



orphanet

2017 Activity Report

2017 Activity Report

www.orpha.net



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Abbreviation list

BNDMR: French Rare Diseases Data Repository
CEQAS : Cytogenetic European Quality Assessment Service
CHMP : the Committee for Medicinal Products for Human use
CNIL : Commission nationale de l’informatique et des libertés : The French data protection authority
CNSA: French National Solidarity Fund for Autonomy
COMP : the Committee for Orphan Medicinal Products
DG Santé : Directorate General Health and Consumers – European Commission
DIMDI: German Institute of Medical Documentation and Information
ECRIN: European Clinical Research Infrastructure Network
EJHG: European Journal of Human Genetics
EMA: European Medicines Agency
EMBL - EBI: European Bioinformatics Institute
EMQN: European Molecular Genetics Quality Network
EQA: external quality assessment
EUCERD: European Union Committee of Experts on Rare Diseases
FDA: Food and Drugs administration
HGNC : Human Genome Organisation Gene Nomenclature Committee
HPO : Human Phenotype Ontology
ICD: International Classification of Diseases
ICD-10GM: German ICD-10
ICHPT: International Consortium of Human Phenotype Terminologies
IHTSDO: International Health Terminology Standards Development Organisation
INSERM: French National Institute of Health and Medical Research
IRDiRC: The International Rare Diseases Research Consortium
ISO : International Organization for Standardization
IUPHAR: The International Union of Basic and Clinical Pharmacology
MA : marketing authorisation
MedRA: Medical Dictionary for Regulatory Activities

MeSH: Medical Subject Headings
NFU: Netherlands Federation of University Medical Centres
OD: orphan drugs
OJRD: Orphanet Journal of Rare Diseases
OMIM: Online Mendelian Inheritance in Man
ORDO: Orphanet Rare Disease ontology
ORS: Orphanet Report Series
RD: Rare diseases
RD-TAG: The Rare Diseases Topic Advisory Group
RNA: Ribonucleic acid
SNOMED-CT: Systematized Nomenclature of Medicine-Clinical Terms
SOPs: Standard Operating Procedures
UMLS: Unified Medical Language System
UniProtKB : Universal Protein Resource Knowledgebase
URL: uniform resource locator
WHO: World Health Organisation
WP: Workpackage



1. Overview

Orphanet is a unique resource, gathering and producing knowledge on rare diseases so as to contribute to improving the diagnosis, care and treatment of patients with rare diseases. Orphanet aims to provide high-quality information on rare diseases, and ensure equal access to knowledge for all stakeholders. Orphanet also maintains the Orphanet rare disease nomenclature (ORPHA code), essential in improving the visibility of rare diseases in health and research information systems.

Orphanet was established in France by the INSERM (French National Institute for Health and Medical Research) at the instigation of the French Ministry of Health in 1997. This initiative became a European endeavour from 2000, supported by grants from the European Commission: Orphanet has gradually grown to a Consortium of 41 countries, within Europe and across the globe.

1.1. Orphanet's missions

Over the past 20 years, Orphanet has become the reference source of information on rare diseases. As such, Orphanet is committed to meeting new challenges arising from a rapidly evolving political, scientific, and informatics landscape. In particular, it is crucial to help all audiences access quality information amongst the plethora of information available online, to provide the means to identify rare disease patients, to guide patients and doctors towards relevant services for an efficient patient care pathway, and to contribute to generating knowledge by producing massive, computable, re-usable scientific data.

Orphanet works towards meeting three main goals:

- **Improve the visibility of rare diseases in the fields of healthcare and research by maintaining the Orphanet rare disease nomenclature (ORPHA codes): providing a common language to understand each other across the rare disease field.**

In a global community, we need to understand each other, although we may not speak the same language. A stable nomenclature, cross-referenced with other international terminologies is therefore essential. In order to improve the visibility of rare diseases in information systems, Orphanet has developed, and maintains, a unique, multi-lingual nomenclature of rare diseases, around which the rest of the data in our relational database is structured. Each disease is assigned a unique ORPHA code: integrating this nomenclature in health and research information systems is essential in ensuring that rare diseases are visible and that different systems can work together. This nomenclature is aligned with other terminologies: OMIM, ICD-10, SNOMED-CT, MedDRA, UMLS, MeSH, GARD. This cross-referencing is a key step towards the interoperability of databases and information.

- **Provide high-quality information on rare diseases and expertise, ensuring equal access to knowledge for all stakeholders: orientating users and actors in the field in the mass of information online.**

Rare diseases patients are scattered across the globe, as are rare disease experts. Orphanet provides visibility to experts and for patients by providing access to a catalogue of expert services in 35 of the 41 consortium countries by disease, such as centres of expertise, laboratories and diagnostic tests, patient organisations, research projects and clinical trials. This data promotes networking, tackles isolation and helps foster appropriate referrals. Orphanet draws on the expertise of professionals from across the world to provide scientific data on rare diseases (gene-disease relationships, epidemiology, phenotypic features, functional consequences of diseases, etc.). In addition, Orphanet produces an encyclopaedia of rare diseases, progressively translated into the 7 languages of the database (English, French, Spanish, Italian, German, Dutch, Portuguese) with texts also currently available in Polish, Greek, Slovak, Finnish and Russian, freely available online. Orphanet integrates and provides access to high quality information produced around the world, such as clinical practice guidelines and information geared to the general public.

- **Contribute to generating knowledge on rare diseases: piecing together the parts of the puzzle to better understand rare diseases.**

To develop and curate the scientific data in the Orphanet database, Orphanet works with experts from around the globe, from healthcare professionals and researchers, to patient representatives and professionals from the medical-social sector. The wealth of data in Orphanet and the way this data is structured allows additional knowledge to be generated, helping to piece together data that at times can resemble pieces of an irresolvable puzzle. Integration of this data adds value and renders it interpretable. Orphanet provides standards for rare disease identification, notably via the Orphanet nomenclature, an essential key for interoperability. Orphanet provides integrated, re-usable data essential for research on the www.orphadata.org platform and as a structured vocabulary for rare diseases, the Orphanet Ontology of Rare Diseases (ORDO). These resources contribute to improving the interoperability of data on rare diseases across the globe and across the fields of health care and research. They are being integrated in several bioinformatics projects and infrastructures around the world in order to improve diagnosis and treatment. Orphanet is committed to networking with partners across the globe in order to help contribute to generating new knowledge on rare diseases.

The integral role played by Orphanet in the research and care spheres has led to its recognition as an [IRDiRC Recognised Resource](#), and integration in the French node of [ELIXIR](#), a European Research Infrastructure Consortium uniting Europe's leading life science organisations. Orphanet is also a [Human Variome Project Recommended System](#). Orphanet and the ORPHA nomenclature are also cited as key resources in every European legislative text on rare diseases and as key measures in many national plans/strategies for rare diseases.

1.2. Our services and products

[Orphanet](#) is currently a comprehensive resource of information and data on RD, notably in terms of referenced documents. It is also the only project that establishes a link between diseases, the existing textual information concerning RD and the appropriate services for patients, researchers, healthcare professionals and decision makers. Moreover, Orphanet's database content is robust and expert validated, updated continuously, and quality controlled. These unique features make Orphanet an essential tool for different stakeholders, in particular health professionals and researchers, to keep up to date with the constantly evolving knowledge concerning RD.

The data in the database is accessible via a variety of media: the Orphanet website (www.orpha.net), the Orphanet mobile application, the Orphanet data download platform "Orphadata" (www.orphadata.org), the Orphanet Rare Disease Ontology (ORDO), and the Orphanet Report Series reports.

- **The Orphanet website provides access to:**
 - A [comprehensive inventory of rare diseases classified according to a polyhierarchical classification system](#). Each disease is mapped with ICD-10, Online Mendelian Inheritance in Man (OMIM), Medical Subject Headings (MeSH), Unified Medical Language System (UMLS), Genetic and Rare Disease Information Center terms (GARD), Medical Dictionary for Regulatory Activities (MedDRA), and associated genes, within its 'identity card' that also includes the relevant prevalence category, age of onset category, and mode of inheritance. Diseases are also annotated with phenotypic features and frequency using HPO, epidemiological data and their functional consequences.
 - An encyclopaedia covering more than 6,900 rare diseases or group of diseases, with summary texts written by scientific writers and reviewed by world-renowned experts. Summary texts are produced in English and are then translated into French, German, Italian, Portuguese, Spanish, Dutch, Polish, Slovak, Greek and Finnish. For certain selected diseases, emergency guidelines and articles for the general public are produced in French and then translated.
 - An [inventory of high quality articles published by other journals or learned societies](#). More than 3000 articles are available via Orphanet, with the permission of the 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.
 - An [inventory of orphan drugs and of drugs intended for rare diseases](#), at all stages of development, from orphan designation to market authorisation.
 - A catalogue of expert services, validated by national experts in the 35 member countries and providing information on: [specialised expert centres and centres of expertise](#), [medical laboratories](#), [research projects](#), [clinical trials](#), [patient registries and mutation databases](#), [networks](#), [technological platforms](#) and [patient organisations](#).
 - Thematic studies and reports on overarching subjects: the "[Orphanet Report Series](#)" (ORS), published as PDF documents.
 - [OrphaNews](#). The newsletter of the rare disease community, written in English, covering both scientific and political news. This newsletter is also published in [French](#) and [Italian](#).

- **Orphanet data is available via two mobile apps:**
 - **Orphanet:** an app in 6 languages (English, French, Spanish, German, Italian, Portuguese) allowing users to access the list of rare diseases, textual information concerning the disease and associated services, as well as Emergency Guidelines. The app is available via for [iOS](#) and [Android](#).
 - **Orpha Guides:** an app in French giving access to information on French national support mechanisms for patients and their families, as well as information concerning the functional consequences of over 200 rare diseases. The app is available for [iOS](#) and [Android](#).
- **The Orphadata platform (www.orphadata.org)** provides high-quality datasets related to rare diseases and orphan drugs, in a reusable and computable format.
 - Freely available datasets: Orphanet Rare Disease Ontology, Orphanet nomenclature and cross-references with other terminologies, classifications, disorders with associated genes, phenotypes associated with rare disorders, linearisation of rare disorders;
 - Datasets available via Data Transfer Agreement/Licence: Textual information, catalogues of patient organisations, expert centres, clinical laboratories and diagnostic tests, orphan drugs, research activities, and epidemiological data.
- **The Orphanet Rare Disease Ontology ([ORDO](#))**, a structured vocabulary for rare diseases derived from the Orphanet database, capturing relationships between diseases, genes and other relevant features. ORDO provides integrated, re-usable data for computational analysis.
- **The Orphanet Report Series ([ORS](#))** are thematic studies and reports on overarching subject, derived from data in the Orphanet database, published as PDF documents.
- The **Orphanet Knowledge Management Platform (<http://curation.orphanet.org/>)** allows experts in the field of rare diseases to help curate the scientific data in the Orphanet database in a traceable and transparent manner.

1.3. Highlights of 2017

Orphanet international positioning

- The year marked the **20th anniversary of the creation of Orphanet**. To celebrate the occasion, Orphanet teams present and past, as well as institutional representatives and Orphanet's strategic partners, were invited to a dinner in Paris. The representatives of the European Commission and INSERM gave opening speeches, reaffirming their support of this essential resource for the rare disease community. Ségolène Aymé, the evening's guest of honour, was presented by Ana Rath, on behalf of Orphanet teams both past and present, a symbol of recognition and gratitude for her action and involvement as founder of Orphanet.
- The 20th anniversary of Orphanet was also the perfect occasion to give the Orphanet website a complete makeover. The **new look and feel of the Orphanet website** was launched in

March 2017. The new site has been designed to improve navigation. The design is responsive, making it easier to consult on a range of different devices, and the lay-out makes data easier to read.

- At the start of 2017, the **OrphaNews newsletter also underwent a complete makeover**. A new front and back office have improved the look and feel of the newsletter, ease publication processes, and also allow for the implementation of new functionalities. Navigation has been improved through the construction of distinct sections, articles can be shared more easily, and the design is responsive on a range of different mobile devices. Users can now search the archives using an in-house thesaurus of terms, making it easier to find information concerning a certain subject or disease.
- **Orphanet formally invited the newly designated European Reference Networks to collaborate** in order to improve the Orphanet nomenclature and classifications, scientific annotations, encyclopedia and exhaustivity of the directory of expert services in Europe. A workshop was held in April 2017 to present the newly launched Orphanet Knowledge Management System (see *Improving Transparency and Traceability*).
- The **Orphanet Consortium officially extended its reach to Asia and welcomed its 41st member country, Japan**. The Translational Research Informatics Center (TRI) (Currently known as Translational Research Center for Medical Innovation) through the Agency for Medical Research and Development (AMED) has been designated to fulfil this role, and is in the process of building the Orphanet Japan team.
- **Cross-referencing with GARD identifiers in the disease identity cards** was published in 2017 on the Orphanet website, in the scope of the collaboration agreement signed in 2016 with the National Institutes of Health, USA.

Improving transparency and traceability

- **In addition to the general SOPs** available online since 2013, that are updated regularly, the procedures used for the **alignments with ICD-10** and those used to carry out the **linearisation of disorders** are available online since 2014. The following procedures were published online in 2017:
 - **[Orphanet inventory of rare diseases](#)**
 - **[Naming rules for the rare disease nomenclature in English](#)**
 - **[Creation and Update of Disease Summary Texts for the Orphanet Encyclopaedia for Professionals](#)**
 - **[Orphanet inventory of genes related to rare diseases](#)**
 - **[International Advisory Board rules of procedure](#)**
 - **[Orphanet Advisory Board on Genetics Rules of procedures](#)**
 - **[Glossary and representation of terms related to diagnostic tests](#)**
- Orphanet published a dedicated **Orphanet Report Series crediting the experts having contributed to the update of scientific data in Orphanet** in 2017.
- The **Orphanet Knowledge Management Platform** (<http://curation.orphanet.org/>) was launched in 2017. This platform has been developed by partners of the RD-Action consortium in Australia. This platform allows experts in the field of rare diseases to help curate the scientific data in the Orphanet database in a traceable and transparent manner. A RD-Action workshop was held in

April 2017 to present the platform to European Reference Networks (ERNs), who will be key end-users of this tool. The curation platform provides a different visualisation of the data in the Orphanet database, with icons next to editable data to ease the sourcing of expert input. Curators at Orphanet are alerted of the suggestion and a discussion between experts can be initiated using the platform. For the moment, experts have the possibility of registering via the platform, stating the diseases for which they have expertise, and providing suggestions to curate the nomenclature, definitions and abstracts in the Orphanet database. Other types of scientific data, such as genes, phenotypes and epidemiological data will be open for suggestions in a second step. ERNs have been formally invited to curate data concerning their field of expertise using the platform as part of collaborative activities with Orphanet in 2017. The main fields of collaboration initiated include the Orphanet nomenclature and classifications, as well as the update of the expert services directory.

- Led by the University of Tübingen, the [Solve-RD consortium](http://www.solve-rd.eu) www.solve-rd.eu, allocated €15 million by the European Commission Horizon 2020 programme, will work from 2018 to improve the diagnosis of rare diseases, hand in hand with the new European Reference Networks (ERN) on rare diseases. The Orphanet coordinating team at INSERM is leading the work package in charge of collecting standardised genetic and phenotypic information concerning unsolved rare diseases cases from ERN cohorts and the European Genome Archive, and developing an ontology of unsolved cases that will work alongside the Orphanet Rare Disease Ontology (ORDO) and the HPO-ORDO Ontological Module (HOOM) in order to make new diagnostic hypotheses.

Orphanet database updates

- Scientific information: [the Encyclopaedia of RD, the Inventory and classification of RD, the inventory of genes and the inventory of Orphan drugs have all been expanded and updated.](#)
- The catalogue of expert services: [expert centres, medical laboratories, clinical trials, research projects, networks, registries, infrastructures, mutation databases, biobanks and patient organisations have been expanded and updated.](#)

Orphanet documents update

- [The Orphanet Report Series have been updated:](#) List of Rare Diseases, Prevalence of Rare Diseases, Lists of Orphan Drugs, Registries, List of Research Infrastructures useful to Rare Diseases in Europe, Orphanet Activity Reports, List of experts contributing to the database, and User surveys, as well as the Report '*Vivre avec une maladie rare en France*' (*Living with a rare disease in France*). The list of rare diseases was produced for the first time in Polish and Czech.
- [The Orphanet Activity report 2016 was translated into French, Spanish and Polish.](#)
- [The Orphadata user guide was updated.](#)
- [The Orphanet annual user survey was updated](#) so as to collect feedback on the new Orphanet website.

