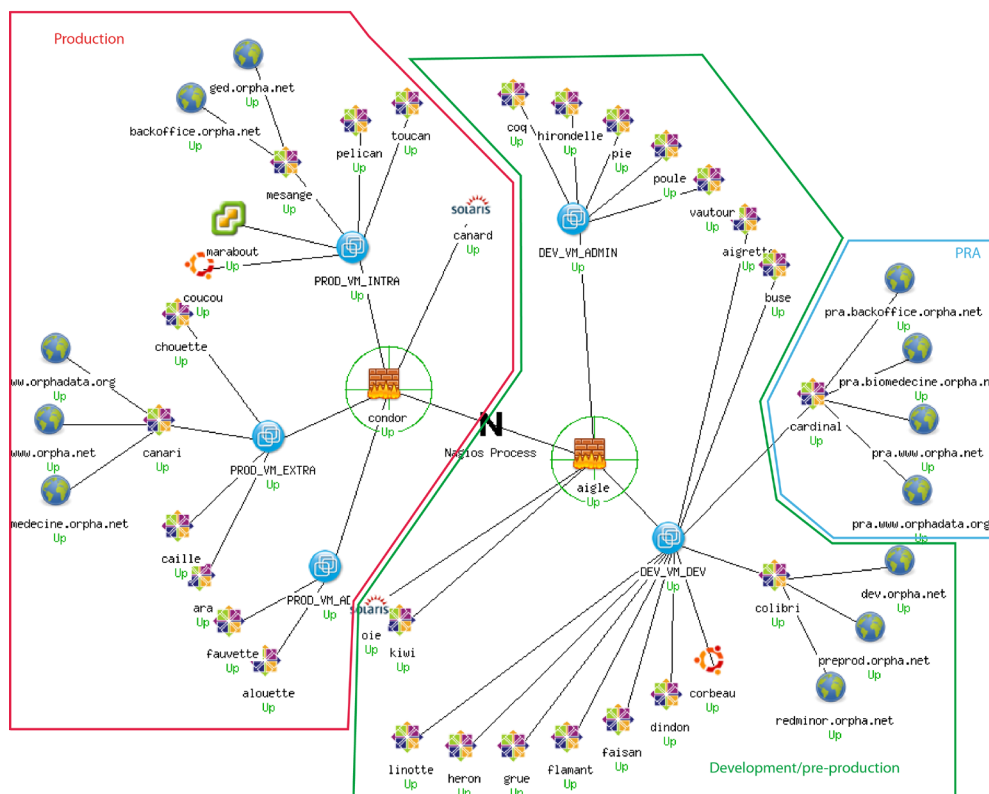
Fig. 5 The Orphanet IT architecture as of 2013

3.3. Orphanet inventory of rare diseases

Orphanet provides a comprehensive inventory of rare diseases classified according to a polyhierarchic classification system of rare diseases. As new scientific knowledge issues arise, the Orphanet RD inventory and classification system is maintained with regular addition/update of diseases employing two non-exclusive sources: documented sources and/or expert advice. The disease database contains 9,264 diseases or groups of diseases and their synonyms as of 2013. This extensive and evolutionary system consists of classifications organised according to the medical and/or surgical speciality that manages specific aspects of each rare disease within a healthcare system. The diseases have been classified within each speciality according to clinical criteria or etiological criteria when diagnostically or therapeutically relevant. The Orphanet classification provides the scope and level of granularity needed by health professionals and can be viewed directly on the website and/or extracted from Orphadata in XML format (www.orphadata.org/cgi-bin/inc/product3.inc.php).

3.3.1. INDEXATION OF RARE DISEASES

Rare diseases are indexed with ICD-10 codes. Indexation with ICD10 codes follows a set of rules depending on if rare diseases are mentioned or not in the tabular list or in the index of ICD10. Rules for attribution of an ICD10 code for diseases that are not listed in the ICD are established.
Indexation by clinical signs uses an in-house thesaurus of phenotypic terms and is carried out with the aim of supplementing the Orphanet assistance-to-diagnosis tool. For each phenotypic term associated with a rare disease, the frequency of its occurrence (very frequent, frequent and occasional) is annotated.
Disease 'identity cards' have been improved with additional cross referencing and epidemiological data. Diseases are linked to one or more OMIM (Online Mendelian Inheritance in Man) numbers and to the list of indexed publications in scientific journals via a specific PubMed query, resulting from mapping Orphanet terms with MeSH descriptors.

Exact mappings between the Orpha nomenclature and other terminologies (Unified Medical Language System (UMLS), MeSH, MedDRA and SNOMED CT) are now available online and downloadable at Orphadata (http://www. orphadata.org/cgi-bin/inc/product1.inc.php). Mappings are done in a semi-automatic way and are manually curated. Updates follow every UMLS release.

3.3.2. ORPHANET RARE DISEASES ONTOLOGY

In January 2014 the Orphanet Rare Disease ontology (ORDO) was released on three websites:

http://bioportal.bioontology.org/ontologies/ORDO

http://www.ebi.ac.uk/ontology-lookup/?termId=Orphanet:98724

http://www.orphadata.org/cgi-bin/inc/ordo_orphanet.inc.php

ORDO was jointly developed in 2013 by Orphanet and the EBI to provide a structured vocabulary for rare diseases capturing relationships between diseases, genes and other relevant features which will form a useful resource for the computational analysis of rare diseases. It is derived from the Orphanet database. It integrates a nosology (classification of rare diseases), relationships (gene-disease relations, epidemiological data) and connections with other terminologies (MeSH, SNOMED CT, UMLS, MedDRA), databases (OMIM, UniProtKB, HGNC, ensembl, Reactome, IUPHAR, Genatlas) or classifications (ICD10). The ontology will be maintained by Orphanet and further populated with new data. Orphanet classifications can be browsed in the OLS view. The Orphanet Rare Disease Ontology is updated monthly and follows the OBO guidelines on deprecation of terms. It constitutes the official ontology of rare diseases produced and maintained by Orphanet (INSERM, US14).

3.4. Orphanet inventory of genes

Genes involved in rare diseases (pathogenic and susceptibility genes) are entered in the database and updated regularly according to new scientific publications. Genes are associated with one or more diseases, to one or more genetic tests, mutation registries and/or research projects in the database. The registered data include: the main name and symbol of the gene (from HGNC), its synonyms, and its HGNC, UniProtKB, Genatlas and OMIM references (in order to cross-reference these websites). Moreover, genes are now cross-referenced with Ensembl (an EBI database that maintains automatic annotation on selected eukaryotic genomes), Reactome (an EBI open-source, open access, manually curated and peer-reviewed pathway database) and IUPHAR (The International Union of Basic and Clinical Pharmacology). The relationship between a gene and a disease is qualified according to the role that the gene plays in the pathogenesis of a disease. Genes are annotated as causative, modifiers (both from germline or somatic mutations), major susceptibility factors or playing a role in the phenotype (for chromosomal anomalies). Candidate genes are also included but only when they are tested for in a clinical setting. These annotations represent a unique, added-value service for researchers.

Epidemiology:
- 4,545 diseases indexed with prevalence data
- 4,401 diseases indexed with mode of inheritance
- 4,404 diseases indexed with age of onset

Mappings and cross referencing :
6,283 diseases indexed with ICD10
4,053 diseases indexed with OMIM
2,132 diseases indexed with UMLS
953 diseases indexed with MedRA
1,673 diseases indexed with SNOMED CT
1,741 diseases indexed with MeSH

The inventory of genes contains:
3,184 genes linked to 3178 diseases, including:
3,084 genes interfaced with UniProt KB
3,101 genes interfaced with OMIM
3,099 genes interfaced with Genatlas
3,154 genes interfaced avec HGNC

2,323 diseases **indexed with Pubmed**

5183 **external links** for 2,983 diseases

2,773 diseases indexed with **clinical signs**

The Orphanet encyclopaedia contains:
- 304 summaries in Dutch
- 4574 summaries in English
- 4060 summaries in French
- 3736 summaries in German
- 4092 summaries in Italian
- 1085 summaries in Portuguese
- 3478 summaries in Spanish
- 293 summaries in Finnish
- 40 in Greek –new!-
- 331 in Polish
- 103 in Slovak –new!-

131 articles for the general public in French and 151 emergency guidelines in French, German, English, Spanish, Italian, Portuguese, and Polish.

Link to external RD literature
22 Reviews articles
560 Clinical genetics reviews
254 Best practice guidelines
100 Guidance for genetic testing
33 General public articles
22 Emergency guidelines
3,154 genes interfaced avec HGNC

Orphanet screen content

orphanet

The portal for rare diseases and orphan drugs

Inserm

Languages: FR | EN | ES | DE | IT | PT | NL

Homepage
Help
Contact us

Rare diseases are rare, but rare disease patients are numerous

Rare diseases | Orphan drugs | Expert centres | Diagnostic tests | Research and trials | Patient organisations | Professionals and institutions | Other information

Search | Search by sign | Classifications | Genes | Encyclopaedia for patients | Encyclopaedia for professionals | Emergency guidelines

Homepage » Rare diseases » Search

SIMPLE SEARCH → OK

:: Amyotrophic lateral sclerosis

Orpha number	:	ORPHA803	ICD-10	: G12.2
Synonym(s)	:	ALS Charcot disease Lou Gehrig disease	OMIM	: 105400 205250 300857 606640 608030 608031
Prevalence	:	1-9 / 100 000		
Inheritance	:	Sporadic Autosomal recessive Autosomal dominant		
Age of onset	:	Adulthood	UMLS MeSH MedRA SNOMED CT	

SUMMARY

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by progressive muscular paralysis reflecting degeneration of motor neurons in spinal tracts, brainstem and spinal cord.

Fig. 6 The disease database content as of 31 December 2013

3.5. Orphanet encyclopaedia

Two distinct encyclopaedias are provided on the Orphanet website: one for health professionals and one for the general public.

3.5.1. HEALTH PROFESSIONALS ENCYCLOPAEDIA

- **Summary information**

The Orphanet abstracts are unique, originally written in English by a member of the Paris-based editorial team and reviewed by an invited expert. Additional information on the diseases (i.e. annotations on epidemiological data, clinical signs, functional consequences of the disease, genes, etc.) is requested from the expert if not already documented in the database, or validation of the existing data is requested. Abstracts are structured in sections according to the Definition of the disease – Epidemiology – Clinical description – Aetiology – Diagnostic methods – Differential diagnosis – Antenatal diagnosis (if relevant) – Genetic counselling (if relevant) – Management and treatment – Prognosis. As of December 2013, 4574 abstracts are available online. They are systematically translated into the six other languages (French, Italian, Spanish, German, Portuguese and Dutch). In addition, as of 31 December 2013, 293 abstracts are available in Finnish, 331 in Polish, 103 in Slovak and 40 in Greek.

- **Practical genetics articles**

These articles are co-produced by Orphanet and the European Journal of Human Genetics (EJHG), the official journal of the European Society of Human Genetics. Freely-accessible articles are published in the EJHG (Nature Publishing Group) and accessible from Orphanet.

- **Orphanet Emergency Guidelines**

These guidelines are intended for pre-hospital emergency health care professionals (a dedicated section is included for their use) and for hospital emergency departments. These practical guidelines are produced in collaboration with French reference centres and patient organisations, and are peer-reviewed by emergency health care physicians from learned societies: 56 emergency guidelines in French are now online. They are being translated into six languages (English, German, Italian, Portuguese, Spanish and Polish). Currently, 22 emergency guidelines are available in English, 22 in Spanish, 25 in Italian, 18 in Portuguese, 7 in Polish and one in German. There are 32 new guidelines since 2012.
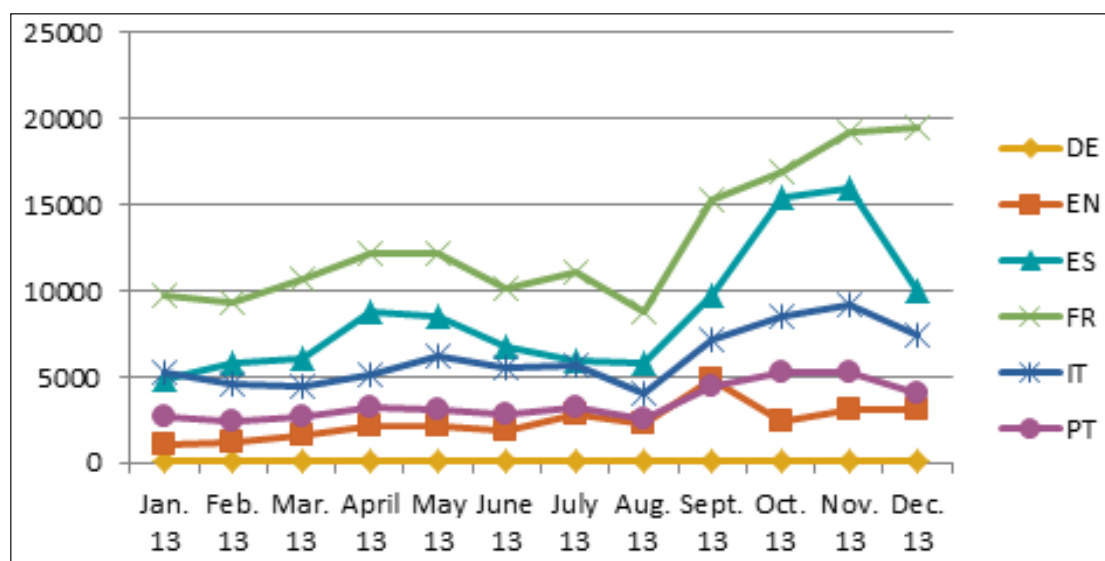

Fig. 7 Consultations of the emergency guidelines by language in 2013

Emergency guidelines were viewed around 340,000 times in 2013, versus 200,000 in 2012, representing an increase of 70% in one year. This global increase reflects the expansion of the collection into the different languages.
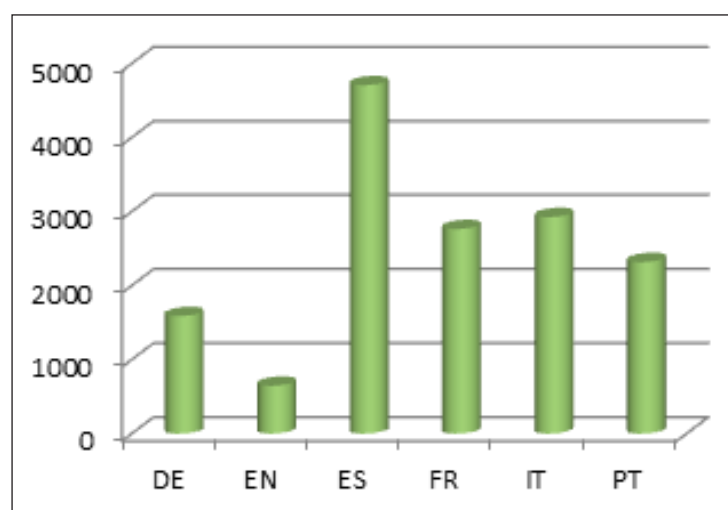

Language	Number of guidelines
German	1
English	22
Spanish	22
French	56
Italian	25
Portuguese	18

Table 1. Available emergency guidelines per language in 2013

Fig. 8 Number of views of the Emergency guidelines by language

The ratio of the number of consultations for each language to the number of guidelines shows that this collection is a success in several languages such as French, Italian, Spanish and Portuguese. Despite the fact that there is only one guideline in German, it is highly consulted. On the other hand, the disappointing number of consultations in English can be explained by the existence of a larger number of equivalent documents elsewhere in this language which are produced by learned societies. To avoid dissipation of time and work, both of which are precious to the rare disease community, Orphanet has established collaborations with these learned societies to provide links to these already existing and valuable resources (please refer to paragraph 3.5.4).

3.5.2. GENERAL PUBLIC ENCYCLOPAEDIA

The general public encyclopaedia was initially a French project intended to give complete, honest, and up-to-date information to patients and their relatives on the diseases that concern them. Starting from 2011, the general public encyclopaedia texts have been enriched with paragraphs on functional consequences of rare diseases including: disabilities resulting from the disease, medical and social measures to prevent/limit them and consequences of disabilities in daily life.
As of 31 December 2013, 131 in-house French texts are available online. Documents from this encyclopaedia are downloaded more than 360,000 times per month, which corresponds to more than 4.3 million downloads in 2013.
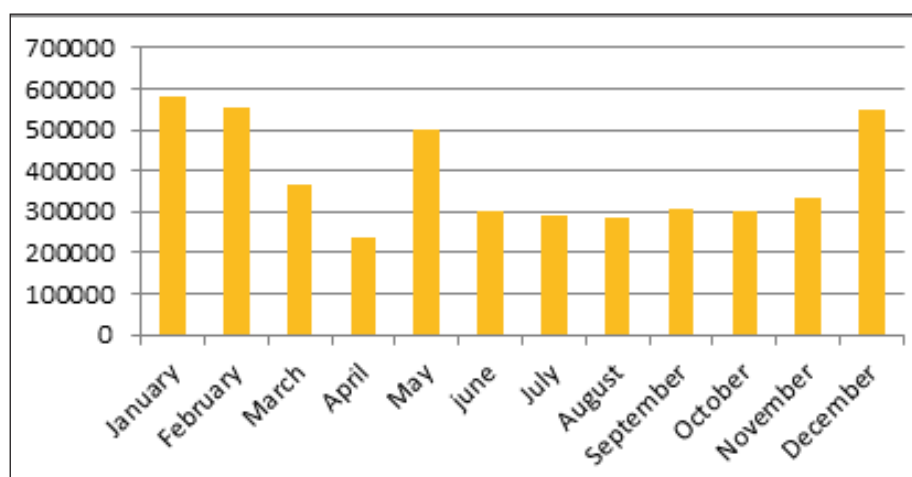
Fig. 9 Total number of downloaded Orphanet general public encyclopaedia texts in 2013

3.5.3. ADDITIONAL PRODUCTS IN 2013

Disability factsheets

As part of the collaboration between CNSA (French National Solidarity Fund for Autonomy) and INSERM, Orphanet now provides a new collection of texts named "disability factsheets" in the Orphanet Encyclopaedia of Disability devoted to the disabilities associated with each rare disease. This new collection is addressed to the professionals in the field of disability as well as to the patients and their families. These texts have been elaborated in order to better understand and to assess the needs of people with disabilities associated with a rare disease and to promote guidance and appropriate support in the national health care system as well as in the care and social support system.

Each card contains a description of the disease (adapted from the corresponding text from the Orphanet encyclopaedia for professionals) and a focus on disability-related measures and consequences in everyday life (taken from the corresponding text of the Orphanet general public encyclopedia).

These texts are available on the Orphanet website via the link «Disability factsheet» at the bottom of the page describing the disease as well as from the tabs «Encyclopedia for professionals» and «Encyclopaedia for general public.» Thirteen of these cards are available online since November 2013.

3.5.4. LINKS TO EXTERNAL RARE DISEASES LITERATURE

With the purpose of expanding the number of articles available online and to disseminate articles matching Orphanet's quality criteria, the editorial team is also in charge of identifying articles suitable for publication on the website produced by other journals or learned societies. Authorisations from the copyright holder are requested so as to give access to the full text.

We can distinguish six distinct externally produced texts accessible from the Orphanet website:

- **Review articles**

Review articles of good quality published in peer-reviewed journals can be linked to a disease and published on the Orphanet website with the permission of the copyright holder. As of 31 December 2013, 59 review articles (excluding those published in the Orphanet Journal of Rare Diseases) were available on the website.

- **Clinical Genetics Review**

These are peer-reviewed disease descriptions focused on genetic aspects with an implication in the diagnosis, management, and genetic counselling of patients and families with specific inherited conditions.
These review articles can be linked to a disease and displayed on the Orphanet website with the permission of their copyright owners. As of 31 December 2013, the clinical genetic review collection comprised 600 articles from GeneReviews, of which 53 were published in 2013.

- **Best practice guidelines**

These guidelines are recommendations for the management of patients, issued by official organisations. There are two kinds of best practice guidelines: anaesthesia guidelines and clinical practice guidelines. They are both produced by learned societies and published either in scientific journals or on learned society or health agency websites. A methodology of assessment has been developed to review the guidelines and link only the most accurate ones. These guidelines can be linked to a disease and displayed on the Orphanet website with the permission of their copyright owners. As of 31 December 2013, 255 best practice guidelines were available on the website, of which 143 were published in 2013.

- **Guidance for genetic testing**

This collection comprises summary recommendations intended to disseminate best practice in genetics testing. They include Gene Cards (published in the European Journal of Human Genetics) and charts from the APGNM (Association nationale des praticiens en génétique médicale). As of 31 December 2013, 100 recommendations were available on the website.

- **Articles for general public**

Publication of general public-intended texts, externally produced by expert centres or patient organisations (produced in compliance with a reliable methodology), in all other languages are now selected and, if permission is granted, the texts are loaded on the Orphanet website.
33 articles are available on the website and 5 of those have been published in 2013.

- **Emergency guidelines**

Orphanet has established a collaboration with The British Inherited Metabolic Disease Group (BIMDG) to provide links to the emergency guidelines they produce. Currently 22 external emergency guidelines are available in English.

3.6. Orphanet directory of expert resources

Orphanet provides a directory of:
- Centres of expertise
- Medical laboratories
- Patient organisations
- Clinical trials
- Patient registries
- Mutation registries
- Biobanks
- Ongoing research projects

Data is collected either from national official sources, or proactively from non-official sources by information scientists in each country. Data follows a validation process before publication, and is quality controlled. The aim of this multi-step process is to generate high-quality, accurate and robust data: complete, valid, consistent,

unique, and uniform with other data of the database.

For data coming from official sources, no pre-release validation is required. When issued from non-official sources, data is submitted to a pre-release validation process that is defined by each country following rules established at the national level and eventually with health authorities, to ensure data relevance for the rare disease community. A second round of validation is performed at the Orphanet coordination level on a monthly basis against the criteria of relevance for rare diseases, coherence with data from other countries and proper indexing with disease classification systems. A third round of quality control is carried out on online published data following a process defined at national level (i.e. annual revision by the Scientific Advisory Board, or by competent authorities).

Regularly, published data is verified and updated (at least once a year).

The 37 countries in which Orphanet collects data are the following:

Armenia, Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lebanon, Lithuania, Luxembourg, Morocco, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tunisia, Turkey, the United Kingdom and Western Australia.

Data collection and/or updates are managed either by the teams at country level when they have sufficient funding for a dedicated professional, or by the coordinating team on behalf of the Orphanet national team.

In 2013, countries managing both data collection and updates at a country level are: Austria, Belgium, Canada-Quebec, Croatia, Czech Republic, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Lithuania, Latvia, Morocco, the Netherlands, Poland, Portugal, Spain, Slovakia, Sweden, Switzerland and the United Kingdom.