Orphanet website information

- In 2017 Orphanet launched a YouTube channel to host video tutorials aimed at helping users understand the Orphanet nomenclature of rare diseases, and search for a disease/gene on the website. Videos are available in English and French, with other languages (subtitles) added progressively.

- A cartographical representation of European Reference Networks was added to the website, enabling users to better visualise the composition and geographical coverage of these networks.
- A pilot was launched with four Orphanet national teams (Germany, the Netherlands, Spain and Switzerland) for the registration of panels of genes in the Orphanet database.
- Cross-references with the LOVD database were added to the gene identity cards on Orphanet.
- In 2017, the Orphanizer ([Phenomizer-Orphanet](#)) tool was launched in beta allowing users to retrieve a differential diagnosis using a set of phenotypes from HPO. This tool has been developed by the Charité, Berlin, Germany and is currently being revised before relaunch in 2018.
- A tab to access the Orphanet data on functional consequences of handicaps was added to the website in 2017.
- The presentation of networks was improved on the website: details of participants in a network are included in the network page, and vice-versa.
- The standard notation for ORPHA numbers changed from ORPHAXXX to ORPHA:XXX to comply with terminology notation practices.
- ORDO V2.3 and V2.4 were launched in 2017.
- Orphadata free-access data sets were made available in .JSON format. The Orphanet nomenclature was made available in Polish.

Codification of RD using ORPHA codes

- The implementation of ORPHA codes in national and regional health information systems is ongoing. In addition to the progression of this implementation in [Germany and France](#), pilot experiences are being conducted in [Hungary, Latvia and Norway](#). ORPHA codes are currently being used in centres of expertise in [the Netherlands and Slovenia](#). ORPHA codes are also being implemented in national patient registries in [Portugal, UK and Spain](#), in addition to regional registries in other countries such as Italy. In [Switzerland](#), the Hôpitaux Universitaires de Genève and CHUV implement ORPHA codes in digital patient records since 2015. The use of ORPHA codes as a complement to already existing coding systems is being explored in most EU Member States, as recommended by the European Commission Expert Group on Rare Diseases. A [mapping exercise](#) of the use of ORPHA codes in Europe was carried out in the context of RD-Action and was made available in 2017.

Users satisfaction

- **Users are satisfied with the utility of the services provided by Orphanet:** in the 2017 satisfaction survey, on average 86% of respondents stated that the services they knew of and used were very useful or useful to them.
- **7.8 million PDF documents downloaded in 2017.**
- **9.3 million visitors last year from 235 countries.**

A freely accessible site available in **7 languages**

30 million pages viewed in 2017

7.8 million PDF documents downloaded in 2017

An **IRDiRC Recognized Resource** and **HVP Recommended System**



Diseases

6,151 rare diseases with unique identifiers : ORPHA numbers

3,898 genes for 3,739 rare diseases

2,963 diseases annotated with HPO terms

5,648 diseases annotated with prevalence/incidence data

Rare disease summaries in 12 languages

4,595	English
3,334	Italian
3,282	French
3,165	German
3,169	Spanish
1,180	Portuguese
662	Dutch
167	Finnish
831	Polish
423	Greek
103	Slovak
255	Russian

Directory of expert resources in 41 countries worldwide

22,184	professionals
7,400	expert centres
2,599	patient organisations
1,648	medical laboratories
44,129	diagnostic tests
1,745	research laboratories
1,997	research projects
1,792	clinical trials
727	patient registries
270	mutation databases
142	biobanks

Figure 1 Orphanet in numbers (January 2018)

2. Orphanet consortium

2.1. The RD-ACTION Joint Action

Orphanet has become a backbone for the rare disease community, with the substantial amount of data developed being not only essential as leverage both for scientific projects as well as policies related to rare diseases in Europe, but also for increasing the awareness and the dissemination of knowledge on RD. Orphanet is mentioned in the European Union's principal documents on RD (e.g. the Commission Communication "Rare diseases: Europe's challenges" of 11 November 2008 and the Recommendation of the Council on an Action in the field of rare diseases of 8 June 2009) as the source of current information on RD in the EU as well as a strategic element of any national plan/strategy on RD, which each Member State was encouraged to develop by the end of 2013. It is also mentioned as a key tool for information on RD in the directive on the application of patients' rights in cross-border healthcare (2011).



Because of this assessment, the evolution of the Orphanet database of rare diseases into a more European, sustainable model has been set as one of the main objectives of RD-ACTION (www.rd-action.eu), the new Joint Action on RD co-funded by the 3rd EU Health Programme and launched on 17th September 2015 in Luxembourg. This instrument combines funding from the European Commission and each of the participating Member States, as well as from Switzerland, Canada and Australia, as collaborating stakeholders.

Following the two previous Joint Actions (Orphanet Joint Action and EUCERD Joint Action) RD-ACTION demonstrates the renewed support of the European Commission (EC) in the field of rare diseases, through its Directorate General for Health (DG SANTE). This work will last three years (until June 2018) and follows the logic of coherence and continuity vis-à-vis the previous actions, but aims to go further in terms of concrete implementation and consolidation of policies. This action is coordinated by Orphanet (INSERM, US14), bringing together 63 European and non-European participants.

RD-ACTION has three main objectives:

- contribute to the implementation, by member states, of the recommendations of the EC Panel in relation to policies on these diseases,
- support the development of Orphanet and make it sustainable,
- help Member States to introduce the ORPHA codes in their healthcare systems to make rare diseases visible.

RD-ACTION was designed in the spirit of integration and coherence so that the data produced by Orphanet can contribute in the necessary analysis of policy recommendations and political action that will then guide the production, operation and dissemination of this data. Participants will ensure effective communication between each of the member states and the EC Panel, in order to concretely support the implementation of their recommendations. Most of the Orphanet country coordinators contribute to the work of RD-ACTION's work packages, therefore participating to the RD codification and policy implementation.

2.2. Orphanet's Governance

To ensure optimal governance and efficient management of the workflow, [Orphanet's governance](#) is organised by three different boards:

- The **Management Board**, composed of country coordinators, is in charge of identifying funding opportunities, approving the global strategy of the project and thus guide the project in its endeavour to provide an optimum service for the end-users, and considering the inclusion of new teams as well as ensuring the continuity of the project.

External boards:

- The **International Advisory Board**, composed of international experts, is in charge of advising the Management Board regarding the overall strategy of the project.
- The **Genetic Advisory Board**, composed of geneticists is in charge of advising Orphanet on topics related to the gene database and the database of genetic tests and laboratories.

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

In the framework of the RD-Action Joint Action 2015-2018, most of the Orphanet activities are co-funded by the EC. As a result, the Orphanet Management board also refers to the General Assembly of the RD-Action project (please refer to www.rd-action.eu for additional information).

2.3. Expansion of the consortium

Since its creation, the quality of data provided by Orphanet has built its reputation and as a result Orphanet has grown as a European consortium, gradually expanding to a Consortium of 35 countries to the East and to the South. In 2011, Orphanet went further west to include Canada. The consortium expanded towards Australasia, with Western Australia joining in 2012. In 2014, Georgia and Tunisia joined the consortium followed by Argentina (the first South American country), in 2015. Japan officially joined Orphanet in 2017 and collaboration is underway to explore the possibility of creating an Orphanet – China team.

Please refer to the organisational chart at the end of this document for more information about the participating Institutions and team members.

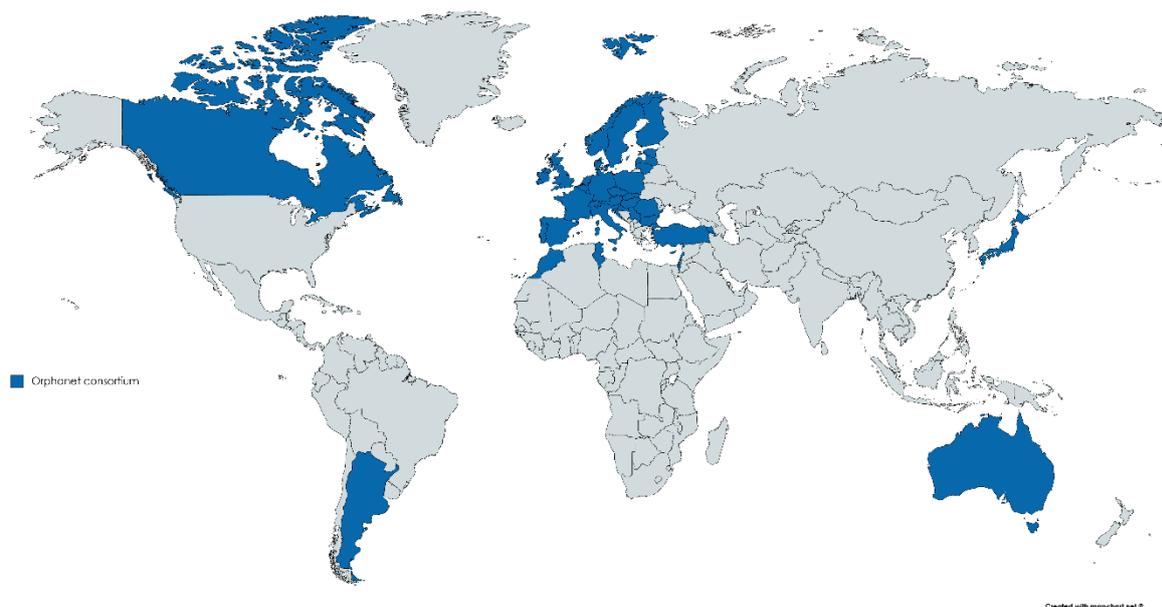


Figure 2 Orphanet members and contact points (December 2017)

2.4. Orphanet members and scope of their activity

2.4.1. COORDINATING TEAM

INSERM (the French National Institute of Health and Medical Research) , having run Orphanet since 1997, coordinates the Orphanet coordinating team. The INSERM team is based at Service Unit 14.

The coordinating team is responsible for the coordination of consortium activities, the hardware and software aspects of the project, the database of rare diseases (including nomenclature in English, classifications, ontology, gene-disease relationships), the production of the encyclopaedia, technology transfer/business development, partnerships, and the global communications strategy, as well as the training of all members of the consortium and 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 their designation stage to their marketing authorisation.

A transition in the distribution of activities is underway so as to allow Orphanet consortium members to take on responsibilities in the core activities (starting with the production of the encyclopaedia) in addition to the collection and translation activities described in 2.4.2.

2.4.2. MEMBERS

The establishment of a catalogue of resources can only be achieved by the consolidation of data collected at the country level. The identification of expert services 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 provide a suitable work environment for the information scientists, in terms of documentation, secretarial facilities and access to the network.

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

Translations of the Orphanet content in the national language are also managed by the national teams, provided that they have a sufficient budget. At the end of 2017 Belgium, France, Germany, Italy, Spain and Portugal are undertaking the translation of the entire website's content into their national language, while the Polish, Finnish, Slovak teams are translating the summary texts encyclopaedia. The Orphanet nomenclature is currently translated into the 7 languages of the website, and also into Polish. In 2018 the website is being progressively translated into Polish.

From 2016, the transition to a more distributed model for the production of the encyclopaedia was launched, with members of the Orphanet Sweden, Slovakia and Ireland teams assuming responsibility for part of the production of texts in English.

The development of the [Orphanet Knowledge Management Platform](#), a platform allowing experts in the field of rare diseases to help curate the scientific data in Orphanet, was carried out in 2016 by partners of the RD-Action consortium in Australia.

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

2.4.3. ORPHANET CONTACT POINTS

All national contact points are located in high-profile institutions. However, in these countries no dedicated funding is allocated to Orphanet activities, therefore there is no active data collection on expert services. The national contact point is in charge of validating the already available national information and the data submitted by national professionals through the online registration tool.

3. Orphanet: Products and services

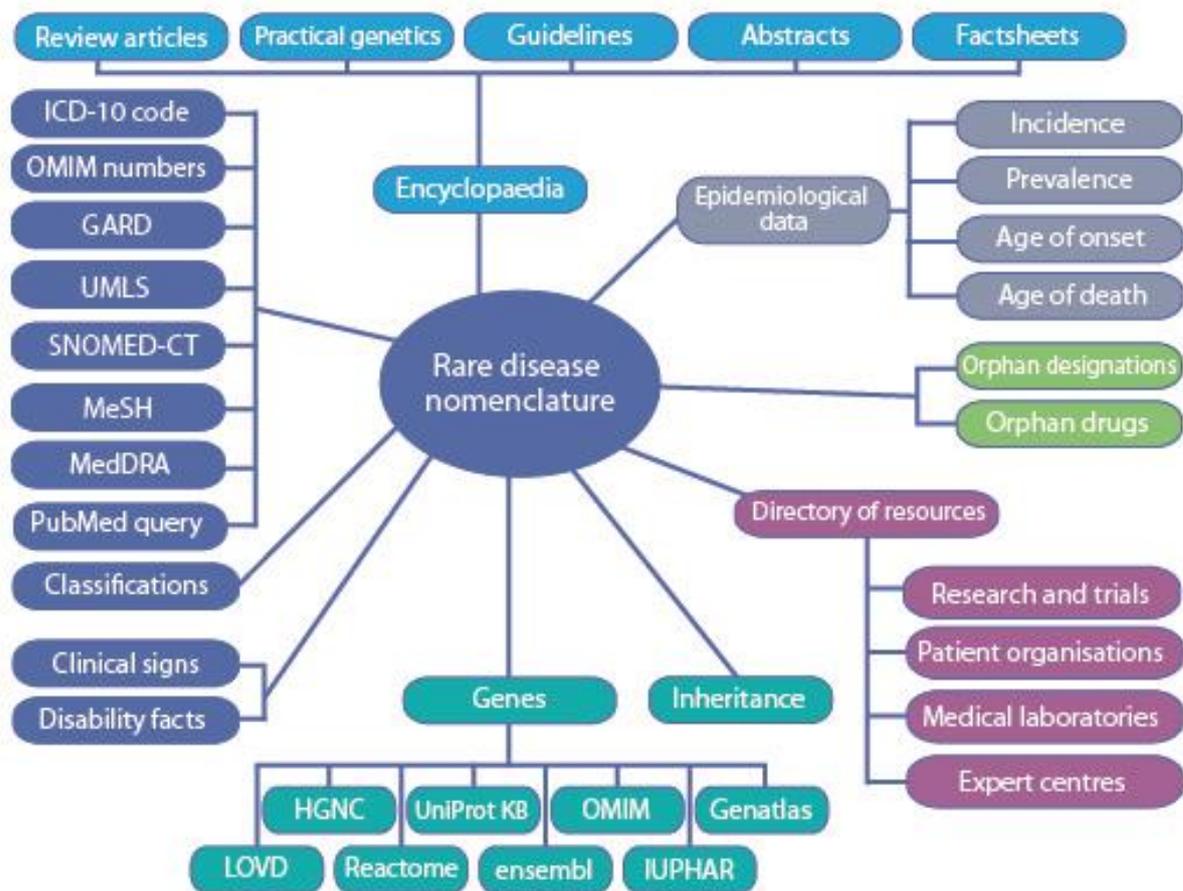


Figure 3 The Orphanet database

Orphanet is an evolutive, relational knowledge database with added value, as the scientific content produced in-house is expert-validated (list of expert reviewers having contributed to the scientific content is presented each year as [a dedicated Orphanet Report](#)) and integrated with other available resources, as shown in the diagram presented in Figure 3 and described hereafter.

Disorders in the Orphanet disease database correspond to rare diseases (defined in Europe as having a prevalence of not more than 1/2,000 persons in the European population), rare forms of common diseases, and diseases for which prevalence figures are unknown but are potentially rare. Some diseases that are non-rare in Europe but that are rare in other countries, like the USA, can be considered for inclusion if their addition is necessary in order to represent expert services in these countries.