The directory of expert resources in 37 countries worldwide contains the following data:
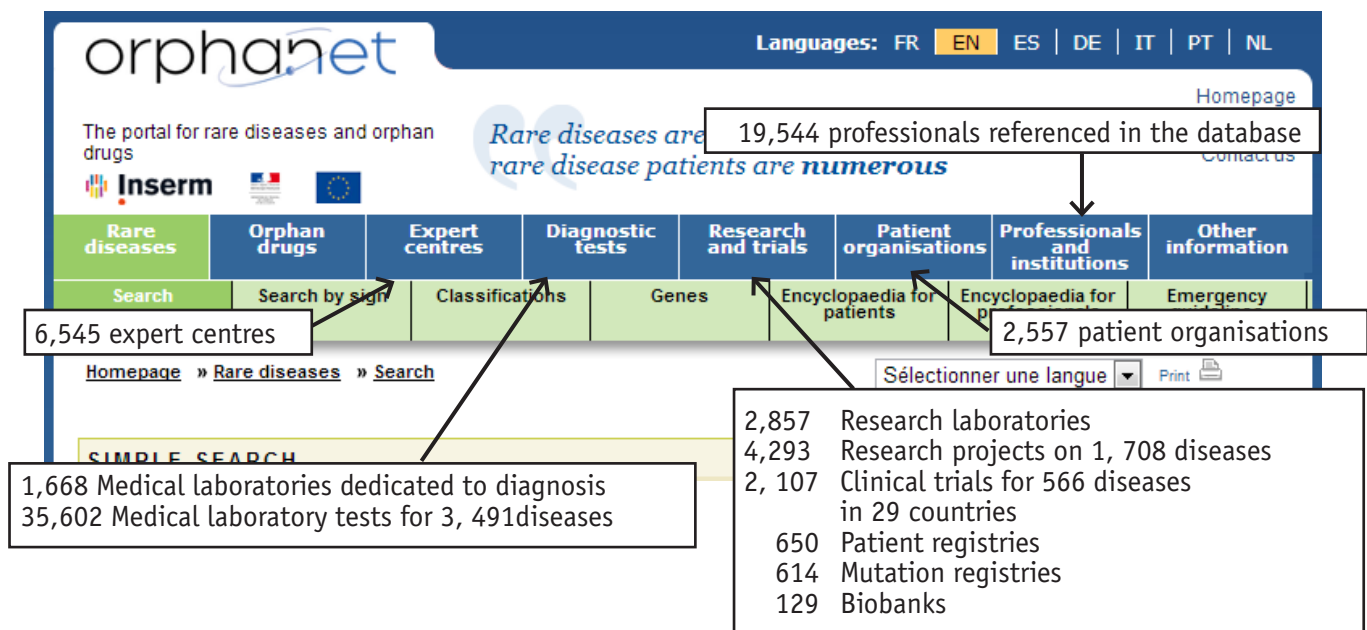

Fig.10 2013 Directory of expert resources in 37 countries

3.6.1. ADDITIONAL FUNCTIONALITIES IN 2013

In December 2013, Orphanet released a web-based registration tool for professionals to register/update their activities related to rare diseases.

A personal workspace allows them to check and update their activities already registered with us and also to declare any new activities related to rare diseases.

3.6.2. DATA QUALITY VALIDATION OF MEDICAL LABORATORIES

Medical laboratories listed in Orphanet are those offering tests for the diagnosis of a rare disease or a group of rare diseases, and those performing genetic testing whatever the prevalence of the disease. These medical laboratories must be accredited and this involves a procedure by which an authoritative body gives formal recognition that a body or person is competent to carry out a specific task (ISO 9000, 2000 Quality management systems – fundamentals and vocabulary). Information on accreditation of medical laboratories is reviewed by Eurogentest and experts in the field.

Moreover, medical laboratories can undergo an external quality assessment (EQA) whereby a set of reagents and techniques are assessed by an external source and the results of the testing laboratory are compared with those of an approved reference laboratory (WHO). This allows a laboratory to compare its performance for an individual test or technique against that of other laboratories.

Information on EQA participation is provided annually by CF Network, CEQA, EMQN and UKNEQAS cytogenetics with the consent of the concerned laboratories. For other EQA providers, information is validated, by Orphanet upon reception of an EQA participation certificate; otherwise the information provided on the Orphanet website is deemed 'not validated' and associated with a [!] sign.

3.7. Orphanet directory of Orphan Drugs

The list of Orphan Drugs includes all those substances that have been granted an orphan designation for a disease considered as rare in Europe, whether they were further developed to become drugs with marketing authorisation (MA) or not. The Orphanet database also includes drugs without an orphan designation as long as they have been granted a marketing authorisation issued by the European Medicines Agency (EMA - centralised procedure) with a specific indication for a rare disease. Some drugs (substance and/or trade name) are included in the database because they are tested in a clinical trial performed on a rare disease, but they do not have a regulatory status.
Drugs with a regulatory status in Europe are collected from reports issued by the two Committees of the EMA: the COMP (Committee for Orphan Medicinal Products) and the CHMP (Committee for Medicinal Products for Human use).
Orphan drugs are published on the Orphanet website, under the Orphan drugs tab and data is also released within an Orphanet Report Series that is issued every three months.

The database of orphan drugs and substances contains the following data:
- For EUROPE

    - 766 substances linked to 974 orphan designations (regarding 393 diseases).
    - 156 European marketing authorisations (of which 68 already had an orphan designation and 88 had no previous orphan designation) (regarding 182 diseases).
- For USA

    - 386 substances linked to 445 orphan designations (regarding 306 diseases)
    - 163 USA marketing authorisations after orphan designation (regarding 157 diseases).

3.8. Orphadata

Since Orphanet is increasingly well-known as the reference source for documentation on rare diseases, a growing number of requests for its high quality data are received. To meet the needs of massive data extraction, orphadata.org was created (www.orphadata.org). Orphadata is intended to contribute to accelerating R&D and to facilitate global adoption of the Orphanet nomenclature.

On this website, the whole Orphanet dataset has been directly accessible in a reusable format since June 2011. Orphadata was developed within the context of the Rare Diseases Portal project funded by DG Research and Innovation (RTD) and the Orphanet Europe Joint Action contract funded by DG Sanco. The dataset is a partial extraction of the data stored in Orphanet and is updated monthly. Freely accessible in six languages (English, French, German, Italian, Portuguese and Spanish) the Orphadata dataset encompasses:

Products freely accessible on Orphadata:

  1. Diseases and cross-referencing
  2. Epidemiological data
  3. Orphanet classifications
  4. Diseases with their clinical signs
  5. Thesaurus of clinical signs
  6. Diseases with their associated genes
  7. Orphanet Rare Disease Ontology

Products accessible on Orphadata after signature of a Data Transfer Agreement
  1. Textual information
  2. Patient organisations
  3. Expert clinics
  4. Clinical laboratories
  5. Orphan drugs
  6. Research activities
Data is available either freely (Academia) or for a fee (Industry).

Orphadata provides a guide for users that defines and describes the elements of the dataset.

Since January 2013, Orphadata products were downloaded more than 118,000 times, with an average of 9,880 times per month.
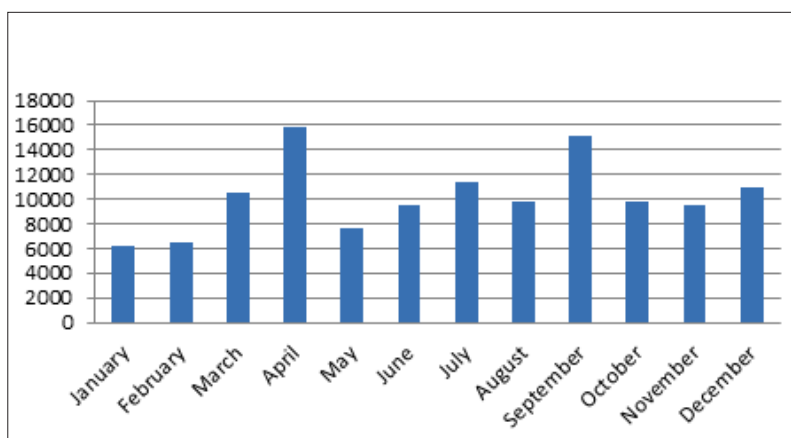
Fig.11 Total number of downloaded products from the Orphadata website in 2013

The most requested Orphadata product is the inventory of diseases with clinical signs.
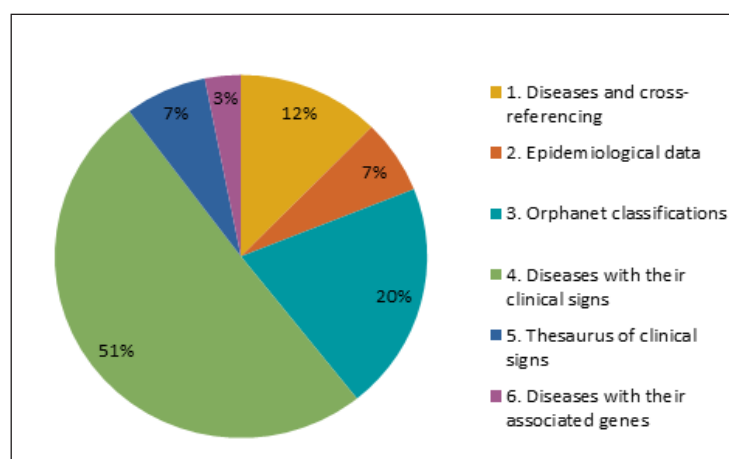
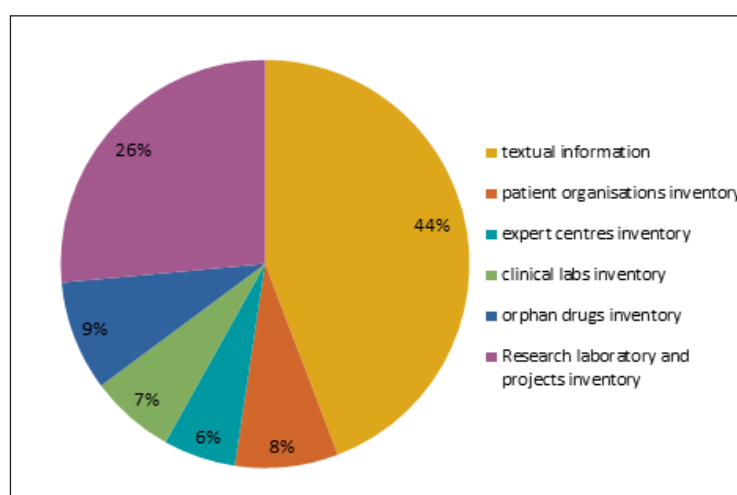**Fig.12 Distribution of downloads of the freely available datasets**

- 12% — 1. Diseases and cross-referencing
- 7% — 2. Epidemiological data
- 20% — 3. Orphanet classifications
- 51% — 4. Diseases with their clinical signs
- 7% — 5. Thesaurus of clinical signs
- 3% — 6. Diseases with their associated genes

Fig.13 Distribution of downloads of the datasets requiring a Data Transfer Agreement

- 44% — textual information
- 8% — patient organisations inventory
- 6% — expert centres inventory
- 7% — clinical labs inventory
- 9% — orphan drugs inventory
- 26% — Research laboratory and projects inventory

3.9. Orphanet Report Series (ORS)

Orphanet reports are a series of texts providing aggregated data covering topics relevant to all rare diseases. New reports are regularly put online and are periodically updated. These texts are published as PDF documents accessible from the homepage and from every other page of the website.

New versions of these publications are advertised in OrphaNews.

The Orphanet Report Series are heavily downloaded: in 2013, more than 1,675,000 Orphanet Report Series were consulted. This represents an increase of 100% compared to 2012 (approximately 800,000 downloads).