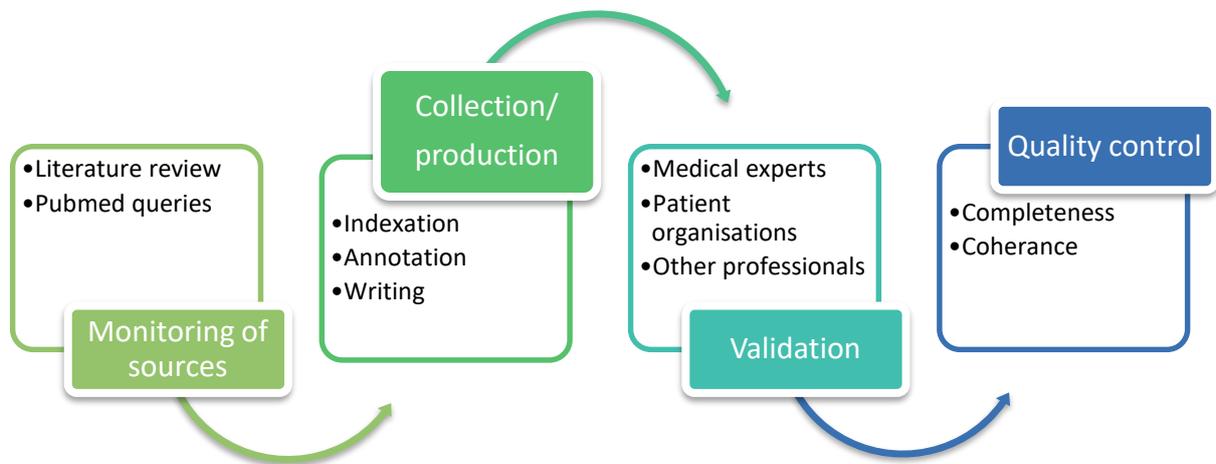


Figure 4 Orphanet data production methodology

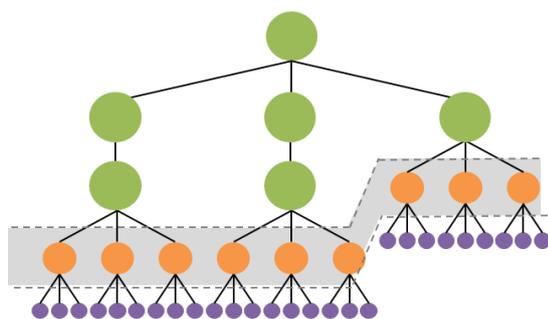
The update of the scientific content of the database is performed using a four step methodology (Figure 4) which consists of a survey of sources, allowing for the collection and production of data by identifying new syndromes, genes or treatments, for the update of classifications of diseases, and is the basis for the production of various texts (encyclopaedia, guidelines, etc.). All texts and data (annotations on epidemiological data, phenotypes, functional consequences of the disease, genes, etc.) are externally validated (either by internationally recognised experts, learned societies and/or patient organisations, according to the type of text or data). A final step of quality control is carried out to ensure the coherence and completeness of the database.

All the teams that make up the Orphanet consortium are responsible for the collection, validation and submission of data on expert services in their country. In order to publish data which is relevant and accurate (complete, valid and consistent with other data from the database), validation and quality control is carried out 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. Orphanet content: Inventory of rare diseases

Orphanet provides a comprehensive inventory of rare diseases classified according to a polyhierarchical classification system. As new scientific knowledge issues arise, the Orphanet RD inventory and classification system is maintained with regular additions/updates of diseases based on peer-reviewed publications. 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 aetiological criteria, when diagnostically or therapeutically relevant. The Orphanet classification provides the scope and level of granularity (Figure 5) needed by health professionals with different specialties, including categories (e.g. rare neurological disease), clinical groups (e.g. rare ataxias), disorders (e.g. Machado-Joseph disease) and subtypes (e.g. Machado-Joseph disease type 1).



Groups:

- Categories, clinical groups

Disorders:

- Diseases, clinical syndromes, malformation syndromes, morphological anomalies, biological anomalies, particular clinical situations

Subtypes:

- Etiological, clinical, histopathological

Figure 5 Schema of the Orphanet nomenclature and classifications

Since 2014, each entity in the nomenclature is assigned precisely one of these categories, allowing more accurate information on their typology and exact count. In addition, for diseases now recognised as part of another disease, Orphanet redirects users towards the disease that is now accepted according to recent literature. The disease database contains 9,408 clinical entities¹ and their synonyms (including 6,151 disorders²). The nomenclature and classifications can be viewed directly on the www.orpha.net website and/or extracted from Orphadata in [XML and JSON formats](#).

¹ Diseases, malformation syndromes, morphological anomalies, biological anomalies, clinical syndromes, particular clinical situation in a disease or syndrome, group of phenomes, etiological subtypes, clinical subtypes, histopathological subtypes, data from January 2018.

² Diseases, malformation syndromes, morphological anomalies, biological anomalies, clinical syndromes, particular clinical situation in a disease or syndrome, data from January 2018.

The Orphanet nomenclature is aligned to other terminologies so as to provide a backbone for semantic interoperability between different systems. Rare diseases are aligned with ICD-10 codes (see Table 1). This process follows a set of rules, depending on whether rare diseases are mentioned or not in the tabular list or in the index of ICD-10. Rules for attribution of an ICD-10 code for diseases that are not listed in the ICD are established. More details on the process can be found in Orphanet’s [ICD-10 coding rules for RD procedure](#). The ICD-10 alignment is manually curated.

Codes	Aligned ORPHA numbers
ICD-10	7,067

Table 1 Number of disorders, groups of disorders or subtypes aligned to ICD-10 codes (January 2018)

Diseases are mapped to one or more OMIM numbers (see Table 2). Exact mappings between the Orpha nomenclature and other terminologies (UMLS, GARD, MeSH and MedDRA) are available online (see Table 2). Mappings to SNOMED-CT are produced in collaboration with IHTSDO and are available upon request to IHTSDO. Mappings are carried out in a semi-automatic way and are manually curated. Updates follow UMLS releases once a year.

All mappings are qualified (exact; narrow-to-broad; broad-to-narrow) and information on the validation status is available. Further annotations are carried out for ICD-10 terms: specific code, inclusion or index term, code attributed by Orphanet, with indication of the validation status.

Terminologies/resources	Mapped disorders, groups of disorders & subtypes
UMLS*	4,833
MeSH*	1,753
SNOMED CT*	5,813
MedDRA	1,164
OMIM**	4,491
GARD	3,933

*Table 2 Number of mapped diseases (groups of disorders, disorders and sub-types) per terminology (January 2018) *Exact mappings **All mappings*

The Orphanet nomenclature is annotated with phenotypes. From 2015 Orphanet disorders are annotated with the Human Phenotype Ontology, a standard and controlled terminology covering phenotypic abnormalities in human diseases, recognised as the reference in the domain, and a designated IRDIRC Recognized Resource. Each phenotypic term is associated with the frequency of occurrence (obligate, very frequent, frequent, occasional, very rare, excluded), and whether the annotated HPO term is a major diagnostic criterion or a pathognomonic sign of the rare disease. As a result of this work, 2,963³ diseases are annotated with HPO terms. Further annotations to HPO are being carried out. In 2017, the Orphanizer tool ([Phenomizer-Orphanet](#)) tool was launched in beta

³ As of January 2018.

allowing users to retrieve a differential diagnosis using a set of phenotypes from HPO. This tool has been developed by Sebastian Köhler from the Charité, Berlin, Germany and is currently being revised before relaunch in 2018.

Orphanet provides **epidemiological and natural history information** on each rare disease. Disease inheritance and age of onset categories are provided (Table 3). Prevalence, annual incidence, prevalence at birth and lifetime prevalence data are now documented in addition to the prevalence intervals available on the website (for Europe, USA and worldwide) (Table 4). Minimum, maximum and mean figures for each item are documented according to geographic zones, when information is available in Orphadata. The number of cases or families reported in the literature is also indicated for very rare diseases. Data sources and validation status are supplied for all data. This new epidemiological data is available for more than 5,600 diseases (groups of diseases, disorders and sub-types) and constitutes a unique and global source of information which we hope is useful to all users concerned, namely policymakers, the research community and the orphan drug industry involved in orphan drug development. The data are made available for download on www.orphadata.org.

Natural history data	Number of groups of disorders, disorders and sub-types
Average age of onset	5,672
Mode of inheritance	5,327

Table 3 Number of disease (groups of diseases, disorders and sub-types) per natural history data (January 2018)

Epidemiological data	Number of groups of disorders, disorders and sub-types
Point prevalence	5,646
Prevalence at birth	504
Lifetime prevalence	46
Annual incidence	552

Table 4 Number of diseases (groups of disorders, disorders and sub-types) per epidemiological data (January 2018)

Orphanet also provides **information on activity limitation/participation restriction (functional consequences)** described in rare diseases, using the Orphanet Functioning Thesaurus, derived and adapted from the International Classification of Functioning, Disability and Health – Children and Youth (ICF-CY, WHO 2007). The provided information is assessed from the whole patients' population affected by the disease, receiving standard care and management (specific and/or symptomatic management, prevention and prophylaxis, devices and aids, care and support). Functional consequences are organised by their frequency in the patient population. Each functional consequence is recorded with: frequency in the patients' population, temporality, degree of severity, loss of ability when relevant, defined by the progressive and definitive loss of a skill or participation over the course of the disease. There are currently 300 clinical entities indexed with the thesaurus.

3.1.1. ADDITIONAL FUNCTIONALITIES IN 2017

In 2017 Orphanet launched a YouTube channel to host video tutorials aimed at helping users understand the Orphanet nomenclature of rare diseases, and search for a disease or a gene on the website. Videos are available in English and French, with other languages (subtitles) added progressively.

The Orphanizer (Phenomizer-Orphanet) tool was launched in beta allowing users to retrieve a differential diagnosis using a set of phenotypes from HPO. This tool has been developed by the Charité, Berlin, Germany and is currently being revised before relaunch.

Cross-referencing to GARD (Genetic and Rare Disease Information Center, National Institutes of Health) identifiers were added to the disease identity cards.

A new tab to access the Orphanet data on functional consequences of handicaps was added to the website in 2017.

3.2. Orphanet content: Orphanet inventory of genes

Genes involved in rare diseases are entered in the database and updated regularly according to new scientific publications. Genes are associated with one or more diseases, with one or more genetic test, and mutation databases and/or research projects. The data registered includes: annotation with the main name and symbol of the gene (from HGNC) and its synonyms, as well as its HGNC, UniProtKB, GenAtlas and OMIM references (in order to cross-reference these websites), in addition to Ensembl (an EMBL-EBI database that maintains automatic annotations for selected eukaryotic genomes), Reactome (an EMBL-EBI open-source, open access, manually curated and peer-reviewed pathway database) and IUPHAR (International Union of Basic and Clinical Pharmacology) databases. The relationship between a gene and a disease is manually qualified according to the role that the gene plays in the pathogenesis of a disease: causative (both from germline or somatic mutations), modifiers (germline), major susceptibility factors, or playing a role in the phenotype (for chromosomal anomalies). For the disease-causing germline mutations, the information, whether pertaining to a gain or loss of function for the protein, is also provided when available. 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 diagnostic and therapeutic research.

Information on the typology of the gene (i.e. gene with protein product, non-coding RNA, disorder-associated locus), its chromosomal location and all former symbols and synonyms is also provided.

3.2.1. ADDITIONAL FUNCTIONALITIES IN 2017

Cross-references with the LOVD database were added to the gene identify cards on Orphanet.

3.3. Orphanet content: Orphanet encyclopaedia

Three distinct encyclopaedias are provided on the Orphanet website: one for health professionals, one for the general public, and one related to disabilities.

3.3.1. HEALTH PROFESSIONALS ENCYCLOPAEDIA

- **Summary information**

Textual information on a disease can be presented in the form of a definition, an abstract, or as an automatically generated text (7,500 entities in the database have one of these forms of textual information).

Orphanet texts (apart from the automatically generated) are unique and written in English by a member of the editorial team. Definitions and abstracts are then reviewed by an invited world-renowned expert. Abstracts and definitions are structured in up to 10 sections: Disease definition – Epidemiology – Clinical description – Aetiology – Diagnostic methods – Differential diagnosis – Antenatal diagnosis (if relevant) – Genetic counselling (if relevant) – Management and treatment – Prognosis. Summary information for 4,595 rare diseases was available online at the start of 2018.

They are progressively translated into the six other languages of the website (French, Italian, Spanish, German, Portuguese and Dutch). In addition, 167 abstracts are now available in Finnish, 423 in Greek, 831 in Polish, 255 in Russian, and 103 in Slovak. For an additional 2,905 entries in the disease inventory, textual information is provided through automatically generated texts (for diseases labelled as a group of diseases, deprecated entries, subtypes of disorders, particular clinical situations for which there is an orphan designation and conditions for which there is a pharmacogenetic test in the inventory).

- **Orphanet Emergency Guidelines**

These guidelines are intended for pre-hospital emergency healthcare 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 (*SFMU* in France): as of January 2018, 85 emergency guidelines in French are available online. They are being translated into the following six languages: English, German, Italian, Portuguese, Spanish and Polish. 20 emergency guidelines are available in English, 45 in Italian, 24 in German, 35 in Spanish, 17 in Portuguese, and 16 in Polish.

Emergency guidelines were downloaded more than 134,800 times in 2017.

Epidemiology:

5,646 diseases annotated with point prevalence data

Natural history:

5,327 diseases annotated with mode of inheritance

5,672 diseases annotated with age of onset

Mappings:

7,067 diseases mapped to ICD-10

4,491 diseases mapped to OMIM

4,833 diseases mapped to UMLS

1,164 diseases mapped to MedDRA

1,753 diseases mapped to MeSH

3,933 diseases mapped to GARD

Genes:

3,898 genes linked to 3,739 rare diseases

3,869 genes interfaced with HGNC

3,823 genes interfaced with OMIM

3,804 genes interfaced with Genatlas

3,818 genes interfaced with UniProtKB

3,830 genes interfaced with Ensembl

488 genes interfaced with IUPHAR-DB

3,150 genes interfaced with Reactome

2,236 diseases interfaced with a Pubmed query

2,963 diseases indexed with HPO terms (clinical signs)

300 clinical entities indexed with CIF-derived terms

5,597 external links for 5,277 diseases

In-house produced texts: 122 articles for the general public in French, 85 emergency guidelines in French, translated in German, English, Spanish, Italian, Portuguese, and Polish. 50 Disability factsheets in French

Link to external RD literature

539 Review articles
663 Clinical genetics reviews
426 Clinical practice guidelines
137 Guidance for genetic testing
1470 General public articles
22 Emergency guidelines

The Orphanet encyclopaedia contains the following summary texts:

- 4,595 English
- 3,334 Italian
- 3,282 French
- 3,165 German
- 3,169 Spanish
- 1,180 Portuguese
- 662 Dutch
- 167 Finnish
- 831 Polish
- 423 Greek
- 103 Slovak
- 255 Russian

The screenshot shows the Orphanet search interface for 'Achondroplasia'. It includes a search bar with the text 'Achondroplasia', a search button, and a list of search filters: Disease name (selected), OMIM, Gene name or symbol, Orpha number, and ICD-10. Below the search bar, the disease name 'Achondroplasia' is displayed with a 'Suggest an update' button. The 'Disease definition' section states: 'Achondroplasia is the most common form of chondrodysplasia, characterized by rhizomelia, exaggerated lumbar lordosis, brachydactyly, and macrocephaly with frontal bossing and midface hypoplasia.' The 'ORPHA-15' section lists various identifiers: Synonym(s): -, Age of onset: Neonatal, MeSH: D000130, Prevalence: 1-9 / 100 000, ICD-10: Q77.4, GARD: 8173, Inheritance: Autosomal dominant, OMIM: 100800, MedDRA: 10000452, UMLS: C0001080. The 'Summary' section is partially visible. The 'Antenatal diagnosis' section is also partially visible. The 'Management and treatment' section is partially visible. The 'Prognosis' section is partially visible. The 'Expert reviewer(s): Dr Michael BOBER - Angela DUKER - Last update: April 2013' is visible at the bottom.

Figure 6 The disease database content as of January 2018

3.3.2. GENERAL PUBLIC ENCYCLOPAEDIA

The general public encyclopaedia was initially a French project supported by the First French National Plan for Rare Diseases in 2005 intended to give complete, reliable, and up-to-date information to patients and their relatives on the diseases that concern them. Since 2011, the general public encyclopaedia texts have been enriched with paragraphs on the functional consequences of rare diseases, including disabilities resulting from the disease, medical and social measures to prevent/limit them and consequences of these disabilities in daily life.

One hundred and twenty-two in-house French texts are available online. Fifteen have been translated into Spanish. Documents from this encyclopaedia were downloaded 4.15 million times in 2017. In 2016, because of the lack of dedicated funding, the production of Orphanet's in-house general public encyclopaedia was interrupted. However, Orphanet disseminates high quality texts intended for the general public that are produced by third parties (see sections Links to External Rare Disease Literature).

3.3.3 DISABILITIES ENCYCLOPAEDIA

As part of the collaboration between CNSA (French National Solidarity Fund for Autonomy) and INSERM, Orphanet provides since 2013 a collection of texts named "disability factsheets" in the Orphanet Encyclopaedia of Disability devoted to the disabilities associated with each rare disease. This 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 text contains a description of the disease (adapted from the corresponding summary 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). Since 2016 many of these texts were produced as stand-alone texts, independent of the General public encyclopaedia.

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 "Encyclopaedia for professionals" and "Disability" tabs. Fifty of these texts are available online and they are also available in the Orpha Guides app. They have been downloaded approximately 50,900 times in 2017 (Figure 7). This represents an increase of 31% compared to the 38,800 downloads in 2016. Translations into Spanish of these texts started in June 2016, with 25 translated at the end of 2017.

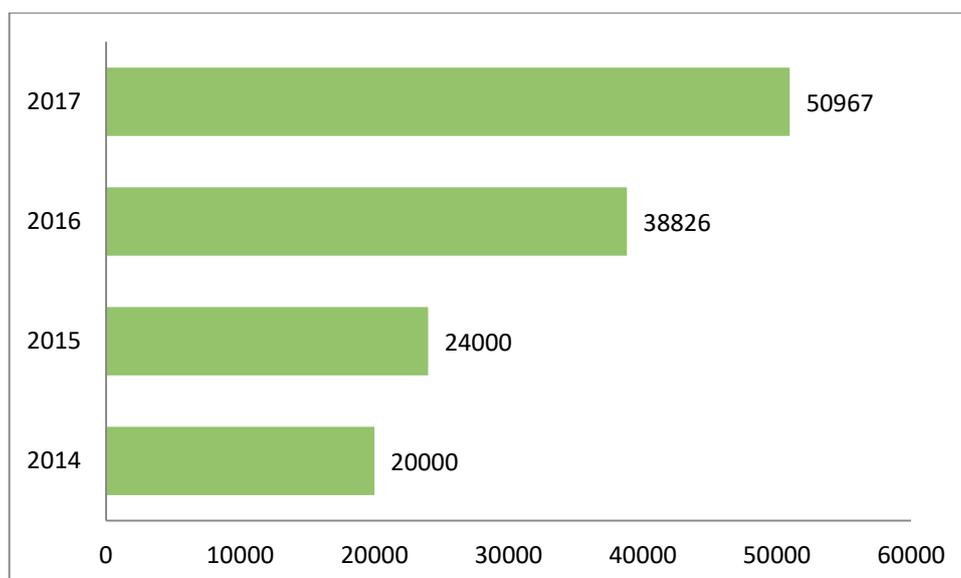


Figure 7 Evolution of number of downloads per year of the French Disability factsheets in since 2014

3.3.4. DIAGNOSTIC CRITERIA

Information on diagnostic criteria is presented in 26 concise documents intended to avoid serial misdiagnosis and to facilitate early therapeutic management. This information, identified as being recognised by experts in the field as a reference in the domain, is extracted from peer-reviewed journals, with a reference to the original paper given at the top of the page.

3.3.5. LINKS TO EXTERNAL RARE DISEASE LITERATURE

With the purpose of disseminating high quality articles through the Orphanet website, Orphanet identifies and assesses articles produced by peer-reviewed journals and learned societies in any of the languages of the Orphanet consortium. Articles are evaluated according to a set of quality criteria. Authorisations from the copyright holder are requested so as to give access to the full text. Numbers of external texts per category are presented in Table 5.

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

- **Review articles**

539 review articles (of which 223 were published in the Orphanet Journal of Rare Diseases) were online at the start of 2018.

- **Clinical Genetics Review**

These are peer-reviewed disease descriptions focusing on genetic aspects with an implication in the diagnosis, management, and genetic counselling of patients and families with specific inherited conditions. The clinical genetic review collection comprises 663 articles from GeneReviews (start of 2018).

- **Clinical 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 or expert networks and published either in scientific journals or on the learned societies' or health agencies' websites. A methodology of assessment has been developed to review the guidelines based on the AGREEII instrument in order to disseminate only the most accurate ones, after permission of the copyright holder is obtained⁴. The Orphanet website gives access to 426 best practice guidelines at the start of 2018.

- **Guidance for genetic testing**

This collection comprises summary guidance intended to disseminate the best practices in genetic testing. They include Gene Cards (published in the *European Journal of Human Genetics*). 137 guidance documents are available via the website at the start of 2018.

- **Articles for the general public**

Dissemination of general public-intended texts in all languages, externally produced by expert centres or patient organisations (produced in compliance with a reliable methodology), are now selected. 1,470 articles were available on the website at the start of 2018. The breakdown by language is presented in Table 5.

- **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 are accessible via Orphanet.

- **Emergency guidelines**

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

- **Disability factsheets**

20 disability factsheets are available in Danish, produced by Sjaeldenborger, the Danish Rare Diseases alliance.

⁴ *Clinical Practice Guidelines for Rare Diseases: The Orphanet Database*, Sonia Pavan , Kathrin Rommel, María Elena Mateo Marquina, Sophie Höhn, Valérie Lanneau, Ana Rath, PLOS One, Published: January 18, 2017, <https://doi.org/10.1371/journal.pone.0170365>

	Article for general public	Review article	Clinical practice guidelines	Guidance for genetic testing	Clinical genetics review
Croatian	27	-	-	-	-
Czech	29	-	-	-	-
English	232	426**	131	136	663
Finnish	13	-	-	-	-
French	100*	38	111	1	-
German	105	30	155	-	-
Greek	34	-	-	-	-
Hungarian	27	-	1	-	-
Italian	56	33	1	-	-
Polish	32	-	-	-	-
Portuguese	31	-	1	-	-
Romanian	31	-	-	-	-
Russian	34	-	1	-	-
Slovak	26	-	-	-	-
Spanish	43	12	22	-	-
Swedish	307	-	-	-	-

**including 223 Orphanet Journal of Rare Diseases reviews

* not including the in-house produced articles (n=112)

Table 5 Total number of Orphanet external content (January 2018): type of text per language

3.4. Orphanet content: Orphanet catalogue of expert services

Orphanet provides a catalogue of:

- Centres of expertise/genetic counselling clinics and networks of centres of expertise
- Medical laboratories and diagnostic tests
- Patient organisations and umbrella organisations
- Patient registries
- Mutation databases
- Biobanks
- Ongoing research projects
- Clinical trials
- Platforms and infrastructures

The Orphanet catalogue of expert services is produced by collecting data either from official national sources, or proactively from non-official sources by information scientists in each country of the Orphanet consortium. 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 the other data of the database.

For data from official sources, no pre-release validation is required, but quality control is performed. 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 to make sure data meets the criteria of relevance for rare diseases, to check coherence across the database and to ensure proper linking with the disease classification system. 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). At least once a year, professionals are invited to verify and update the expert services they are involved in.

The 35 countries in which Orphanet members collected data in 2017 are the following:

Argentina, Armenia, Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Morocco, the Netherlands, Poland, Portugal, Romania, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tunisia, the United Kingdom and Western Australia. Updates were received by the online registration tools for data regarding Denmark, Georgia, Lebanon and Luxembourg were managed at the coordinating team on behalf of the Orphanet contact points.

Data collection outside the Orphanet consortium:

Patient organisations in countries outside the Orphanet consortium can be registered in the database if they are an alliance and/or a member of EURORDIS and if they have a legal status or they are registered in an official journal. However, Orphanet does not ensure the regular update of this information. A disclaimer informing the users of this is available on the resource page of the website.

Research related resources (research projects, clinical trials, patient registries, biobanks and mutation databases) funded by funding agencies in countries outside of the Orphanet consortium are collected

by the coordinating team if the funding agency is [a member of the IRDiRC consortium](#). Patient registries outside of the Orphanet consortium can also be registered if they fulfill inclusion criteria (Please refer to the [technical procedures](#) for an exhaustive list of inclusion criteria).

The catalogue of expert services in the Orphanet consortium contains the following data:

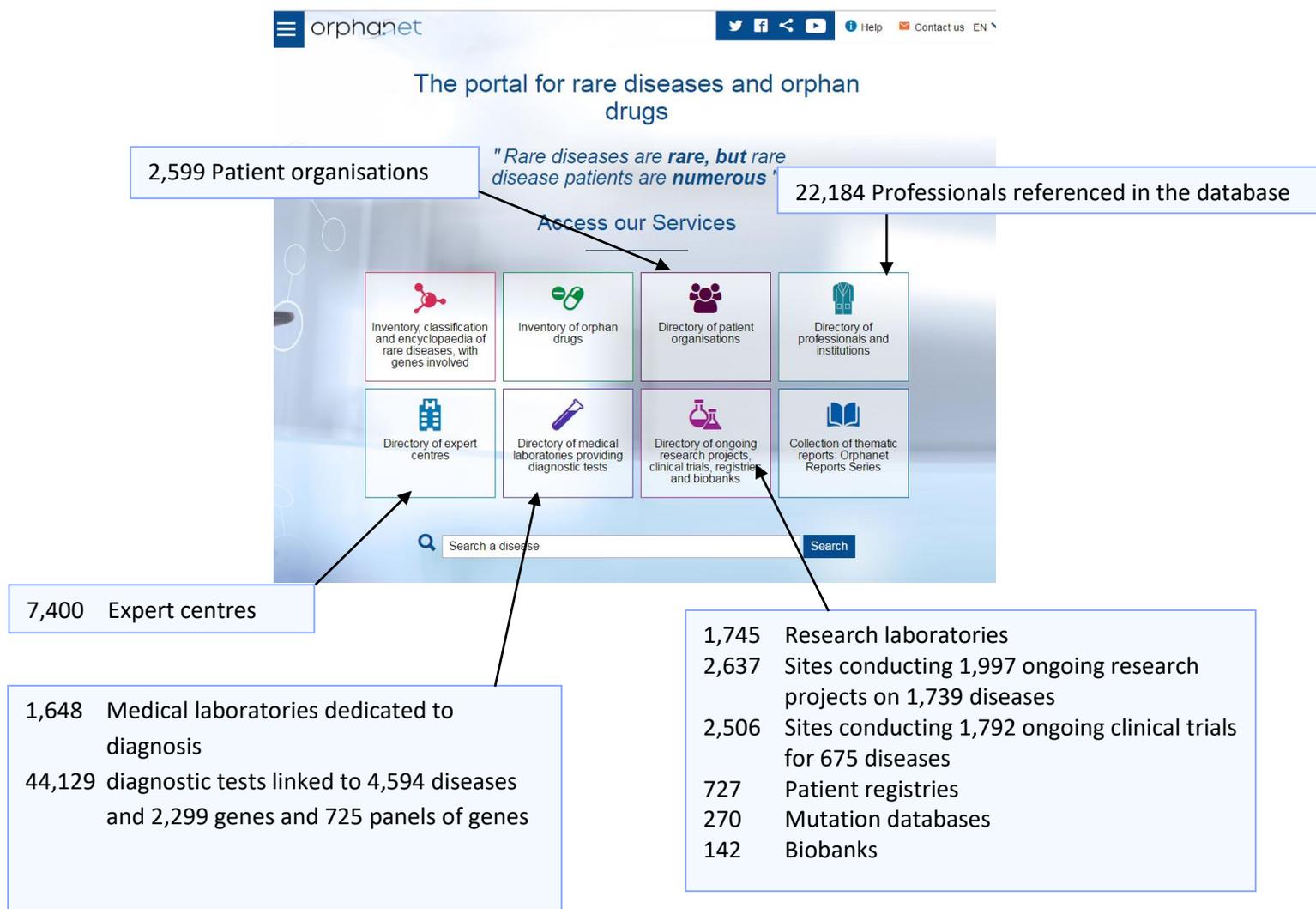


Figure 8 Directory of expert services

3.4.1. 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. Information on quality management for medical laboratories and diagnostic tests is provided in Orphanet. Medical laboratories can 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). 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 those of other laboratories.

Information on EQA participation is provided annually by Cystic Fibrosis Network, Cytogenetic European Quality Assessment Service (CEQAS) and European Molecular Genetics Quality Network (EMQN) with the consent of the concerned laboratories. For other EQA providers, information on participation can be provided by the laboratory itself.

3.4.2. ADDITIONAL FUNCTIONALITIES IN 2017

The presentation of networks was improved on the website: details of participants in a network are included in the network page, and vice-versa.

A cartographical representation of European Reference Networks was added to the website, enabling users to better visualise the composition and geographical coverage of these networks.

3.5. Orphanet content: 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 have been 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). Orphanet also collects information on Orphan Drugs from Food and Drug Administration in the USA (FDA).

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 updated every trimester.

The database of orphan drugs and substances contains the following data (as of the end of 2017):

For Europe:

- **1,550** Orphan Designations linked to **1193** substances and covering **566** diseases
- **288** Marketing Authorizations (of which **103** already had an Orphan Designation and **183** without Orphan Designation), covering **259** diseases

For the USA:

- **760** Orphan Designations linked to **618** substances and covering **430** diseases
- **351** Marketing Authorizations (of which **344** already had an Orphan Designation and **7** without Orphan Designation), covering **318** diseases

3.6. Orphanet products: Orphanet Report Series

Orphanet Reports (ORS) 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 page of Orphanet's website. New versions of these publications are advertised in OrphaNews.

The ORS are heavily downloaded: in 2017, more than 655,000 ORS were downloaded (Table 6).

	English	French	German	Spanish	Italian	Dutch	Polish	Portuguese
List of rare diseases in alphabetical order	48,767	16,5429	37,113	24,737	53,655	8,650	38,576	5,775
Prevalence of rare diseases by alphabetical list	37,781	5,480	6,036	5,112	4,843	NA	NA	982
List of orphan drugs in Europe	15,999	3,585	1,607	1,826	2,327	452	NA	324
Prevalence of rare diseases by decreasing prevalence or cases	7,964	7,432	3,106	10,806	4,342	NA	NA	1,770
Registries	19,108	NA	NA	NA	NA	NA	NA	NA
Orphanet ICD10 coding rules	8,030	NA	NA	NA	NA	NA	NA	NA
Orphanet linearisation rules	837	NA	NA	NA	NA	NA	NA	NA
Research Infrastructures for rare diseases in Europe	3,426	NA	NA	NA	NA	NA	NA	NA
Vivre avec une maladie rare en France	NA	38,444	NA	NA	NA	NA	NA	NA

(N.A. = ORS not available in this language)

Table 6 Number of downloads of selected Orphanet Report Series in 2017 by language

3.7. Orphanet's IT infrastructure

The whole IT infrastructure is under the responsibility of INSERM. The production servers are located in one of the largest civil data centres in France, the CINES (Centre Informatique National de l'Enseignement Supérieur). To ensure structural security, the development servers are located in another 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. The architecture of the servers is represented in Figure 9.

Many 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. Back-office tools used by the coordinating team in France, and other teams internationally, are accessed through VPN (Virtual Private Network) servers. No major problems were encountered in 2017 and the www.orpha.net website was highly available despite an increasing amount of visitors, which now reaches 2.5 million pages viewed per month. We have made several updates for security reasons (PHP and servers OS) and replace one host server to improve backoffice tools. The uptime measurement by Nagios supervision for www.orpha.net in 2017 was 364d 19h 34m 10s 99.676%.