	English	French	German	Italian	Portuguese	Spanish	Total
List of rare diseases	341,750	362,684	Translation ongoing	436	Translation ongoing	274	705,144
Prevalence or reported number of published cases listed in alphabetical order of disease	86,355	29,277	12,172	14,066	13,433	17,468	172,771
Diseases listed by decreasing prevalence or number of published cases	25,893	24,306	6,100	10,849	16,137	19,268	102,553
Patient Registries in Europe	52,926		-	-	-	-	52,926
Lists of orphan drugs in Europe	118,329	33,161	7,888	19,636	3,122	17,384	199,520
Activity report 2012	139,984	13,965	-	3,555	-	6,970	164,474
Total	766,079	463,393	26,160	44,987	36,247	61,364	1,398,230

Table 2. Number of downloads of selected Orphanet Report Series in 2013 by language

Comparison of the number of downloads of the Orphanet Report Series translated in all 6 languages shows that this collection is most heavily downloaded in English and French.
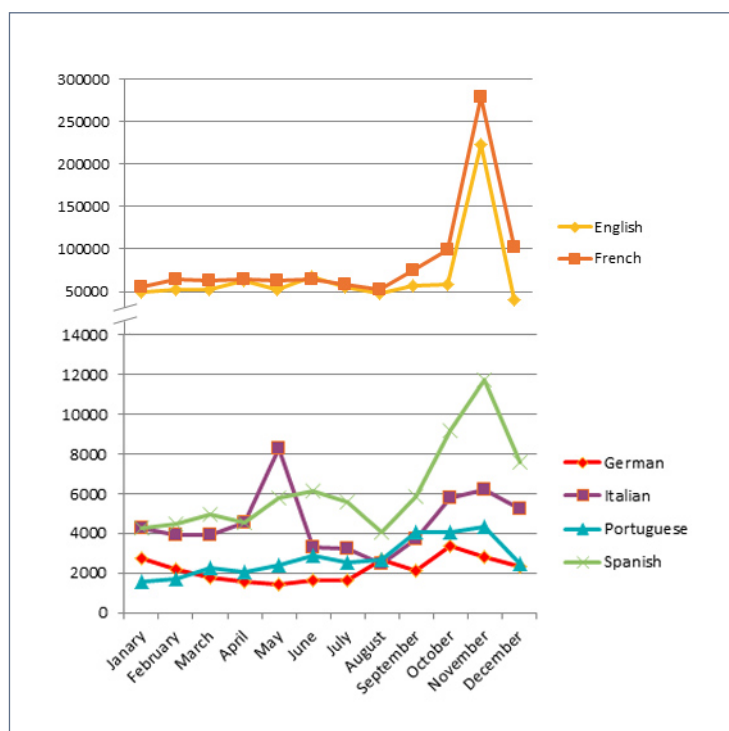
Fig. 14 Number of downloads of the Orphanet Report Series translated in all Orphanet languages

3.9.1. ADDITIONAL REPORTS IN 2013

In 2013, two new reports issued:

- The list of rare diseases in alphabetical order with their associated Orpha number for more effective communication but also for easy retrieval of the Orphacode by clinicians and coders. This was also the most successful ORS in the collection with 705,000 downloads in 2013 in French and English. It will be translated in the other Orphanet languages in 2014.

- The List of Research Infrastructures useful to Rare Diseases in Europe by country, in English.

3.10.   The Orphanet Newsletter

A literature review is performed twice a month in order to update the database and to collect news to report in OrphaNews, a bi-monthly electronic newsletter, to which the subscription is free. OrphaNews presents an overview of scientific and political news about rare diseases and orphan drugs. It is the communication tool of the Rare Disease community and is produced jointly by Orphanet and the EUCERD Joint Action.

OrphaNews in English has more than 14,700 subscribers. Orphanews in French has more than 8,800 subscribers and OrphaNews in Italian has more than 4,000 subscribers.

Fig. 15 2013 Orphanews homepage

3.11.   Orphanet Journal of Rare Diseases (OJRD)

Orphanet Journal of Rare Diseases is an open access, online journal that encompasses all aspects of rare diseases and orphan drugs. The journal publishes high quality reviews on specific rare diseases. In addition, the journal may consider articles on clinical trial outcome reports, either positive or negative, and articles on public health issues in the field of rare diseases and orphan drugs. OJRD was indexed in Medline at the end of its first year of existence (2006) and was selected by Thompson Scientific after only two years in publication. Its current impact factor is 4.32. In 2013, 427 publications were submitted to the journal. Of these, 199 were accepted for publication.

4. Users

4.1. Types of users and use

2013 Orphanet user satisfaction
An online survey was carried out for two weeks in late 2013 (from 21 November to 5 December). The satisfaction of the portal users was assessed by asking them to respond to a short online questionnaire.
The following results present the responses collected in all languages (Dutch, English, French, German, Italian, Portuguese and Spanish).

QUESTION 1

BY WHAT CAPACITY ARE YOU CONSULTING THE ORPHANET WEBSITE **TODAY?** PLEASE SELECT A CATEGORY.

This question aimed to determine the profile of Orphanet's users.
Seven categories were proposed (i.e. health professional, patient/entourage/patient organisation, researcher, industrial, health care manager/policy maker, Education/communication and student), and a free text field was included for other types of users to enter their profession. Only one response was possible.

Answer Options	Response Percent	Response Count
Health professional	47%	1238
Patient/entourage/ patient organisation	22%	871
Research	9%	140
Industry	1%	35
Health care manager/policy maker	2%	41
Education/communication	2%	54
Student	15%	316
Other	3%	127
Answered Question		2822
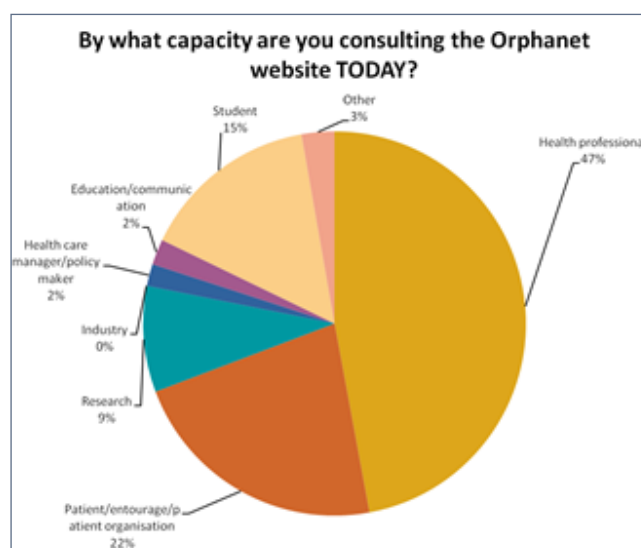
Table 3. Distribution of the 2013 user survey respondents amongst the proposed categories

The largest category of respondents was the health professionals category (47%). The second largest category of respondents was patients and their entourage (including patient organisations, alliances and support groups) with 22% of responses.

Then, for each category, respondents were asked to choose the sub-category that would best describe them.

Health professionals (n=1230):

Answer Options	Response Percent	Response Count
Hospital specialist	37%	460
General practioner	10%	125
Independent specialist	9%	116
Expert in rare diseases	3%	34
Public health services	4%	50
Health service / health insurance	3%	33
Hospital pharmacist	1%	13
Independent pharmacist	1%	15
Biologist with expertise in rare diseases	3%	40
Biologist without expertise in rare diseases	2%	27
Nurse	4%	50
Other healthcare professional (other than nurse)	6%	69
Genetic counsellor	4%	44
Other	13%	154

Table 4. Distribution of the 2013 user survey respondents amongst the health professionalsub-category

Patient/entourage (n= 863):

Answer options	Response percent	Response count
Patient	49%	421
Mother/father/child of a patient	28%	241
Other family member	11%	93
Friend of a patient	6%	54
Member of a patient organisation	2%	15
Patient organisation administration	2%	18
Other	2%	21

Table 5. Distribution of the 2013 user survey respondents amongst the patient/entourage sub-category

Research (n= 133):

Answer options	Response percent	Response count
Academic/clinical researcher	27%	36
Academic/basic researcher	32%	43
Industry researcher	10%	13
Bioinformatician	7%	9
Health economist	3%	4
Social sciences	5%	7
Other	16%	21

Table 6. Distribution of 2013 user survey respondents amongst the research sub-category

The 'Social sciences' category gathers 5% of researchers, underlining the emergence of this domain in the rare diseases field.

Industry (n=36):

Answer options	Response percent	Response count
Biotechnology and pharmaceutical	85%	29
Private health insurance		0
Consultant for Industry	15%	5
Investor / business developer		0
Other		0

Table 7. Distribution of the 2013 user survey respondents amongst the industry sub-category

Health care manager/policy maker (n=41):

Answer options	Response percent	Response count
Governmental administration	41%	17
Hospital administration	37%	15
European administration	0%	0
Other	22%	9

Table 8. Distribution of the 2013 user survey respondents amongst the healthcare manager/policy maker sub-category

Education/communication (n=54):

Answer options	Response percent	Response count
Journalist	7%	4
Librarian	4%	2
Webmaster	2%	1
Teacher (primary/secondary education)	18%	10
Teacher (higher education)	26%	14
Other	43%	23

Table 9. Distribution of the 2013 user survey respondents amongst the education/communication sub-category

Students (n=313):

Answer options	Response percent	Response count
Medical student	74%	231
Other student	26%	82

Table 10. Distribution of the 2013 user survey respondents amongst the student sub-category

Other students are mainly biology students, but also biotechnology, bioinformatics, pharmacy or nursing students.

QUESTION 2
HOW OFTEN DO YOU VISIT ORPHANET?
Over 65% of those who answered this survey are regular users whereas 34% were visiting Orphanet for the first time.

QUESTION 3
WHAT SORT OF INFORMATION ARE YOU LOOKING FOR DURING THIS CONNECTION TO ORPHANET?

This question aims to determine which kind of information visitors sought on Orphanet. More than one choice was possible.
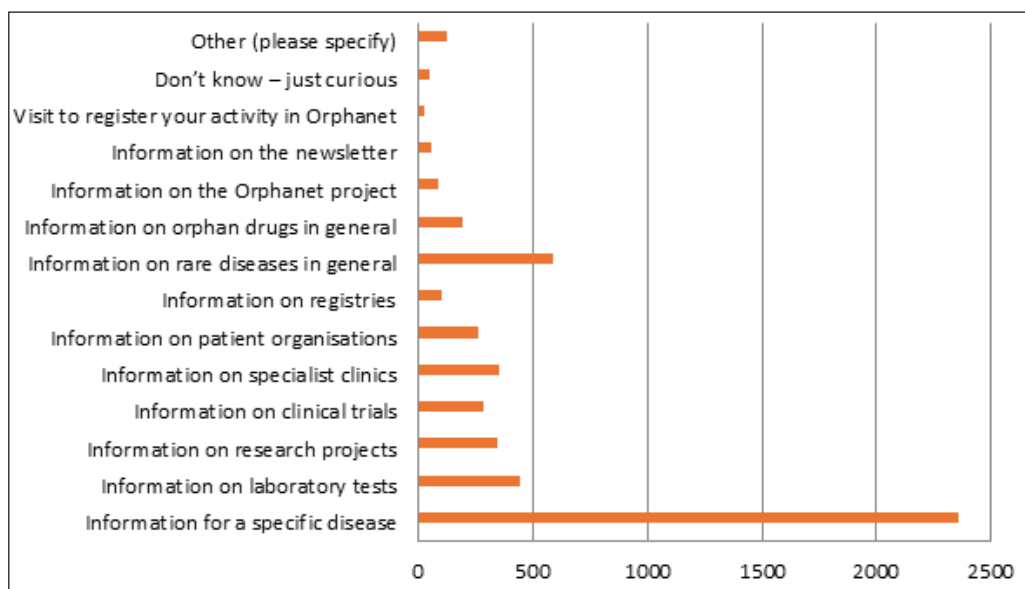
Fig. 16 Information sought on Orphanet by the 2013 user survey respondents

QUESTION 4
DO YOU REGULARLY USE THE FOLLOWING SITES WHEN DEALING WITH RARE DISEASES?