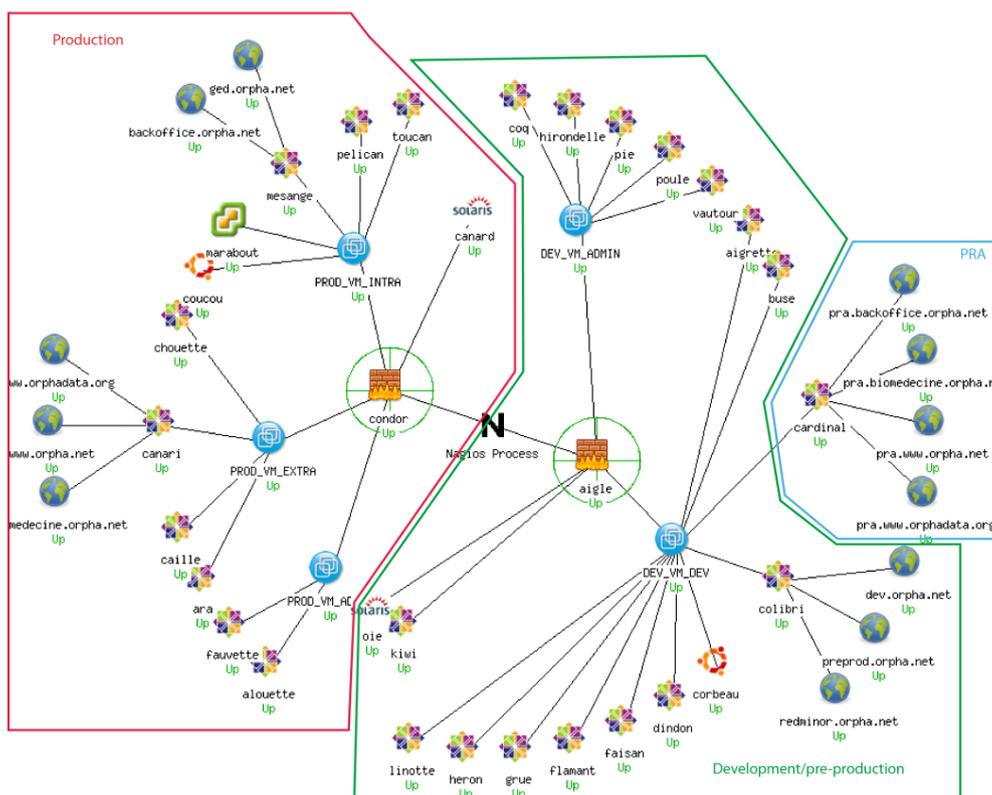


Figure 9 Orphanet's IT architecture in 2017

3.8. Orphanet services: 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 (Fig 10b). Indeed, the typeface is magnified and information is organised in easy-to-spot blocks with distinctive icons that allow users to more readily navigate the site. The disease search function is in the centre of the homepage.

A new look website was launched to mark the 20th anniversary of Orphanet in 2017 (Fig 10b), with much of the redesign work taking place in 2016. This new website version has a responsive design. One new feature is the 'burger menu' present on all pages, that allows users to access each of the products and services provided by Orphanet, no matter what page they are on. The popular Orphanet Report Series, which provides aggregated Orphanet data on a range of rare disease and orphan drug topics, has a dedicated icon block. OrphaNews, the newsletter of the rare disease community and a dissemination tool for RD-ACTION, is easily identified via a dedicated block, as are Orphadata and ORDO.



Figure 10a The Orphanet portal homepage in 2016

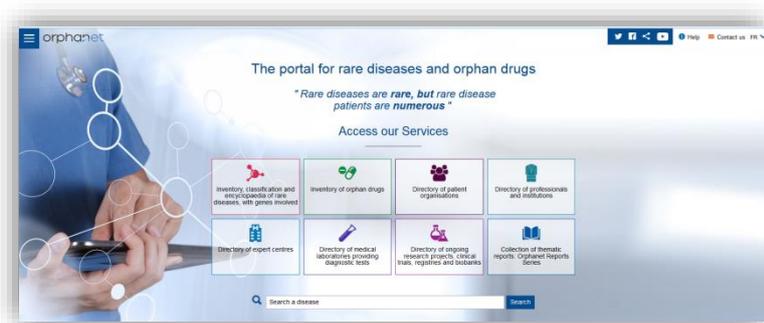


Figure 10b The Orphanet portal homepage in 2017

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. The new look and feel of the website was the first step in the process to improve access to the data in the Orphanet database.

There are two ways to contribute as an expert, or professional in the field of rare diseases, to the Orphanet database: the curation platform and the online registration service. In 2017 Orphanet made available the Orphanet Knowledge Management Platform (<http://curation.orphanet.org/>). This platform allows experts in the field of rare diseases to help curate the scientific data in the Orphanet database in a traceable and transparent manner. Professionals and associations can also provide updates and add activities to the catalogue of expert resources via a [secure account](#); these registrations are manually processed by the Orphanet local teams and undergo a quality control.

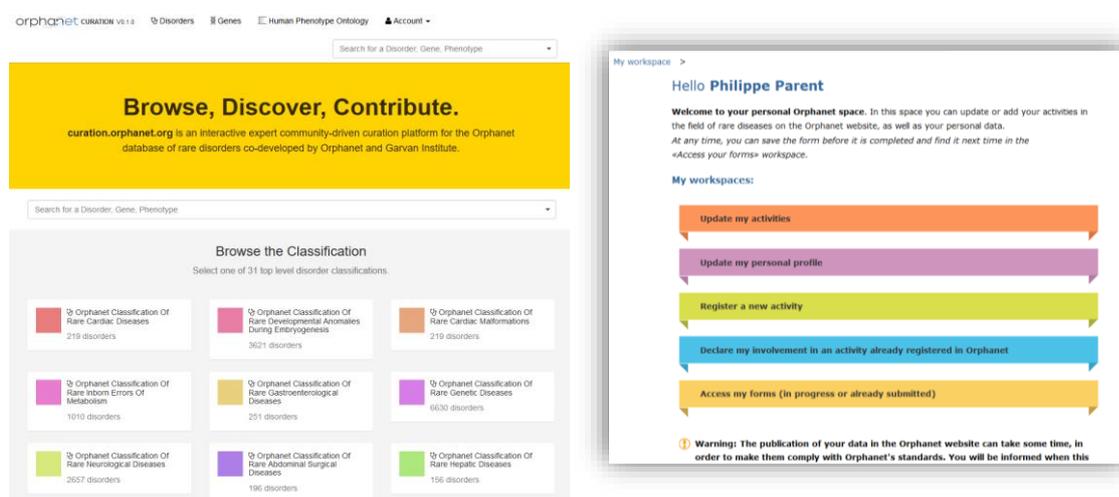


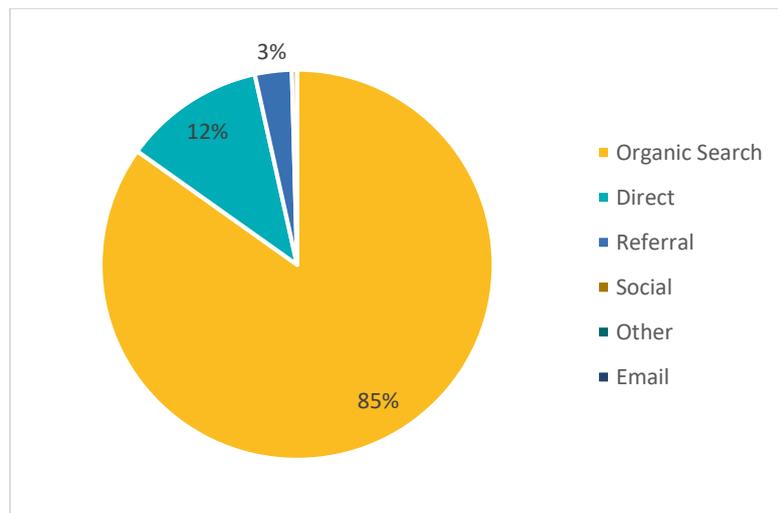
Figure 11 The curation platform (left) and the online registration tool (right)

Two tutorials were made available in 2017 to help users to search for a disease or search for a gene using this new website.

3.8.1. 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 12,800,000 responses.

Users mainly access the www.orpha.net site through search engines, namely organic searches (54% of sessions according to Google Analytics), and Google alone accounts for 83% of queries (Figure 12). Organic searches correspond to listings on search engine results pages that appear because of their relevance to the search terms, as opposed to them being from advertisements. Other sites generating traffic to Orphanet through referrals represent 12% of visits. The remaining visits are in part from social media channels.



*Figure 12 Distribution of the traffic sources
(Source: Google Analytics, 1st of January 2017 to 31st of December 2017)*

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”. The indexation of our site is of the “long tail” type: more than 300,000 different keywords generate traffic to the site.

Google Analytics allows users to trace visits made from mobile devices (Smartphone, tablets): these visits represented 54% of all visits during 2017, a dramatic increase when compared to other years (28% in 2016, 20% in 2015 and 2014, and 23% in 2013). This new version has a responsive design and so provide a much better adaptation to any mobile devices.

3.8.2. THE WEBSITE'S AUDIENCE

ORPHANET IN NUMBERS

- 30 million pages viewed
- 7.8 million PDFs downloaded
- Visits from 235 countries

In 2017, around 30 million pages were viewed, thus on average around 82,700 pages were viewed per day (Figure 13).

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: 7.8 million PDFs were downloaded from the site in 2017.

The users come from 235 countries. The top ten countries are: France, Italy, Brazil, Mexico, Spain, Germany, United States, Colombia, Canada and Belgium.

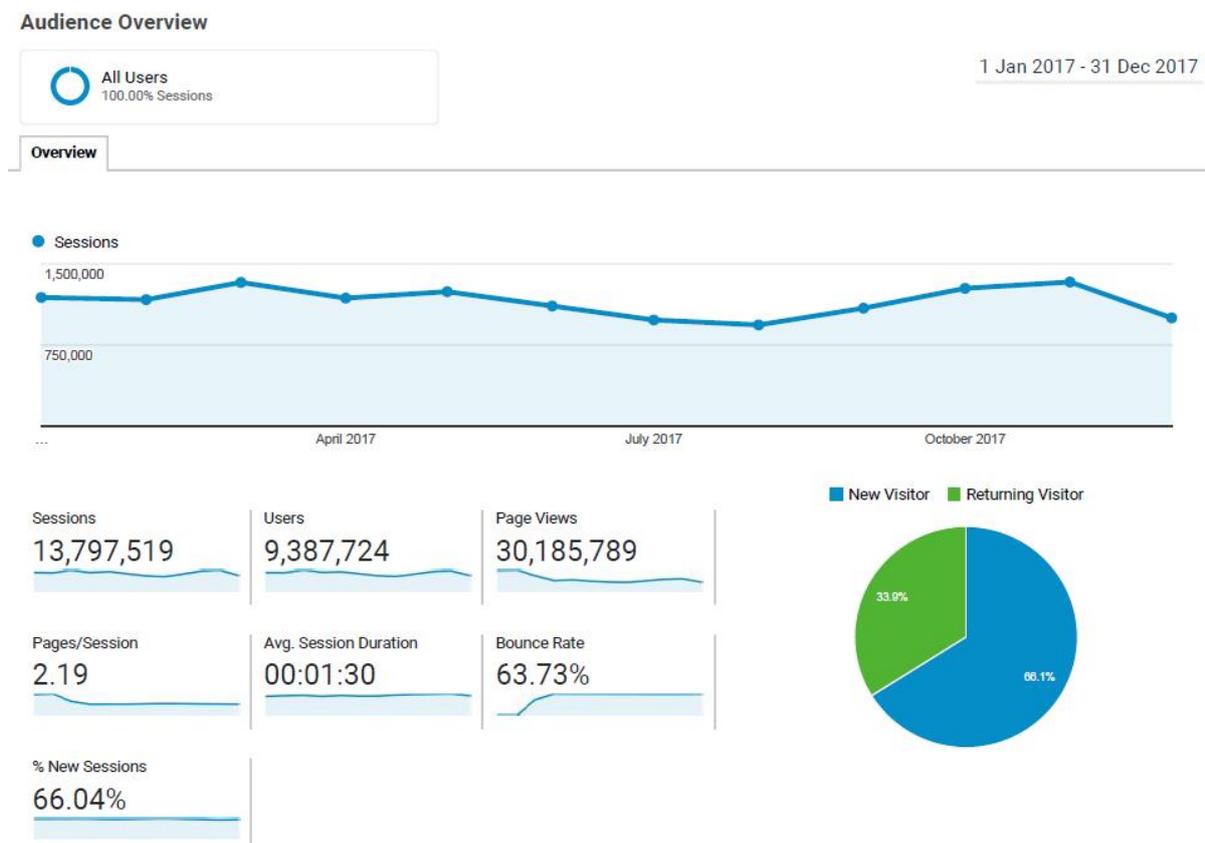


Figure 13 Orphanet website consultations in 2017
(Source: Google Analytics, 1st January 2017 to 31st December 2017)

The tool that is used to track our audience is Google Analytics. It allows 3 parameters to be monitored: sessions, users and page views (this shows a substantial ratio of page views / visitors). It should be noted that the current way in which users and sessions are counted is liable to change. For example, in 2014, the CNIL (*Commission nationale de l'informatique et des libertés* : the French data protection authority) recommended that websites inform users of the measurement tools used on the website, such as Google Analytics. During the summer of 2014 we developed a pop-up

that requires users to accept this measurement. In case of refusal or inaction (no change of page for example), the user and the session are not properly recognised by the tool.

The number of sessions in 2017 was relatively stable compare with 2016 (Figure 14), as were the number of users; although the number of pages per session decreased from 3.49 to 2.19, the average session duration increased by 2 seconds.

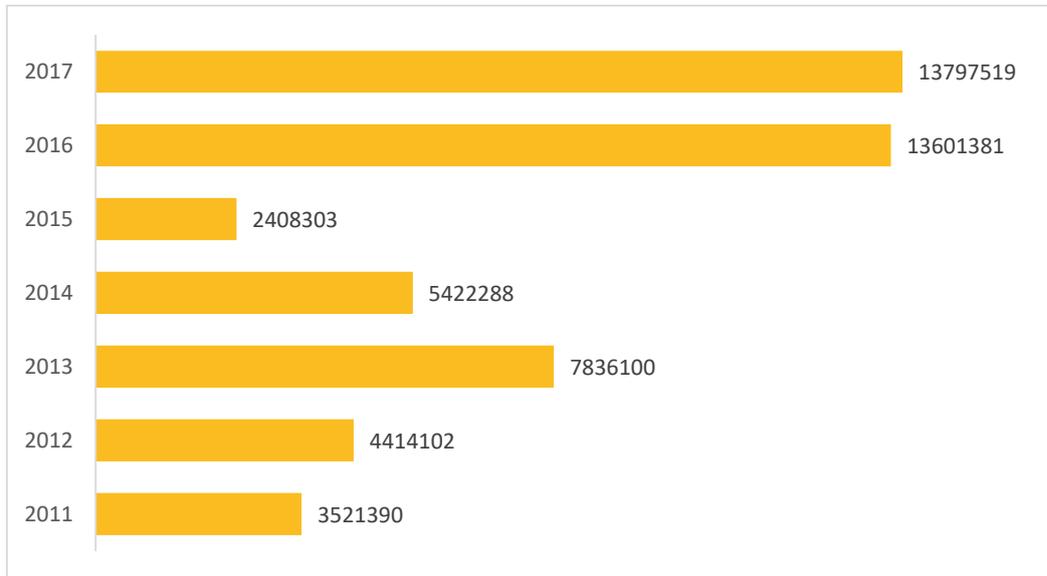


Figure 14 Evolution of number of sessions since 2011 (Source: Google Analytics)

3.8.3. ORPHANET NATIONAL WEBSITES

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 national 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 2017, 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.

3.9. Orphanet services: Orphanet Rare Diseases Ontology

The Orphanet Rare Disease ontology (ORDO) is available on three websites [Bioportal](#), [Orphadata](#) and the [EBI Ontology Lookup Service](#).



ORDO was jointly developed in 2013 by Orphanet and the European Bioinformatics Institute (EMBL-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 nosology (classification of rare diseases), relationships (gene-disease relations, epidemiological data) and connections with other terminologies (MeSH, UMLS, MedDRA, GARD), databases (OMIM, Universal Protein Resource Knowledge Base (UniProtKB), Human Genome Organisation Gene Nomenclature Committee (HGNC), ensembl, Reactome, IUPHAR, Genatlas) or classifications (ICD-10), complete epidemiological data, mappings and genetic annotations. The ontology is maintained by Orphanet and further populated with new data. Orphanet classifications can be browsed in the EBI's ontology lookup service (OLS). ORDO is updated twice a year and follows the OBO guidelines on deprecation of terms. It constitutes the official ontology of rare diseases. The availability of such relationships between medical terminologies allows RDs to be used as a "pivot" to connect different biological, clinical or genetic ontologies. This interoperability allows for the association of new content and the establishment of new research hypotheses on data that were not initially related.

In 2017, ORDO was downloaded 7,137 times, a decrease of 15% as compared to the previous year.

3.10. Orphanet services: Orphadata

Since Orphanet has become 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](#) was created. Orphadata is intended to contribute to accelerating R&D and to facilitate the global adoption of the Orphanet nomenclature.





Figure 15 Screenshot of the Orphadata platform

Via this platform, Orphanet datasets have been made directly accessible in a reusable format since June 2011. The data sets are available in seven languages: English, French, German, Italian, Portuguese, Spanish, Dutch, and in Czech (available in 2018). The nomenclature was made available on the platform in 2017 in Polish. Part of the datasets are available freely via a Creative Commons licence, and some are available via signature of a Data Transfer Agreement for academic research (Table 7) or a licence agreement for for-profit organisations/companies (table 8).

<ul style="list-style-type: none"> An inventory of rare diseases, cross-referenced with OMIM, ICD-10, MeSH, MedDRA, UMLS, GARD and with genes in HGNC, OMIM, UniProtKB, IUPHAR and Genatlas. Annotations on typology of diseases and genes and of gene-disease relationships. Definitions for RD.
<ul style="list-style-type: none"> A classification of rare diseases established by Orphanet, based on the literature and expert consensus classifications.
<ul style="list-style-type: none"> Phenotypes associated with rare disorders (annotations using HPO terms), as well as their frequency.
<ul style="list-style-type: none"> Linearisation of RD : for analytical purposes, each disorder is attributed to a preferred classification (linearisation) by linking it to the head of classification entity.
<ul style="list-style-type: none"> Orphanet Rare Diseases Ontology (ORDO)

Table 7 Products freely accessible on Orphadata

<ul style="list-style-type: none"> • An inventory of Orphan Drugs at all stages of development, from EMA orphan designation to market authorization, cross-linked with diseases.
<ul style="list-style-type: none"> • Summary information on each rare disease in seven languages (English, French, German, Italian, Spanish, Portuguese, Netherlands).
<ul style="list-style-type: none"> • URLs of other websites providing information on specific rare diseases
<ul style="list-style-type: none"> • Epidemiological data related to rare diseases based on the literature (point prevalence, birth prevalence, lifelong prevalence and incidence, or the number of families reported with respective intervals per geographical area, type of inheritance, interval average age of onset and age of death).
<ul style="list-style-type: none"> • A directory of specialised services, providing information on centres of expertise, medical laboratories, diagnostic tests, research projects, clinical trials, patient registries, mutation databases, biobanks and patient organisations in the field of rare diseases, in each of the countries in the Orphanet network.

Table 8 Products accessible on Orphadata after signature of a Data Transfer Agreement/licence agreement

Orphadata provides a [guide](#) for users that defines and describes the elements of the dataset and gives access to Orphanet procedures relevant to the users of the data, such as the [methodology of alignment of ICD10 coding rules for rare diseases](#) and the [methodology of linearisation](#).

Only non-nominative data are accessible, in accordance with personal data protection laws. The dataset is updated once a month. The date of the last release is indicated.

In 2017, **Orphadata products were downloaded more than 212,000 times**, with an average of 17,690 times per month. This represents an increase of 25% compared to 2016 (Figure 16).

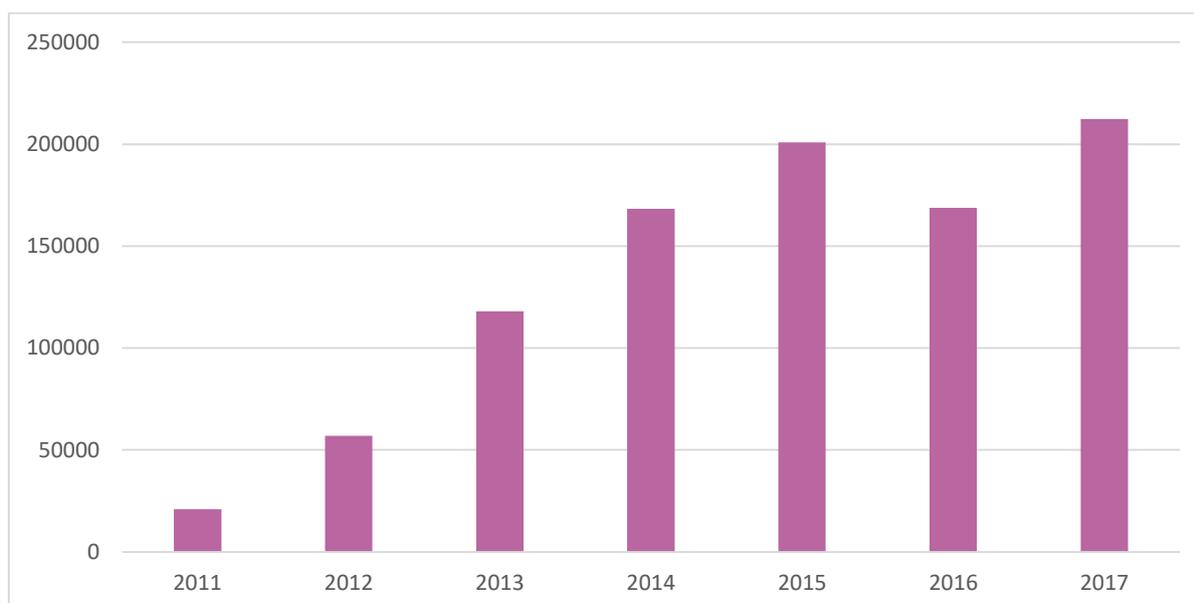


Figure 16 Number of downloads from the Orphadata website since mid-2011

The most requested Orphadata product in 2017 was the inventory of diseases were the classifications of rare diseases (Figure 17a and 17b).

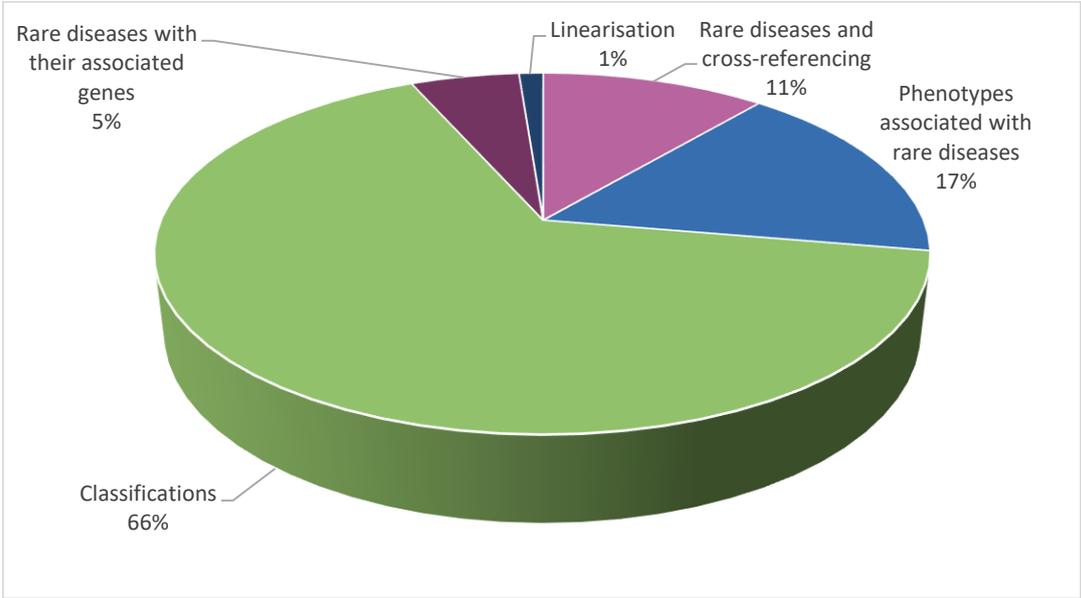


Figure 6a Distribution of the downloads of Orphadata freely available datasets in 2017. [total of 209,028 downloads]

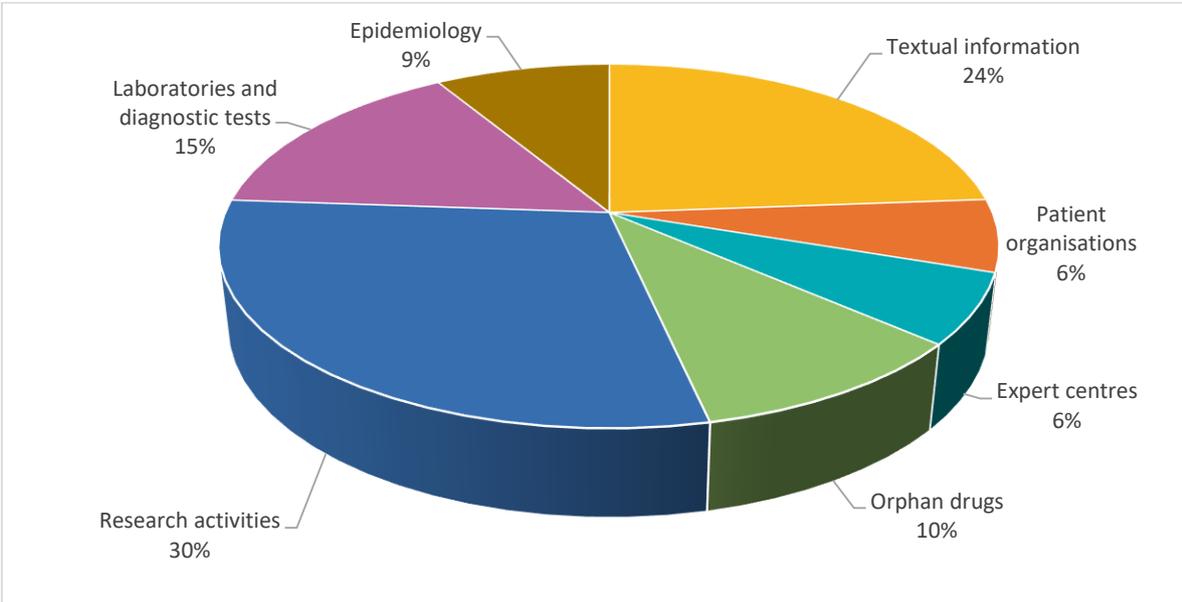


Figure 17b Distribution of the downloads of Orphadata Datasets accessible on demand in 2017 [total of 3243 downloads]

3.10.1. ADDITIONAL FUNCTIONALITIES IN 2017

In 2017, the freely available products on Orphadata were also made available in .JSON format. The nomenclature was also made available on this platform in Polish.

3.11. Orphanet Services: The OrphaNews Newsletter

[OrphaNews](#) is a bimonthly newsletter for the rare disease community, presenting an extensive overview of scientific and political news about rare diseases and orphan drugs. Subscription to this newsletter is free. A literature survey is performed twice a month in order to update the Orphanet database and to collect both scientific and political news to report in OrphaNews. The selection of articles for the newsletter is validated by a multidisciplinary editorial board. News is also submitted from contact points in each of the Orphanet consortium countries.

OrphaNews International is supported by the European Commission's DG SANTE RD-ACTION Joint Action N° 677024 and it is the dissemination tool of this Joint Action. [OrphaNews France](#) is supported by the French Muscular Dystrophy Association (AFM), while [OrphaNews Italy](#) is supported by Genzyme. At the end of 2016 the newsletter was transferred to a new tool (Figure 19) so as to improve the look and feel of the newsletter, navigation in the newsletter, and to provide better search functions via a thesaurus of keywords. The first editions in this new format were published at the start of 2017.



Figure 18 OrphaNews homepage in 2016



Figure 19 OrphaNews new-look homepage in 2017

In 2017 [OrphaNews](#) in English had more than 12,000 subscribers. [OrphaNews](#) in French had more than 8,400 subscribers and [OrphaNews](#) in Italian had more than 5,600 subscribers.

3.12. Orphanet Services: Mobile applications

Orphanet data is available via two mobile apps.



Figure 20 Orphanet mobile app and Orpha Guides mobile app

Orphanet is an app allowing users to access the list of rare diseases, textual information concerning the disease and associated services (expert centres), as well as Emergency Guidelines. The app is available via for [iOS](#) and [Android](#). This application is available in all languages of the Orphanet website.

Orpha Guides is an app in French giving access to information on French national support mechanisms for patients and their families, as well as information concerning the functional consequences of over 100 rare diseases. The app is available for [iOS](#) and [Android](#).

3.13. Orphanet Journal of Rare Diseases

Orphanet Journal of Rare Diseases (OJRD) 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 Thomson Scientific after only two years of being in publication. Its 5 year impact factor is 4.185.

4. Users: 2017 satisfaction survey

An online survey was carried out for 4 weeks in January 2018. The satisfaction of the website users was assessed by asking them to respond to a short online questionnaire. 5,263 users replied to the survey.

The following results present the responses collected in all languages (Dutch, English, French, German, Italian, Portuguese and Spanish). More results from this survey are available in the Orphanet Report Series dedicated to the [2017 survey](#).

In what capacity are you consulting the Orphanet website TODAY?

This question aimed to determine the profile of Orphanet's users. Seven categories were proposed (i.e. health professional, patients/entourage, researcher, industry, healthcare manager/policy maker, and students), and a free text field was included for other types of users to enter their profession. Only one response was possible. Respondents from the 'other' category were reassigned to one of the seven proposed categories when appropriate.

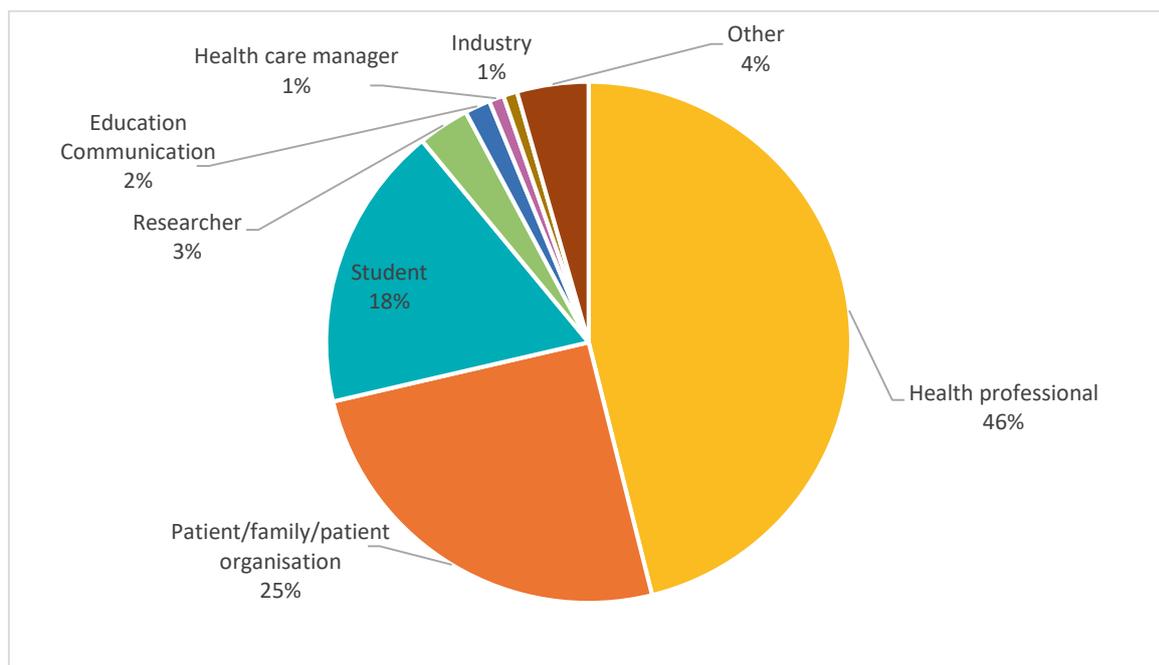


Figure 21 Types of Orphanet user (percentage of total respondents) $n = 5,131$

The largest category of respondents is the health professional category (46%). The second largest category of respondents is patients and their entourage (including patient organisations, alliances and support groups) with 25% of responses. Many students (18%) also replied to the survey. The 'other' category included respondents working in terminology standards, biocuration, as well as non-related socio-professional categories and those generally interested in rare diseases but who did not state their professional category.