This question aimed to determine which other websites are visited by people looking for information on rare diseases. More than one choice was possible.
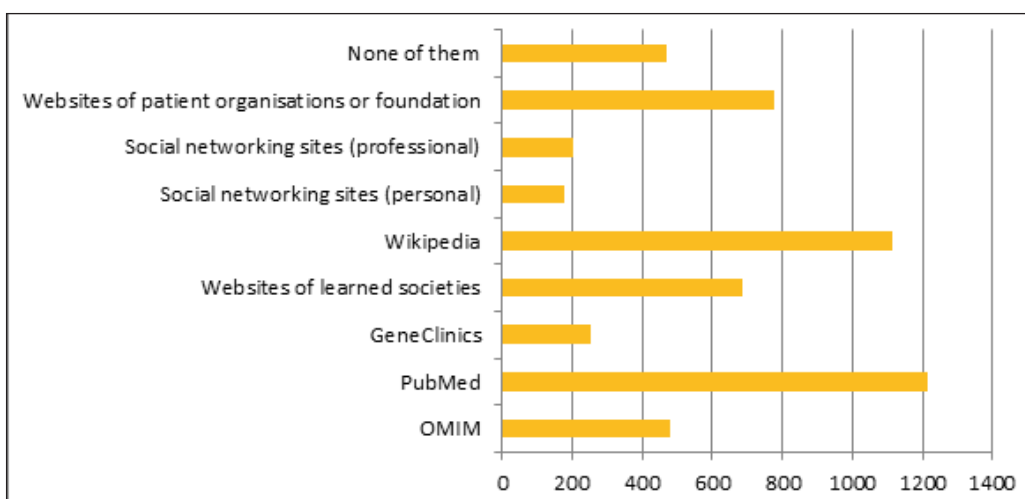
Fig. 17 Other RD websites visited by the 2013 user survey respondents

To obtain information on rare diseases, Pubmed is used by 44% of those who answered this question; Pubmed is massively consulted by healthcare professionals (67%), researchers (72%) and industry professionals (84%). OMIM is mainly used by healthcare professionals (36%), researchers (37%) and not by patients or industry professionals. Websites of patient organisations or foundations are more often consulted by industry professionals (50%) or patients (40%).

This analysis also underlines the fact that Wikipedia remains a main source of information for all categories of respondents.

HOW ARE YOU ACCESSING ORPHANET TODAY?

Answer Options	Very useful	Useful
Via a computer at work	**37%**	1006
Via a computer at home	**52%**	1419
Via a computer at an internet café	1%	30
Via a mobile device (Smartphone, tablet)	10%	267

Table 11. Access to Orphanet by the 2013 usersurvey respondents

Users accessing Orphanet via a mobile device have doubled since last year.

QUESTION 6

HAVE YOU DOWNLOADED THE ORPHANET APPLICATION?

Answer options	Response percent	Response count
Yes	**7%**	189
No	**93%**	2527

Table 12. Download of the Orphanet application by the 2013 user survey respondents

5. Network: the national and international collaborations of Orphanet

5.1. Collaboration with the WHO

The World Health Organisation (WHO) and Orphanet collaborate on the revision of the International Classification of Diseases (ICD-11).

Orphanet has been entrusted as the operating institution to prepare the proposal for ICD-11 related to rare diseases. The Rare Diseases Topic Advisory Group (RD-TAG) has therefore managed the process of the preparation and peer-review of proposals in order to include rare diseases in every relevant chapter of the ICD-11. In 2013, the beta version of ICD-11 was released. It includes over 4,000 rare diseases. The beta version is available for public consultation at http://apps.who.int/classifications/icd11/browse/f/en. The final version is not expected before 2017.

5.2. Collaboration with Health Authorities

5.2.1. NATIONAL PLANS

Orphanet teams actively participate in the preparation of National Plans on Rare Diseases as they are recognised as experts at the national level.

Orphanet is mentioned as the reference portal for rare diseases in the recommendations and proposed measures for the Belgian Plan for Rare Diseases, in the Ministry of Health Report on Rare Diseases in Austria (2012), in the Cyprus Strategic Plan for Rare Diseases (2012), in the French Plan National Maladies Rares, in the German National Plan for Rare Diseases (2013), and in the Greek National Plan for Rare Diseases. It is mentioned as a main source of information in the UK strategy.

Orphanet Germany is currently involved in three activities receiving financial support from the German Ministry of Health: (1) SE-ATLAS (www.se-atlas.de) is a joint project by the Universities of Mainz, Orphanet-Germany, and the Centers for Rare Diseases in Frankfurt and Tübingen, aiming to innovate the presentation of health care facilities for patients with rare diseases in Germany by featuring an interactive geographical map. (2) PORTAL-SE (www.portal-se.de) is a sister project by the Universities of Hannover, Freiburg, Mainz, the Chamber of Physicians of Lower Saxony and Orphanet-Germany to conceptualize a central information portal facilitating access to information on all aspects of rare disease care in a user-group specific manner. Both of these projects do not intend to create new databases. Orphanet-Germany will, according to the German Action Plan on Rare Diseases, remain the central information platform in this respect.

5.2.2. ADOPTION OF THE ORPHANET NOMENCLATURE IN HEALTH INFORMATION SYSTEMS

To improve the traceability of rare diseases in health information systems and to increase the recognition of each rare disease in national health and reimbursement systems, Orphanet has developed an evidence-based standardised nomenclature: the Orphacode. It is composed of a unique and stable Orpha number for each rare disease of the inventory. In 2012, it has been implemented in the French hospital system database that the ORPHA number be used to code all hospitalised patients. The goal is to better identify patients in the health-care system so as to improve knowledge of their healthcare pathways. The ORPHA code has been added in a dedicated part of the coding system, besides the ICD-10 derived code. The French Minsitry of Health issued a directive to rare disease reference centres and competence centres in order to include ORPHA codes in patient records. This will help in capturing data to be included in the French Rare Diseases Data Repository, BNDMR (www.bndmr.fr), which is in development. Coding with the ORPHA codes should be extended to other sectors of the health system in the future.

In July 2013, a 3-year project started to revise the German ICD-10 (ICD-10GM). Orphanet-Germany is partnering in this project by supplying the DIMDI (German Institute of Medical Documentation and Information) with the German translation of the rare disease terms. The project intends to integrate the Orphanet classification of diseases by adding Orpha numbers and it also serves to expand the inventory of rare diseases within the ICD-10GM. Alignment of German disease terms within both database systems should lead to more congruence between both systems.

5.2.3. EXPERT RESOURCES DOCUMENTATION

The Orphanet Belgian team will pilot a nation-wide survey on behalf of the Ministry of health to document Belgian expertise for rare diseases.

5.3. Scientific collaborations and partnerships

Orphanet believes in the effectiveness of data and expertise sharing in order to achieve a deeper understanding of Rare Diseases and to address the specific needs of different stakeholders.
Thanks to the internally produced, expert-reviewed scientific information that Orphanet offers on Rare Diseases it is often solicited by many different projects to contribute its expertise.
It is for these reasons that new collaborations and partnerships are developed regularly and this results in the intense scientific collaborative activity described below.

5.3.1. PARTNERSHIP WITH EUROGENTEST

Orphanet was a partner of EuroGentest 2 until December 2013. In 2012, within this project, a workshop was held to discuss the standards to be used in terms of terminology for rare diseases and for phenotypic descriptions related to genetic variants. Standard terminologies are essential to the clinical research community for the description of phenotypes. The expert group proposed the creation of an international consortium which became a reality in 2013.

A collaboration between Orphanet, HPO (Human Phenome Ontology) and OMIM was established to prepare a proposal for a core set of terms to describe human phenomes. This work was supported by the EuroGenTest contract. A consortium of partners was set up: the International Consortium of Human Phenotype Terminologies (ICHPT). There is now an agreement on 2,372 terms which are proposed to be adopted by all existing terminologies. This core terminology will be made available on a dedicated website in 2014, and mappings with other phenotype terminologies in use (HPO, PhenoDB, LDDB, SNOMED CT, Elements of Morphology amongst others) will be provided in order to ensure inter-operability between databases and patient data worldwide. This project is now overseen by IRDiRC project and was initiated and coordinated by Orphanet.

5.3.2. PARTNERSHIP WITH IUPHAR

A partnership was established with IUPHAR at the end of 2011 to cross-link Orphanet with the IUPHAR database and the cross-linking is ongoing. This project will be expanded in 2014 in order to take into account the evolutions of the IUPHAR database.

5.3.3. PARTNERSHIP WITH IRDIRC

The Orphanet team is a partner of an FP7 research support action entitled "Support IRDIRC".
The International Rare Diseases Research Consortium (IRDiRC) was launched in April 2011 to foster international collaborations in rare disease research. IRDiRC teams up researchers and organisations investing in rare disease research in order to achieve two main objectives, namely to deliver 200 new therapies for rare diseases and the means to diagnose most rare diseases by the year 2020. Orphanet hosts data on research projects funded by IRDiRC members which are research funding agencies. This requires the expansion of data coverage to new countries such as the United States. In addition, Orphanet data is at the disposal of the IRDiRC working groups and is analysed for them on request.

5.3.4. PARTNERSHIP WITH ECRIN

Since 2012 Orphanet is involved in ECRIN-Integrating activities as the leader of the work package on Rare Diseases. ECRIN (European Clinical research Infrastructure Network) is a network dedicated to fostering clinical research and to help organise multinational clinical trials mainly directed towards academics.

5.3.5. PARTNERSHIP WITH RARECARENET

Since mid 2013, Orphanet has a partnership with RareCareNet, providing them with information on expert centres and rare cancer patient organisations. RareCareNet provides Orphanet with information on the epidemiology of rare cancers, and a common effort is currently performed in order to agree on the classification for rare cancers.

5.3.6. PARTNERSHIP WITH GLAXOSMITHKLINE

The partnership formed with GlaxoSmithKline (GSK) was renewed in 2013. The company, which has a division dedicated to rare diseases, wishes to support the development of the disease database and of the Orphadata website, which are considered as strategic resources of interest to the industry.

5.3.7. COLLABORATION WITH SNOMED-CT

Collaboration with the International Health Terminology Standards Development Organisation (IHT-SDO) lead to the agreement that RDs be included in SNOMED CT. Effective revision of SNOMED CT for rare diseases should take place in 2014.

5.3.8. COLLABORATION WITH THE EBI

Collaboration was established with the European Bioinformatics Institute (EBI) at the end of 2011 to cross-link Orphanet's database with their genomic and their biological pathway data resources (ensembl and Reactome) and is currently ongoing.

A new collaboration between Orphanet and the EBI was established in 2013 in order to produce an ontology for rare diseases: The Orphanet Rare Diseases Ontology (ORDO).