How often do you visit Orphanet?

Only one response was possible. Around 50% of those answering the survey are regular users, whereas 27% were visiting Orphanet for the first time.

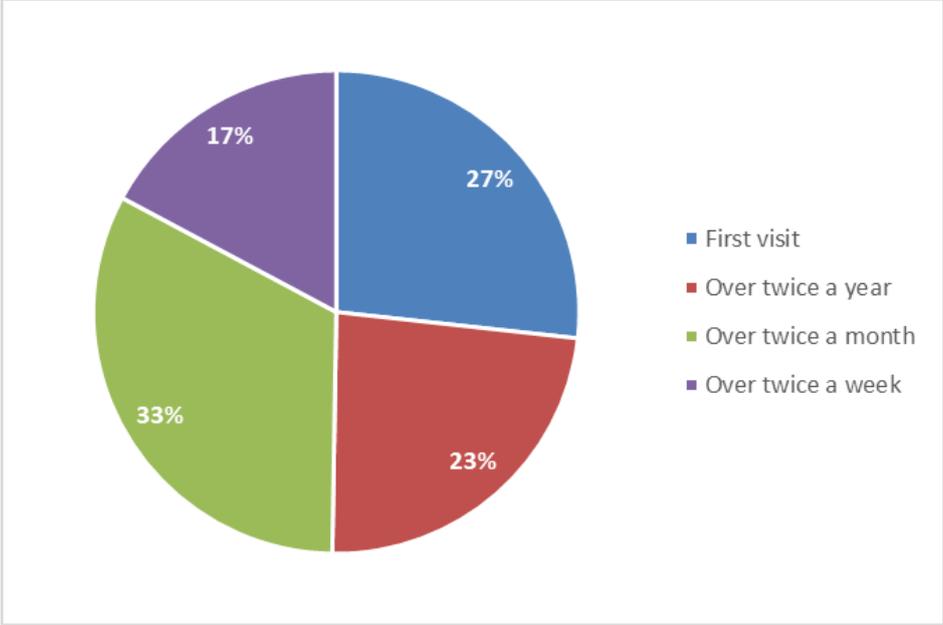


Figure 22 Visiting frequency of respondents (n=4608)

There were 7% more first time users this year compared to last year (20%). There was a slight decrease in users consulting the site more than twice a month (33% compared to 37%, and a slight decrease in the number of respondents stating they use the site over twice a week (17% compared to 19%).

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.

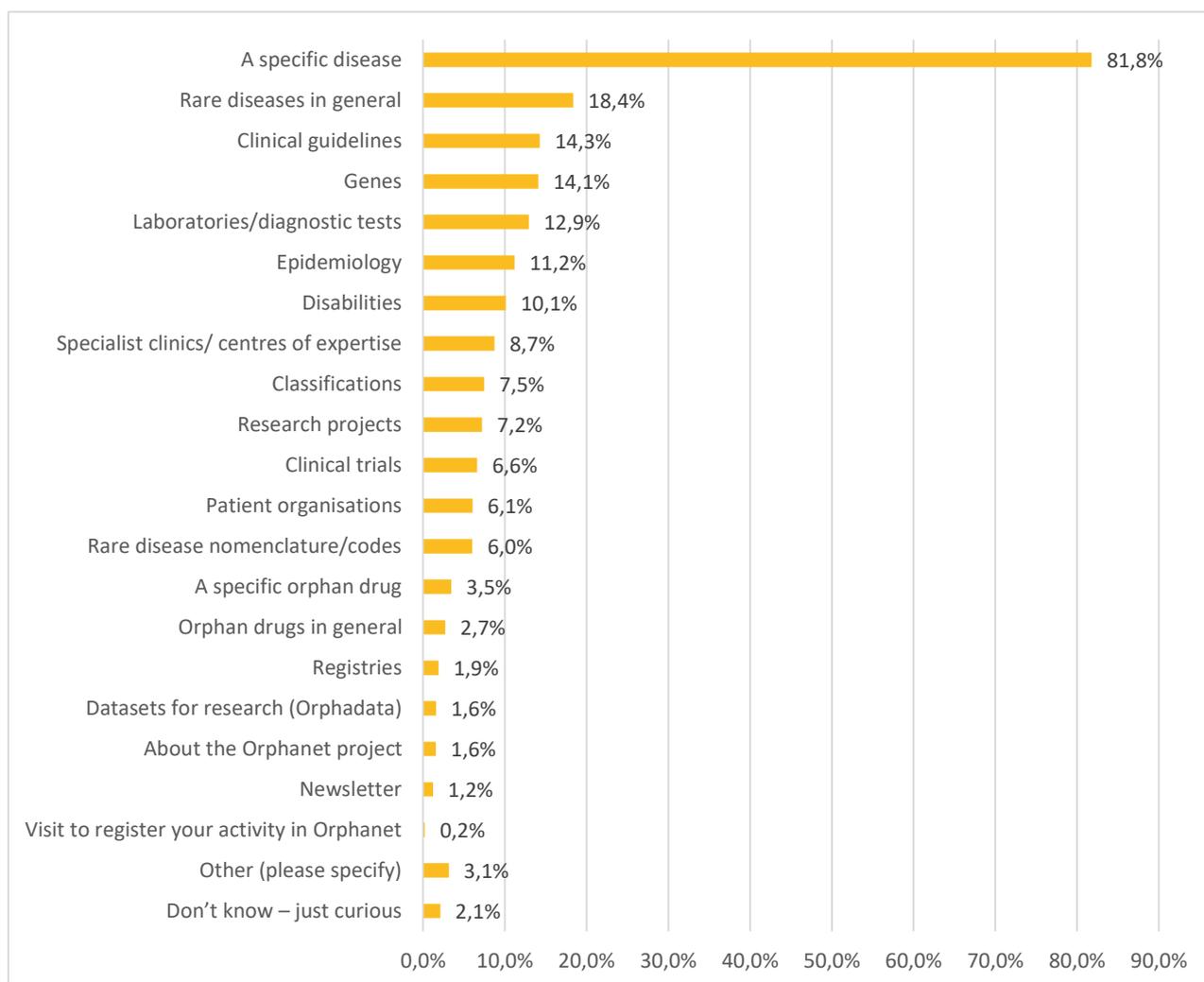


Figure 23 Information sought by respondents during their connection to Orphanet (percentage of total number of respondents n=4972)

The results show a clear trend: most of the respondents were looking for information for a specific disease (82%). Our visitors also look for information on rare diseases in general (18%) clinical guidelines (14%), genes (14%), laboratories/tests (13%) and epidemiology (11%). A smaller percentage of respondents were seeking information concerning other expert resources: specialist clinics (9%), research projects (7%), on clinical trials (7%), patient organisations (6%). 6% of users were looking for information related to the nomenclature and coding of rare diseases and 8% were looking for information pertaining to the classification of rare diseases. The trends are stable compared to the previous year.

How useful would you rank the following Orphanet services for your own use?

The usefulness of Orphanet products was evaluated through this question. All respondents, except those consulting Orphanet for the first time, were asked this questions as the aim was to assess the usefulness of available tools and services for users' needs, based on their experience, and to also assess their knowledge of the existence of range of available services. Only one response was

possible for each product for the 2,777 respondents. The respondent is not obliged to give an answer for every product, but can if they wish. Respondents were asked to rate the services according to their utility for their own use: ++, +, -, - -. Two other options were given: 'I do not use this service', and 'I did not know Orphanet offered this service'. The results show that Orphanet products are highly appreciated but not sufficiently well known.

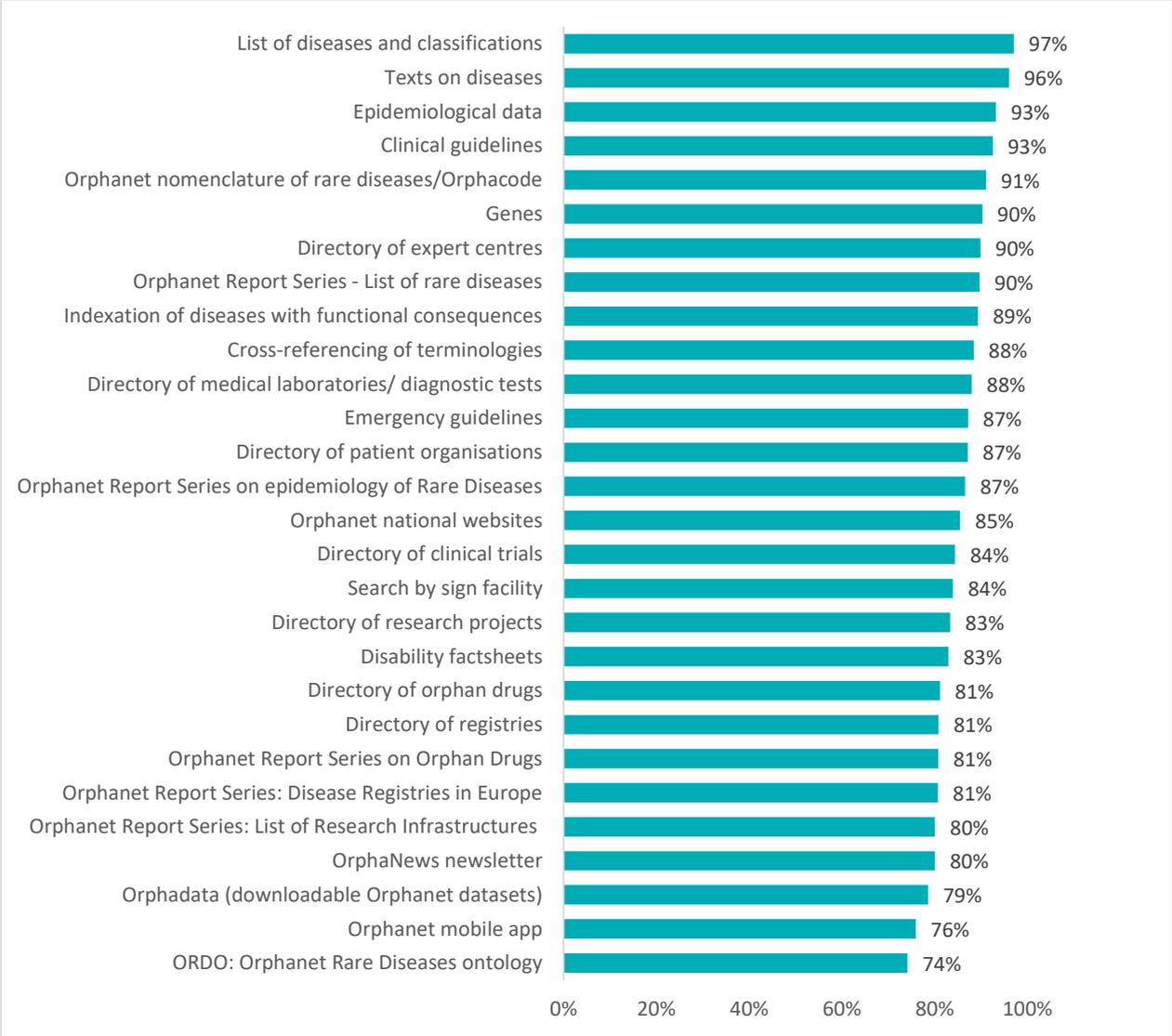


Figure 7 The most useful services offered by Orphanet according to respondents (answers '++' or '+' on the scale of usefulness).

The results show similar trends to previous years' surveys. The most useful Orphanet services, according to our users, are the list of diseases and classifications (97%) and texts on diseases (96%). The data concerning the epidemiology of rare diseases is also highly appreciated (93%), as are the clinical guidelines made available via Orphanet (93%). The Orphanet nomenclature of rare diseases and codes are also highly appreciated (91% of respondents who knew of, and used this service) as are the directory of expert centres (90%), and information on genes (90%). The indexation of diseases with the functional consequences of the disease is highly appreciated by 89% of

respondents. The trends are similar to last year, and show that Orphanet users are generally very satisfied with the products they use and know about.

An analysis of the answer ‘I didn’t know that Orphanet offered this service’ highlights that our users are not sufficiently informed about our range of products and services.

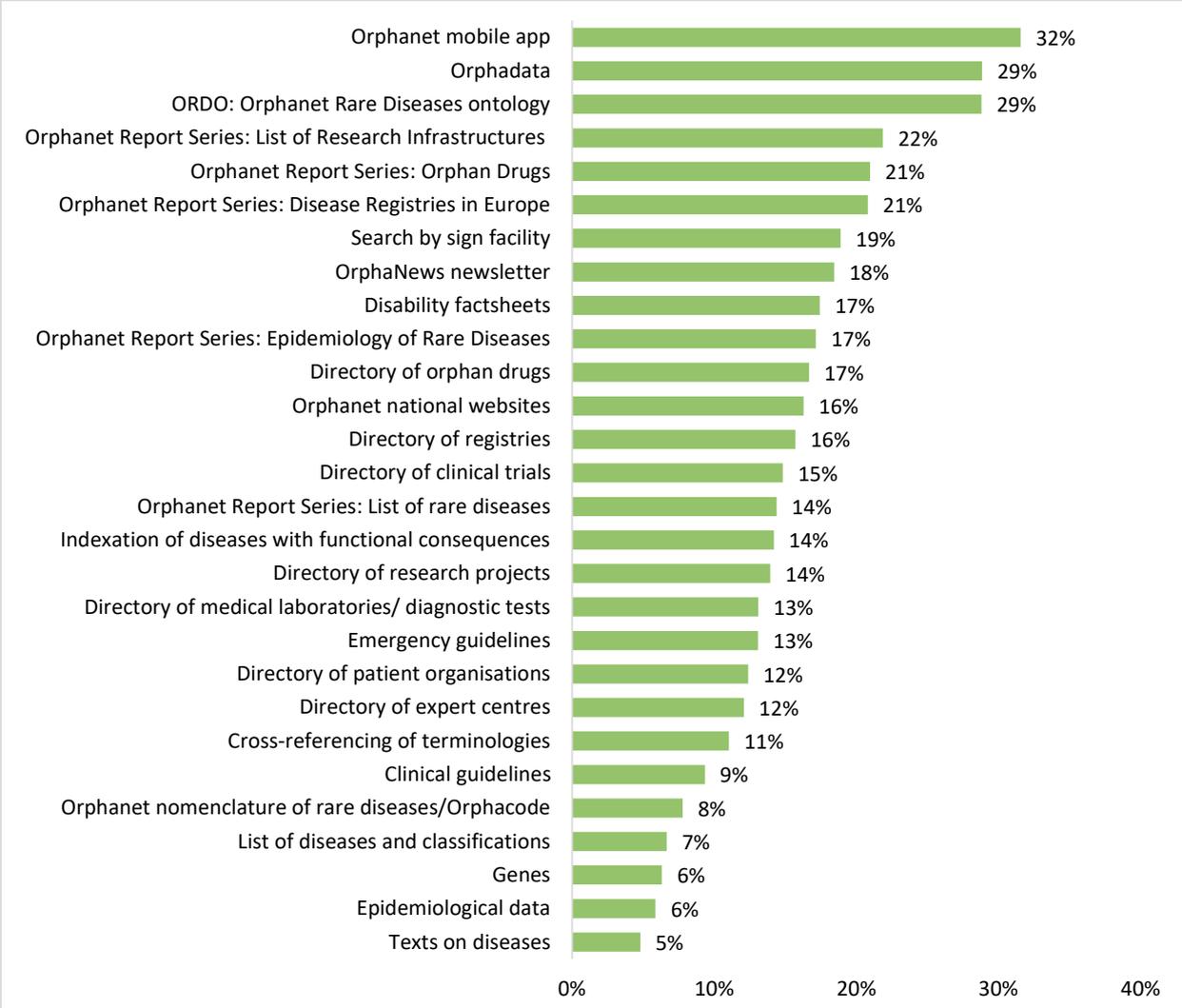


Figure 25 Least well-known Orphanet products (respondents answering ‘I didn’t know this service existed’)

ORDO, the Orphanet Rare Disease Ontology, launched in 2013, is not known to 29% of our users, although amongst its users, it is well appreciated (74% highly appreciate this service). The targeted audience for this service is researchers, and in particular those in the bioinformatics sphere, which may explain why it is relatively unknown to those responding to the survey. It should be noted that ORDO is better known this year (29% compared to 38%). Similarly, Orphadata, the website that allows users to download Orphanet datasets for research purposes, is fairly well appreciated but is one of the least well known services (29% of respondents). This service was launched in 2011, and

is research orientated which may explain why it is not known or used by most or Orphanet's users; it should be noted that last year 36% of users did not know of Orphadata, compared to 29% this year. As previously seen, the Orphanet mobile app is not well known (32% of users answering this question did not know it existed, compared to 36% of respondents in last year's survey).