6. Funding

Orphanet's budget was approximately 3,5M Euros in 2013, originating from 9 different contracts for the core activity funding and from various other contracts in some of the participating countries.
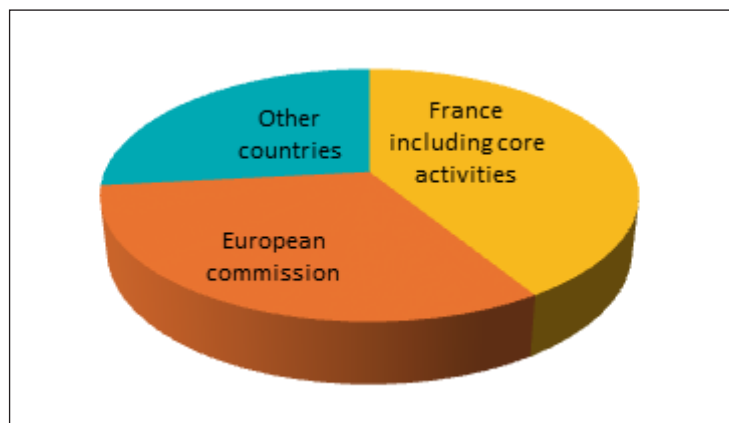
Fig. 18 Orphanet's global budget 2013

Globally, we can distinguish funding for the core activities and for national activities.

6.1. Orphanet's core activity funding

Orphanet's core activities include the infrastructure, the coordination activities (management, management tools, quality control, rare disease inventory, classifications and production of the encyclopaedia) and communication. It excludes the collection of data on expert services in the participating countries.
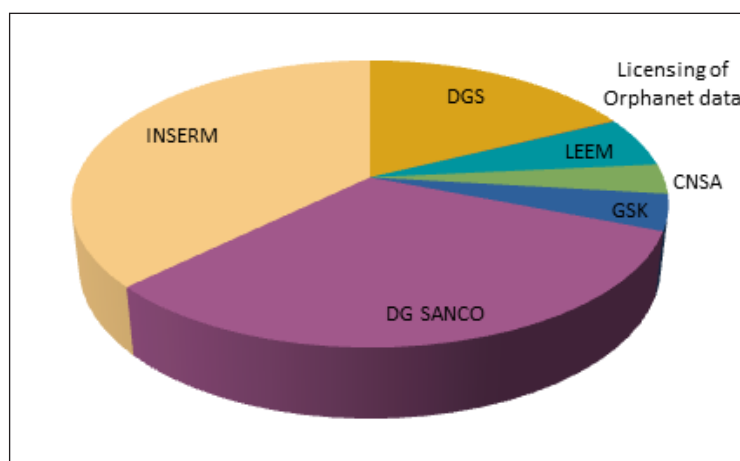
Fig. 19 Orphanet core activities funding 2013

This budget excludes the costs of infrastructure (office space) which are essentially supported by INSERM.
In the last 10 years, the funding of Orphanet's core activities has quadrupled reflecting the growth of the project.
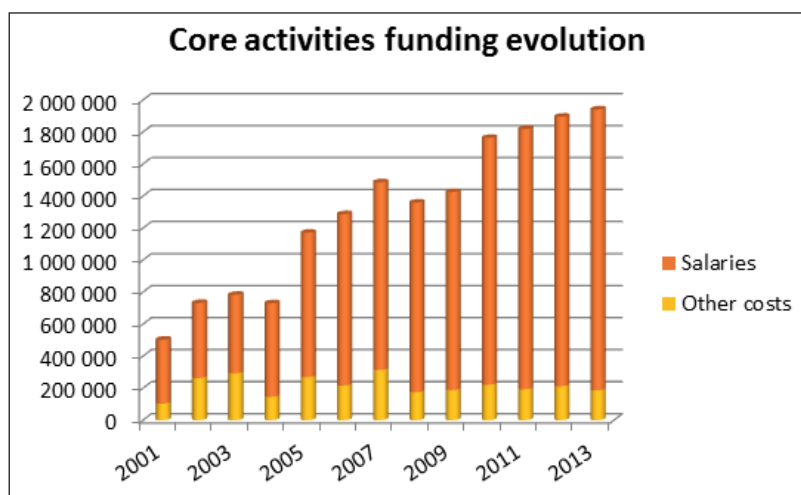
Fig. 20 Core Activities funding evolution 2001-2013

Although there has been an extremely positive increase over the years, the current budget remains limited in comparison to the needs of maintaining and updating a database of this size. What is clear from the figure above is that apart from the salaries, the budget required for running the activities has dramatically decreased in proportion when compared to the needs and to previous years.

6.1.1. EUROPEAN FUNDING

The European Commission funds the inventory of rare diseases, the encyclopaedia and the collection of data on expert services in European countries (since 2000, DG Public Health and Consumers Protection grant N°s S12.305098; S12.324970; SPC.2002269-2003220, 2006119, 20091215 and since 2004, DG Research grant N°s LSSM-CT-2004-503246; LSHB-CT-2004-512148; LSHB-CT-2006-018933; Health-F2-2008-201230, HEALTH-F2-2009-223355).

In 2013, Orphanet was funded by the DG Sanco grant 20102206 (Orphanet Europe Joint Action).

6.1.2. OTHER CURRENT FINANCIAL PARTNERSHIPS FOR CORE ACTIVITY FUNDING

Inserm Institut national de la santé et de la recherche médicale	The "Institut National de la Santé et de la Recherche Médicale" finances Orphanet's core activities. Inserm Transfert is in charge of ensuring licencing benefits and intellectual property transfer concerning Orphanet data.
RÉPUBLIQUE FRANÇAISE MINISTÈRE DES AFFAIRES SOCIALES ET DE LA SANTÉ	The French Directorate General for Health finances Orphanet's core activities (DGS).
European Union flag	The European Commission finances the database of diseases, the encyclopaedia in English, coordination, communication and IT of the project.
CNSA Caisse nationale de solidarité pour l'autonomie	The "Caisse nationale de solidarité pour l'autonomie" supports the indexing of rare diseases with the International Classification of Functioning, Disability and Health (ICF).
AFM Association Française contre les Myopathies	The "Association Française contre les Myopathies" finances OrphaNews France and OrphaNews Europe, as well as data collection on clinical trials.
leem Fondation Sous l'égide de la Fondation de France	The "Fondation des Entreprises du Médicament" finances the collection of data on orphan drugs and clinical trials.
gsk GlaxoSmithKline	Glaxo Smith Kline finances the extension of the database's disease annotation and free access to this data.
RÉPUBLIQUE FRANÇAISE MINISTÈRE DES AFFAIRES ÉTRANGÈRES ET EUROPÉENNES	The French "Ministère des affaires Etrangères" finances the cooperation with Canada.
EuroGentest	EuroGentest financed the creation of a thesaurus of clinical signs to harmonise international phenotype nomenclatures.

6.1.3. CURRENT NON FINANCIAL PARTNERSHIPS FOR CORE ACTIVITY FUNDING

Non financial partners are those that provide services in kind and/or share their expertise for Orphanet core activities.

	Collaboration with the World Health Organisation (WHO) in the process of revising the International Classification of Diseases.
GENATLAS	Cross-referencing with Genatlas which collaborates in updating the data on genes involved in rare diseases.
UniProt	Cross-referencing with UniProt KB which collaborates in updating the data on genes linked to proteins involved in rare diseases.
HGNC	Cross-referencing with HGNC which collaborates in updating the data on genes involved in rare diseases.
OMIM®	Cross-referencing with OMIM (The Online Mendelian Inheritance in Man), and OMIM has added Orphanet to the list of external links provided on its website.
REACTOME	Cross-referencing with Reactome.
e!Ensembl	Cross-referencing with Ensembl.
IUPHAR	Cross-referencing with The International Union of Basic and Clinical Pharmacology DataBase (IUPHAR-DB).
LOVD	The LOVD (Leiden Open Variation Database) platform has been updated with links to Orphanet's gene pages.
EuroGentest	EuroGenetest collaborates with Orphanet in the field of quality management of medical laboratories.

6.2. Financial and non-financial partnerships for national activities

Orphanet's national activities are also supported by national institutions, specific contracts and/or contributions in kind. In European countries, data collection at the national level is also supported by the European Commission.

6.2.1. PARTNERSHIPS PROVIDING FUNDING FOR NATIONAL ACTIVITIES

Institutional partners host Orphanet national team activities and contribute to the project by allocating a budget and the time of some of their professionals. For European countries, this kind of partner is defined as an "associated partner".
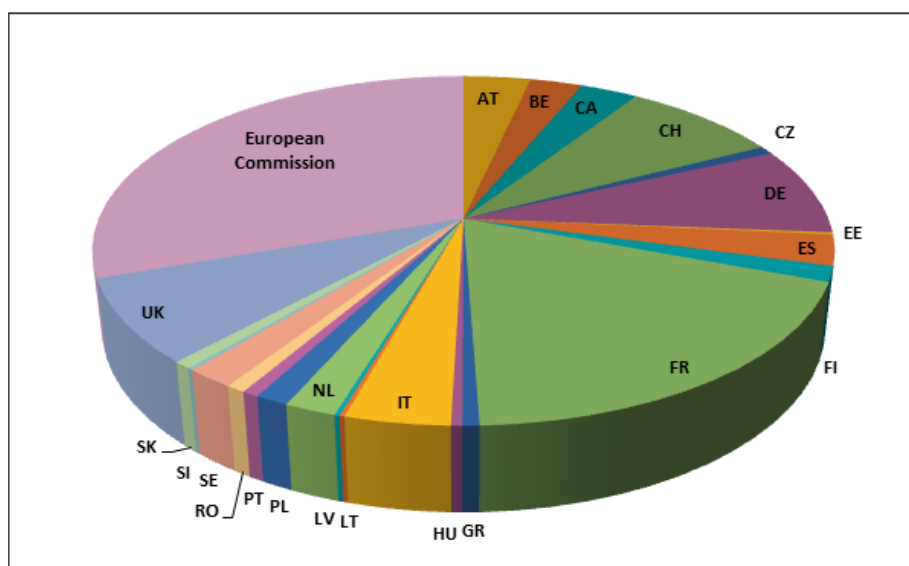
Fig. 21 Funding sources for national activities in 2013

AUSTRIA	
Gesundheit Österreich GmbH	The "Gesundheit Österreich GmbH" (GÖG) is an associated partner in the Orphanet Europe Joint Action as of April 2011.
MEDIZINISCHE UNIVERSITÄT WIEN	The Medical University of Vienna is an associated partner in the Orphanet Europe Joint Action as of April 2011 and hosts Orphanet Austria since 2005. It further provides part-time funding (in kind) for the work of the country coordinator.
BUNDESMINISTERIUM FÜR GESUNDHEIT	The Austrian Ministry of Health provides funding to the Orphanet Europe Joint Action as of April 2011.
BELGIUM	
federal public service HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT	The Federal Public Service Health, Food Chain Safety and Environment is an associated partner in the Orphanet Europe Joint Action as of April 2011.
isp wiv	The "Wetenschappelijk Instituut Volksgezondheid – Institut Scientifique de Santé Publique" is an associated partner in the Orphanet Europe Joint Action as of April 2011.
CANADA	
CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada	Canadian institute of Health Research is the host institution of Orphanet Canada, finances a position for the project manager and provides additional administrative support for the project.
RÉPUBLIQUE FRANÇAISE MINISTÈRE DES AFFAIRES ÉTRANGÈRES Québec COOPÉRATION FRANCE-QUÉBEC	La "Commission permanente de coopération franco-québécoise" finances the teams' missions between France and Québec .
Santé et Services sociaux Québec	The Québec "Ministère de la Santé et des Services sociaux" finances a project manager position in Quebec and some administrative support.
Centre universitaire de santé McGill McGill University Health Centre	The Department of Medical Genetics of the McGill University Health Centre is the host institution of Orphanet-Quebec and provides the medical coordinator.
RQMO	Le "Regroupement québécois des maladies orphelines" provides the project coordinator and administrative support.

CYPRUS	
	The Department of Medical and Public Health Services is an associated partner in the Orphanet Europe Joint Action as of April 2011.
CZECH REPUBLIC	
	The Charles University Prague - 2nd School of Medicine is an associated partner in the Orphanet Europe Joint Action as of April 2011.
	Czech Association of rare diseases finances the activity of the Czech team since April 2012.
ESTONIA	
	The University of Tartu is an associated partner in the Orphanet Europe Joint Action as of April 2011.
FINLAND	
	Rinnekoti Foundation is an associated partner in the Orphanet Europe Joint Action as of January 2013.
FRANCE	
	The "Fondation Groupama pour la santé" contributes to the development of the mobile application.
	The "LFB Biomédicaments" helps finance the development and update of emergency guidelines and the French encyclopaedia for the general public.
	The "Agence de la biomédecine" finances the monitoring of the list of laboratories, the creation of tools for collecting, managing and monitoring annual activity, as well as funding the compilation of data collected in France.
	The "Caisse nationale de solidarité pour l'autonomie" supports the development of the French encyclopaedia for the general public with information on the functional consequences of rare diseases, as well as the production of fact sheets on rare disabilities not necessarily related to rare diseases.
	The INVS, Institut de Veille Sanitaire, supports Orphanet.
GERMANY	
	The Federal Ministry of Health Germany provides funding to the Orphanet Europe Joint Action as of April 2011.
	The Medical School of Hanover (MHH) supports data collection, and is an associated partner in the Orphanet Europe Joint Action as of April 2011.
GREECE	
	The Institute of Child Health, Athens is an associated partner in the Orphanet Europe Joint Action as of April 2011.

HUNGARY	
	The National Institute for Health Development ("*Országos Egészségfejlesztési Intézet*") is an associated partner in the Orphanet Europe Joint Action as of August 2012.
ITALY	
	The Italian Health Ministry finances Orphanet-Italy activities through current research funding.
	The Bambino Gesù Children's Hospital is an associated partner in the Orphanet Europe Joint Action as of April 2011.
	Genzyme Italia finances OrphaNews Italia.
	The Senate of the Italian Republic donated the proceeds of a Christmas concert to finance Orphanet-Italy activities
LATVIA	
	"Centre for Disease Prevention and Control of Latvia" (Slim bu profilakses un kontroles centrs) is an associated partner in the Orphanet Europe Joint Action as of April 2012.
LITHUANIA	
	The Vilnius University Hospital, "Santariškių Klinikos" Centre for Medical Genetics is an associated partner in the Orphanet Europe Joint Action as of April 2011.
NETHERLANDS	
	The "Leids Universitair Medisch Centrum" is an associated partner in the Orphanet Europe Joint Action as of April 2011. It hosts Orphanet Netherlands and co-funds the work of prof. dr. van Ommen.
	The Centre for Medical Systems Biology is a joint activity of six institutions in the Netherlands, led by LUMC and including VUMC. The CMSB co-funds the rare disease work of the country coordinator, prof. dr. Van Ommen, and the chair of the Dutch Scientific Advisory Board, prof. dr. Cornel. From April 2011 on the CMSB also funds the work of the project manager.
POLAND	
	The "Instytut Pomnik Centrum Zdrowia Dziecka" (Children's Memorial Health Institute) is an associated partner in the Orphanet Europe Joint Action as of April 2011.
	The Polish Ministry of Health contributes to the translation of the Orphanet encyclopedia in Polish.
PORTUGAL	
	IBMC - Institute for Molecular and Cell Biology is the host institution of Orphanet-Portugal since 2009 and is a partner in the Orphanet Europe Joint Action as of April 2011; it partly funds the national activities, namely the full salary of the project coordinator.
	ICBAS - Instituto de Ciências Biomédicas Abel Salazar, the Biomedical Sciences Institute at the University of Porto, is an Orphanet partner since 2009; it is responsible for the full salary of the national coordinator, a full-time Professor at that institution.

	DGS - The Directorate-General of Health, at the Portuguese Ministry of Health, officially supports Orphanet-Portugal, and provided a specific grant for 2012, including part of the salary of the information scientist, as well as divulgation materials and activities, among others.
	The pharmaceutical company Pfizer supports financially the Orphanet-Portugal, under some planned activities.
	The pharmaceutical company Biomarin supports financially the Orphanet-Portugal, under some planned activities.

ROMANIA

	The "Universitatea de Medicina si Farmacie "Gr.T.Popa" Iasi" is an associated partner in the Orphanet Europe Joint Action as of April 2011.

SLOVAKIA

	The Children's University Hospital in Bratislava is an associated partner in the Orphanet Europe Joint Action as of April 2011.

SLOVENIA

	The University Medical Centre Ljubljana is an associated partner in the Orphanet Europe Joint Action as of April 2011.

SPAIN

	The Spanish Ministry of Health, Social Services and Equality - Office for Health Planning and Quality is an associated partner in the Orphanet Europe Joint Action as of April 2011.
	The Centre for Biomedical Network Research on Rare Diseases (CIBERER) has been the partner for Orphanet in Spain since April 2010 and an associated partner in the Orphanet Europe Joint Action as of April 2011. CIBERER finances the main activities of the Spanish team.

SWEDEN

	The "Karolinska Institutet" is an associated partner in the Orphanet Europe Joint Action as of April 2011.
	Karolinska University Hospital of Stockholm supports the Orphanet Sweden activities.

SWITZERLAND

	University Hospitals of Geneva is the host institution of Orphanet Switzerland and finances a part-time position for the coordinator and provides some administrative support for the project.
	Since 2011, Orphanet Switzerland is funded by the Swiss Conference of the Cantonal Ministers of Public Health. The support finances the position of the coordinator (part-time), two information scientists (1 full-time from April 2011 and 1 part-time) and a webmaster from the Health On The Net Foundation (HON).

TURKEY	
AiFD	The Association of Research-Based Pharmaceutical Companies gives non-restricted support for the Turkish translation of the Orphanet webpage and the document including over 10,000 rare genetic diseases together with their detailed description. They supported the creation of the Orphanet-Turkey website and help Orphanet Turkey to prepare and print leaflets representing Orphanet, Orphanet-Turkey and their activities for health care professionals and the general public.
UNITED KINGDOM	
MANCHESTER 1824 The University of Manchester	The University of Manchester is an associated partner in the Orphanet Europe Joint Action as of April 2011.
nowgen engagement • education • training	Nowgen in Manchester hosts Orphanet-UK's activities and contributes to the project by allocating the time of some professionals.

6.2.2. INSTITUTIONAL PARTNERSHIPS PROVIDING SERVICES IN KIND FOR NATIONAL ACTIVITIES

All the Institutions hosting the national Orphanet teams provide their office space, all the necessary supplies to run the team activities and allocate the time of some of their professionals. For European countries, this kind of partner is defined as a "collaborating partner".

ARMENIA	
	The Center of Medical Genetics and Primary Health Care hosts Orphanet-Armenia's activities and contributes to the project by allocating the time of some professionals.
AUSTRALIA	
	The Office of Population Health Genomics, Department of Health, Western Australia hosts Orphanet-Australia's activities and contributes to the project by allocating the time of some professionals.
BULGARIA	
	The Bulgarian Association for Promotion of Education and Science (BAPES), hosts Orphanet-Bulgaria's activities and contributes to the project by allocating the time of some professionals.
CROATIA	
	The Zagreb University hosts Orphanet-Croatia's activities and contributes to the project by allocating the time of some professionals.
IRELAND	
	The Our Lady's Children's Hospital, Crumlin hosts Orphanet-Ireland's activities and contributes to the project by allocating the time of some professionals.
	Nowgen in Manchester, UK hosts Orphanet-Ireland's activities and contributes to the project by allocating the time of some professionals.
ISRAEL	
	The Schneider Children's Medical Center of Israel hosted Orphanet-Israel's activities and contributed to the project by allocating the time of some professionals until June 2013.
	The Meir Medical Center of Israel hosts Orphanet-Israel's activities and contributes to the project by allocating the time of some professionals since June 2013.
LEBANON	
	The Saint Joseph University hosts Orphanet-Lebanon's activities and contributes to the project by allocating the time of some professionals.
LUXEMBOURG	
	The Ministry of Health of Luxembourg hosts Orphanet-Luxembourg's activities and contributes to the project by allocating the time of some professionals.
MOROCCO	
	The National Institute of Hygiene hosts Orphanet-Morocco's activities and contributes to the project by allocating the time of some professionals.

NORWAY
The Norwegian Directorate of Health hosts Orphanet-Norway's activities and contributes to the project by allocating the time of some professionals.
SERBIA
The Institute of Molecular Genetics and Genetic Engineering , University of Belgrade, hosts Orphanet-Serbia's activities and contributes to the project by allocating the time of some professionals.
TURKEY
The Istanbul University hosts Orphanet-Turkey's activities and contributes to the project by allocating the time of some professionals.

6.2.3. NON-FINANCIAL PARTNERSHIPS IN 2013

BELGIUM
A partnership exists with RaDiOrg.be, a EURORDIS member, which continued to play a role in the validation of data on Belgian patient organisations in Orphanet.
The Orphanet team hosted by the Scientific Institute of Public Health collaborates internally with the Service "Infectious Diseases in the general population" to validate data on reference laboratories and tests for infectious diseases.
The College of Human Genetics in Belgium, which represents the 8 recognized genetic centres, are collaborating with the Orphanet team to improve and simplify the process of registration and update of data on genetic testing activities in the Orphanet database.
The National Institute of Health and Disability Insurance provides information on the recognized reference centres that work under a convention.
BULGARIA
The Association of Medical Students in Plovdiv has been actively promoting Orphanet use in its community. Together, BAPES and ASM-Plovdiv have organised a series of workshops, dedicated to Orphanet.
The Bulgarian National Alliance of People with Rare Diseases has partnered with BAPES in order to promote Orphanet among rare diseases patients in Bulgaria, as well as to list the Bulgarian patient associations on the Orphanet database.
CZECH REPUBLIC
The Czech Medical Genetics society helps Orphanet CZ in the collection of information on DNA diagnostic laboratories in the country, information on rare diseases clinics - dysmorphology, genetic counselling and information on patient support groups. They have a joint partnership for the development of the Czech National Plan for rare diseases following the Czech National Strategy from 2009. The Czech National Plan is developed under the auspices of the Ministry of Health - Department of Medical Services.
The Ministry of Health of the Czech Republic officially supports Orphanet.

ESTONIA	
	The Ministry of Social Affairs of Estonia officially supports Orphanet.
FINLAND	
	The Ministry of Social Affairs and Health of Finland officially supports Orphanet.
	Terveysportti (www.terveysportti.fi) is a web service for medical professionals published by Duodecim Medical Publications Ltd, which is owned by the Finnish Medical Society Duodecim. Orphanet was included in Terveysportti's searches concerning the 300 "most common rare diseases". As a result, Orphanet will have a higher profile among the Finnish health care professionals.
FRANCE	
	The Ministry of Health officially supports Orphanet.
	The French High Authority for Health (HAS) and Orphanet cooperate for the online publication of National Protocols for Diagnosis and Care (NHDP) produced by the HAS.
	The "Agence nationale de sécurité du médicament et des produits de santé" (ANSM) provides Orphanet with data on clinical trials in France.
	"Air France" provides patients and professionals with a quota of airline tickets for patients to travel to medical experts or experts to patients with rare diseases. Orphanet provides expertise on the merits of applications.
	Orphanet has delegated to "Maladies Rares Info Services", the French helpline for information on rare diseases - 0810 69 19 20, the role of replying to unsolicited electronic messages received by Orphanet.
GERMANY	
	The Federal Ministry of Health Germany officially supports Orphanet.
	The "Allianz Chronischer Seltener Erkrankungen e.V." (ACHSE) works together with Orphanet Germany on informational services for patients.
	The "Kindernetzwerk e.V. - für Kinder, Jugendliche und (junge) Erwachsene mit chronischen Krankheiten und Behinderungen" provides data on associations in Germany.
	The "Deutsche Gesellschaft für Humangenetik e.V." supports Orphanet by supplying the German team with addresses and information on laboratories and diagnostics.
	Nationale Kontakt- und Informationsstelle zur Anregung und Unterstützung von Selbsthilfegruppen (NAKOS) officially supports Orphanet.
GREECE	
	The Ministry of Health and Social Solidarity of the Hellenic Republic officially supports Orphanet.

HUNGARY	
	The State Secretary of Health within the Ministry of Human Resources officially supports Orphanet.
ISRAEL	
	The Israeli Ministry of Health officially supports Orphanet.
ITALY	
	The "Istituto Superiore di Sanità" officially supports Orphanet.
	Telethon collaborates with Orphanet for the collection of data concerning research projects.
	Uniamo, the Italian Federation of support groups on rare diseases, collaborates with Orphanet in the organization and promotion of events dedicated to rare diseases, in order to increase public awareness on this particular issue.
	AIFA collaborates with Orphanet for the collection of data concerning clinical trials.
	Netgene collaborates with Orphanet for the diffusion of information on rare diseases.
	Farmindustria promotes Orphanet publications.
	Osservatorio Malattie Rare (O.Ma.R.) collaborates with Orphanet for the diffusion of information on rare diseases and the promotion of events
LATVIA	
	The Ministry of Health of the Republic of Latvia officially supports Orphanet.
	The Rare Diseases Society in Latvia aims to promote equal rights and opportunities for patients with rare diseases.
	Palidzesim.lv is a non-governmental organisation in Latvia which financially supports children and families to confirm a diagnosis of a rare disease by sending patients or medical samples abroad.
LITHUANIA	
	The Ministry of Health of the Republic of Lithuania officially supports Orphanet.
NETHERLANDS	
	The Ministry of Health, Welfare and Sport of the Netherlands officially supports Orphanet.
	The Erfocentrum provides information to the general public on genetic, mainly rare, disorders. Collaboration has been established to increase the number of Dutch texts available on the Orphanet.
	The VSOP (Vereniging Samenwerkende Ouder- en Patiëntenorganisaties) provides information regarding patient organisations dedicated to rare disease and participates in the validation of information on Dutch expert centres.
	The Dutch Federation of University Medical Centres and Orphanet NL collaborate in establishing a comprehensive list of Dutch expert centres.

POLAND	
	The CMHI supports Orphanet Poland in all activities inside and outside the institution; e.g. organising conferences for professionals, parents and media, discussions on rare disease with all stakeholders and improving access to orphan drugs.
	The patient organisation, Ars Vivendi, provides patients and parents with information about Orphanet services and cooperates with Orphanet Poland.
PORTUGAL	
	INFARMED - the National Authority for Medicines and Health Products, collaborates with a regularly updated list of orphan drugs approved and available in Portugal, as well as its quantities used.
	ACSS - the Central Administration of Health System acknowledges that Orphanet-Portugal is the reference source of information on rare diseases and orphan drugs in Portugal.
	CES - the Social Studies Center, at the School of Economics at the University of Coimbra, has been collaborating in the update and validation of the list of bona fide Patient Associations in the country.
	NEDR - the Nucleus for Study of Rare Diseases of the Portuguese Society of Internal Medicine collaborates in the update and validation of activities about rare diseases ongoing in Portugal.
	Aliança - the Portuguese Alliance of Rare Diseases Organizations has been collaborating in several joint actions with Orphanet-PT, including the update and validation of Patient Associations and the joint organization of the Rare Diseases Day each year.
	FCT - The "Fundação para a Ciência e a Tecnologia" collaborates by updating information on research projects and clinical trials taking place in the field of rare diseases and/or orphan drugs ongoing in Portugal. The Orpha number is requested in every project in the life sciences dealing with rare diseases.
	SPGH - The Portuguese Society of Human Genetics collaborates by updating information on professionals, genetic counselling clinics, medical labs and diagnostic tests available in the country.
ROMANIA	
	The Ministry of Health collaborates with Orphanet Romania in updating data on the Romanian medical system. It officially supports Orphanet.
	Orphanet Romania collaborates with the Romanian Medical Association in updating data on health professionals.
	Orphanet Romania collaborates with the Romanian Society of Medical Genetics to set up programs for the development of a national network of diagnosis, investigation and prevention in Centres of Medical Genetics and to promote collaboration with associations of people with genetic/malformative diseases.
	Orphanet Romania collaborates with Romanian Prader Willi Association in order to bring together the efforts of patients, specialists and families to ensure a better life for all people with genetic diseases.
SLOVAKIA	
	The Ministry of Health of the Slovak Republic officially supports Orphanet.

SLOVENIA	
REPUBLIC OF SLOVENIA **MINISTRY OF HEALTH**	The Ministry of Health of Slovenia officially supports Orphanet.
IGRE INŠTITUT ZA GENOMSKE RAZISKAVE IN EDUKACIJO	Orphanet Slovenia collaborates with the Institute of Genomic Research and Education IGRE with the aim of disseminating information about the Orphanet project and web services on the national level.
SPAIN	
MINISTERIO DE SANIDAD Y POLÍTICA SOCIAL	The Ministry of Health and Social Affairs of Spain officially supports Orphanet.
SWEDEN	
REGERINGSKANSLIET	The Ministry of Health and Social Affairs of Sweden officially supports Orphanet.
SWITZERLAND	
HON Health On the Net Foundation Non Governmental Organization www.healthonnet.org	The Health On the Net Foundation supports the technical aspect of the project by developing online forms to collect data. In addition, it hosts the website www.orphanet.ch and helps to update the homepage.
PRORARIS Alliance Maladies Rares – Suisse Allianz Seltener Krankheiten – Schweiz Alleanza Malattie Rare – Svizzera	ProRaris, the Swiss Alliance of patients with rare diseases has established a close collaboration with Orphanet Switzerland in order to identify relevant information services for patients and professionnals and in the organisation and promotion of events dedicated to rare diseases, in order to increase public awareness on this particular issue.
IG Seltene Krankheiten CI Maladies rares CI Malattie rare	Orphanet Switzerland is member of the «Community of Interest for Rare Diseases» launched in August 2011. This community brings together all the relevant stakeholders in the field of rare diseases in Switzerland in order to develop, in collaboration with the Federal Office of Public Health, a national strategy for rare diseases.
TURKEY	
	The Turkish Ministry of Health officially supports Orphanet. It collaborates with Orphanet Turkey for data collection and the dissemination of Orphanet in Turkey.
UNITED KINGDOM	
DH Department of Health	The Department of Health officially supports Orphanet.
Ataxia UK Caring today, researching for tomorrow	Ataxia UK and Orphanet cooperate in the exchange of information, in the validation and online publication of research projects regarding Ataxia and in the endorsement and boosting of Orphanet and Ataxia UK activities.
A network of centres of expertise dyscerne for dysmorphology	Dyscerne and Orphanet cooperate in endorsing and boosting Dyscerne and Orphanet activities, raising standards in the diagnosis and management of rare dysmorphic conditions, improving dissemination of information on these conditions, developing and sharing information and educational tools for healthcare professionals.
RARE DISEASE | UK	Orphanet collaborates with Rare Disease UK in the sharing of data and expertise, in the endorsement and promotion of Orphanet and Rare Disease UK activities, and in the development of the UK Strategy for Rare Diseases. Rare disease UK is also a post-validator of information on Orphanet regarding patient organisations in the UK.

Genetic Alliance UK Supporting. Campaigning. Uniting.	Orphanet collaborates with Genetic Alliance UK in the sharing of data and expertise, in the endorsement and boosting of Orphanet and Genetic Alliance UK activities, in seeking to raise awareness, improve the quality of services and information available to patients and families and to improve the quality of life for those affected by genetic conditions. Genetic Alliance is also a post-validator of information on Orphanet regarding patient organisations in the UK.
ERNDIM QUALITY ASSURANCE IN LABORATORY TESTING FOR IEM	ERNDIM is a post-validator of information on Orphanet UK regarding medical laboratories performing biochemical diagnosis of rare diseases.

7. Communication

7.1. Communication documents

In 2013, A5-size flyers to present Orphanet and Orphanet services were designed, printed and distributed:
- Leaflet on Orphanet in 3 languages (English, French and German)
- Leaflet on Orphadata (English)
- Leaflet on the Orphanet application for iPhone and iPad (English)
- Leaflet on Orphacodes (English)
- Leaflet on the Orphanet database structure and main products (English)

7.2. Invitations to give lectures at conferences in 2013

Orphanet representatives, as specialists in the field of rare diseases, were invited to give lectures and to participate in more than 120 conferences worldwide. These lectures focused on presenting the Orphanet database (53), public health policies (16), RD research (7), orphan drugs (3), and medical and genetic approaches (37 presentations).

7.3. Booths at conferences in 2013

Orphanet booths were held in 18 different congresses in 2013 (see below). In 2013, for the first time, Orphanet had a booth at the annual meeting of the American Society of Human Genetics, which was held in Boston (USA) from the 23rd to 26th of October 2013.
List of congresses where Orphanet booths were held:
- Rare Disease Day 2013, Hamburg, 28 February 2013
- 24th Annual Meeting of the German Society of Human Genetics in cooperation with the Austrian Society of Human Genetics and the Swiss Society of Medical Genetics", Dresden, 20-22 March 2013
- Board of Clinical Genetics meeting Budapest, 11 April 2013
- 3rd Fetch-Associations-Rheumatology meeting, Hôpital Cochin, Paris, 23 May 2013
- Congress of the Italian Association of Chromosome 22 deletion "Aidel 22", Rome, 24-25 May 2013
- Scientific Conference on Autism, VI Awareness Day on Autism, Rome, 2 April 2013
- European Society of Human Genetics, Paris, 8-12 June 2013
- French General Practitioner Congress, Nice, 28-29 June 2013

- 9th European Cytogenetics Conference, Dublin, 29 June – 02 July 2013
- 2013 DEBRA International Congress, Rome, 20 September 2013
- Hungarian Society of Human Genetics meeting, Budapest, 26 September 2013
- International Meeting of Angelman syndrome, Rome, 11 October 2013
- Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) Patient Education Day, Montreal, 19 October 2013
- American Society of Human genetics, Boston, October 23-26 October 2013
- IV. National EUROPLAN Conference, Budapest, 25 October 2013
- Canadian College of Medical Geneticists (CCMG), Toronto, 7-9 November 2013
- RARE, Montpellier, 28-29 November 2013
- Research and Innovation Conference in Manchester, 3 December 2013

8. The Orphanet team as of December 2013

COORDINATING TEAM
INSERM US14 - FRANCE

Coordinator of the Orphanet Joint Action
Ségolène Aymé

Administration, finances and communication

Financial officer
Christiane Lajeune / Corentin Fort

Assistant
Mariane Bellanger

Communication officer
Céline Angin

Chief Medical Officer - Orphanet Deputy Director
Ana Rath

Coding and classifications
Bertrand Bellet
Janine-Sophie Giraudet-Le Quintrec
Catherine Gonthier
Natacha Marpillat
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