The most well-known products remain the texts on diseases with only 5% not aware of their existence; only 6% of respondents did not know about the epidemiological data made available by Orphanet or information on genes, and only 7% of respondents did not know about the existence of the list of diseases and classification.

This analysis will help the Orphanet team structure outreach activities in the future, especially for newer services such as the Ontology and Orphadata.

5. Networking: Orphanet's national and international collaborations

Orphanet believes in the effectiveness of sharing data and expertise 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, Orphanet is often solicited by many different projects to contribute its expertise.

It is for these reasons that new collaborations and partnerships are developed regularly, resulting in the intense scientific collaborative activity described below.

5.1. National plans or strategies for rare diseases

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

Orphanet is mentioned either as the reference portal for rare diseases or main source of information on rare diseases in the recommendations and proposed measures of the majority of national plans or strategies adopted to date.

Germany

Orphanet Germany was involved in two activities receiving financial support from the German Ministry of Health in 2017: (1) [SE-ATLAS](#), 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](#) is a sister project by the Universities of Hannover, Freiburg and Mainz, the Chamber of Physicians of Lower Saxony, and Orphanet-Germany, to conceptualise 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.

The Netherlands

The Minister of Health, Welfare and Sport in the Netherlands appointed the NFU, the Netherlands Federation of University Medical Centres, to coordinate the identification and documentation of Dutch centres of expertise for rare diseases together with Orphanet Netherlands and the VSOP (umbrella organisation of parent and patient organisations for genetic, congenital and rare disorders). The potential centres of excellence have been evaluated based on the EUCERD criteria established at the European level that include the presence of guidelines, protocols, standards and indicators of care, and equally evaluate scientific research, the relationship with patient organization(s) and how the continuity of the centre is ensured within the institute. The NFU published the procedure on the NFU website (in Dutch;

www.nfu.nl/patientenzorg/complexezorg/procedure-expertisecentra). In the first round, 288 potential centres from the University Medical Centres were evaluated, in the second round 125 potential centres from both University Medical Centres and non-university major "top-clinical" hospitals were assessed. The minister assigned from both rounds centres of expertise as official Dutch centres of expertise. These 302 centres are listed on the Orphanet website by the Dutch information scientist. The list can also be found on the Erfocentrum website www.erfelijkheid.nl.

Italy

The **Italian Health Ministry included Orphanet as a reference** in the new version (July 2016) of the Ministerial Decree of December 09, 2015, on Prescription Appropriateness (Italian title of the Decree: "[Condizioni di erogabilità e indicazioni di appropriatezza prescrittiva delle prestazioni di assistenza ambulatoriale erogabili nell'ambito del Servizio sanitario nazionale](#)"). The Decree sets up specific conditions for laboratories performing genetic tests in Italy ("Condizioni di erogabilità", as reported in "[Allegato 1](#)" of the Decree). In particular, with regard to genetic tests, the document contains the following reference to Orphanet database: "In order to identify single genes, refer to genes reported in the Orphanet database with diagnostic value"). This reference to Orphanet into the Italian legal framework marks an important milestone in its consolidation as a legitimate source of information on rare diseases in Italy. Orphanet was also highly mentioned in the National Plan for Rare Diseases 2013-2016 and the Ministry of Health identified Orphanet as a reference source of information for rare diseases and orphan drugs.

5.2. Nomenclature and terminologies

5.2.1. 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 ORPHA nomenclature. It is composed of a unique and stable ORPHA number for each entry of the inventory. The ORPHA number can be used for codification purposes.

In 2014, the Commission Expert Group on Rare Diseases adopted a [recommendation](#) on ways to improve codification for rare diseases. In this document, Member States are encouraged to consider and explore the feasibility of the use of ORPHA codes at a national level and to include the codification of rare diseases as an area of their national plans/strategies for rare diseases. Support for the large number of Member States who have already expressed their interest in using ORPHA codes (as a complement to existing coding systems) is provided via a dedicated work package (WP5) of the current Joint Action for rare diseases RD-ACTION (www.rd-action.eu). This work package has notably produced [a survey of current codification situations](#) in the Member States, a [review document of existing technical implementations for RD coding](#), and a [Standard procedure and guide for coding with Orphacodes](#), as well as a [beta version of a master coding file](#), and [specifications for](#)

[the implementation of this file. Specifications for an integrated coding application with Orphacodes](#) have also been produced.

A [mapping exercise](#) of the use of ORPHA codes in Europe as carried out in context of RD-Action and will be available in 2017. A number of countries have already taken some concrete steps in implementing ORPHA codes in their healthcare systems (Portugal, Germany, France, Belgium, Italy, Norway, Latvia, Czech Republic, Hungary, Cyprus, Switzerland) and national Orphanet teams are playing a key role in particular in the following countries:

France

In 2012, it was decreed that the French hospital system database would use ORPHA codes to code all hospitalised patients. The aim is to better identify patients in the healthcare system so as to improve knowledge of their healthcare pathways. The ORPHA code has been added in a dedicated part of the coding system, in addition to the ICD-10 derived code. Also because of the development of electronic health records in France, the French Ministry of Health has set up an advice committee for the codification of RD in which Orphanet plays a major role. A governmental memo was released in January 2016⁵, aimed at centres of reference and centres of competence, making the codification of rare disease patients with ORPHA codes mandatory in the French Rare Diseases Data Repository [BNDMR](#). Orphanet and the BNDMR have developed guidance documents for the codification of rare diseases in the BNDMR. This will help in collecting data that is to be included in the BNDMR, which was deployed from the end of 2016. Coding with the ORPHA codes shall be extended to other sectors of the health system in the future.

Germany

In July 2013, a 3-year project started to revise the German ICD-10 (ICD-10GM). Orphanet Germany is a partner of this project by supplying the DIMDI (German Institute of Medical Documentation and Information) with the German translation of rare disease terms. The project intends to integrate the Orphanet classification of diseases by adding ORPHA codes 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.

The Netherlands

The RIVM, the National Institute for Public Health and the Environment, that coordinates this project on behalf of the Ministry, started to compare the disease classification of the World Health Organization (WHO; WHO-FIC Update and Revision Committee) with the Orphanet classification. RIVM project leaders are working in close collaboration with Orphanet Netherlands on this subject within the work package 5 of the RD-ACTION project.

Italy

In 2017, ORPHA codes have been integrated into the health and research information systems of eight Italian regions.

⁵ http://circulaire.legifrance.gouv.fr/pdf/2016/01/cir_40460.pdf

5.2.2. 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 electronic version of ICD-11. In 2013, the beta version of ICD-11 was released. It included over 5,000 rare diseases and a proposal to include all Orphanet diseases in ICD11 is being submitted. The beta version is available here for public consultation. To date, there are 3718 rare disorders in the ICD Joint Linearisation for Mortality and Morbidity Statistics (60% of all rare diseases in Orphanet). Expert links to Orphanet are transmitted to maintain up-to-date information. A mapping file between ICD11 and ORPHA numbers is under production and will be released by Orphanet at the time of the official ICD11 release.

5.2.3. COLLABORATION WITH SNOMED INTERNATIONAL

A collaboration with SNOMED International is ongoing in order to include RD lacking in SNOMED-CT, and to provide alignments between ORPHA codes and SNOMED-CT terms. It will help with the identification of patients with RD in health information systems in countries having adopted SNOMED-CT. The alignment file will be available in 2019, distributed alongside SNOMED CT by SNOMED.

5.2.4. COLLABORATION WITH NIH-NCATS' GENETIC AND RARE DISEASE INFORMATION CENTER

A partnership was established between Orphanet and the Genetic and Rare Disease Information Center (NIH-NCATS) in 2016. One of the aims of this partnership was to mutualise efforts so as to provide the audiences of both sites with the most complete and up-to-date information on rare diseases. In a first step, the Orphanet and GARD nomenclatures were aligned, so as to allow cross-referencing between the two resources. These alignments can be visualised on the disease identity card on the Orphanet website, and are also included in the nomenclature and cross-references file available on Orphadata.

5.3. Catalogue of services

5.3.1. COLLABORATION WITH RD-CONNECT

A partnership has been established between Orphanet and RD-Connect. The latter is a European funded project (2012-2018) aimed at creating an integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research. This partnership is focused on sharing data on biobanks and registries between Orphanet and RD-Connect in order to enrich both databases.

5.3.2. PORTAIL ROMAND DES MALADIES RARES

A collaboration is in place with the Swiss ‘Portail Romand des maladies rares’ (www.infomaladiesrares.ch) in order to improve the visibility of expert centres on rare diseases registered in Orphanet in Romandy.

5.3.3. SE-ATLAS

A collaboration is in place with SE-Atlas (<https://www.se-atlas.de/>) in order to improve the visibility of expert centres on rare diseases registered in Orphanet in Germany (see 5.2).

5.4. Scientific collaborations and partnerships

5.4.1. PARTNERSHIP WITH INTERNATIONAL UNION OF BASIC AND CLINICAL PHARMACOLOGY (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 is being expanded in order to take into account the evolutions of the IUPHAR database.

5.4.2. PARTNERSHIP WITH THE INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

The INSERM unit that hosts the Orphanet coordinating team is a partner of an FP7 research support action entitled “**Support IRDiRC**”.

[IRDiRC](#) was launched in April 2011 to foster international collaborations in rare disease research. IRDiRC united 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. In 2017, such considerable progress was made towards these goals that three new goals were adopted, namely: all patients coming to medical attention with a suspected rare disease will be diagnosed within one year if their disorder is known in the medical literature, 1000 new therapies for rare diseases will be approved, and methodologies will be developed to assess the impact of diagnoses and therapies on rare disease patients. Orphanet collects data on research-related activities funded by IRDiRC members, which are research funding agencies. This requires the expansion of data coverage to new countries such as the United States and Japan. In addition, Orphanet data is at the disposal of the IRDiRC working groups and their scientific committees and is analysed for them on request.

Orphanet also provides regular data analysis for the following indicators on the IRDiRC website: number of new RD on a monthly basis, number of genes linked to RD, number of RD for which there

is a genetic test available and number of medicinal products with an orphan designation and marketing approval for the treatment of RD in the US and/or Europe.

5.4.3. PARTNERSHIP WITH RARECARENET & JOINT ACTION ON RARE CANCERS (JARC)

Since mid-2013, Orphanet has had a partnership with **RareCareNet**, providing them with information on expert centres and rare cancer patient organisations. RareCareNet in return provides Orphanet with information on the epidemiology of rare cancers, and a common effort is currently performed in order to agree on the classification of rare cancers. This work continues in the context of the EU Joint Action on Rare Cancers, which kicked-off in 2016 (www.jointactionrarecancers.eu). This Joint Action aims to integrate and maximise efforts of the European Union (EU) Commission, EU Member States and all stakeholders to advance quality of care and research on rare cancers. Orphanet is involved in a number of the work packages, in particular on issues such as the collection of epidemiological data of rare cancers, information on expert centres for rare cancers, clinical practice guidelines, and nomenclature and classifications. Cross-talk with the European Joint Action on Rare Diseases, RD-Action, coordinated by Orphanet, is also assured.

5.4.4. COLLABORATION WITH THE EUROPEAN BIOINFORMATICS INSTITUTE

Collaboration was established with the **EMBL - 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, with cross-references being regularly updated.

Orphanet and EMBL-EBI have jointly developed the **Orphanet Rare Disease Ontology (ORDO)** and in 2014, a new version of this ontology was launched (ORDO 2.0) in collaboration with the EBI; subsequent versions have been produced by Orphanet. The Ontology is updated twice a year.

5.4.5. COLLABORATION WITH THE FRENCH INSTITUTE OF BIOINFORMATICS

Orphanet is the French Institute of Bioinformatics' 30th platform. The IFB is a national bioinformatics infrastructure bringing together platforms from the main players in research in France: CNRS, INRA, INRIA, CEA and the INSERM, as well as the Curie and Pasteur Institutes and French universities. At the moment, 30 platforms are members, grouped into six regional centres across France. The IFB's primary mission is to provide the basic services and resources in the field of bioinformatics for scientists and engineers working in life sciences. Notably, IFB is the French node of the European research infrastructure ELIXIR. ELIXIR is a distributed infrastructure for life-science information, uniting Europe's leading life science organisations in managing and safeguarding the massive amounts of data being generated every day by publicly funded research. As a platform of the IFB, Orphanet is also part of this European research infrastructure, offering data and a bio-ontology of rare diseases to advance research in this field.

Orphanet, in particular, participates in the ELIXIR pilot use case on rare diseases in the context of the EXCELERATE project: in 2016 Orphanet contributed to this use case by producing a report on the role of Orphanet, in particular the Orphanet nomenclature, as a vector for interoperability in the field of rare diseases. This project aims to build an ELIXIR registry of data resources and analysis tools that are critical for the development of rare disease research, implement a technical framework for the comparison and standardisation of services useful for rare disease communities, and collaborate with rare-disease communities in organising and running their training courses, workshops and jamborees. One of the principal goals of ELIXIR is to work towards the sustainability of resources and tools such as those offered by Orphanet, which makes this a strategic step in the right direction for Orphanet's future. In this context, Orphanet and ORDO are already cited in the ELIXIR Biosharing platform, a curated, informative and educational resource on inter-related data standards, databases, and policies in the life, environmental and biomedical sciences.

5.4.6. COLLABORATION WITH NIH-NCATS GENETIC AND RARE DISEASE INFORMATION CENTER (GARD)

A partnership between Orphanet and the Genetic and Rare Disease Information Center (NIH-NCATS) was established in 2016. The aim of this partnership is to mutualise efforts so as to provide the audiences of both sites with the most complete and up-to-date information on rare diseases. In a first step, the Orphanet and GARD nomenclatures were aligned, so as to allow cross-referencing between the two resources. In a second step, summary texts from Orphanet (along with a link to the relevant Orphanet disease page and the Orphanet logo) have been included in GARD for the diseases for which GARD does not have a text. This cross-Atlantic partnership will improve the visibility of Orphanet in the United States and is just one of the ongoing efforts to integrate the Orphanet nomenclature, in particular, into the different rare-disease related resources maintained by the NIH (e.g. UMLS, ClinVar, MedGen, GTR).

5.4.7. HARMONISING PHENOMICS INFORMATION FOR A BETTER INTEROPERABILITY IN THE RARE DISEASE FIELD (HIPBI-RD)

HIPBI-RD (www.hipbi-rd.net) is a three-year project financed via the E-Rare 3 ERA-NET mechanism. The project builds on three resources largely adopted by the RD community: Orphanet, and its ontology ORDO, HPO and PhenoTips. It aims to provide the community with an integrated, RD-specific informatics ecosystem that will harmonize the way phenomics information is stored in databases and in patient files worldwide, and thereby contribute to interoperability. This ecosystem will consist of a suite of tools and ontologies, optimised to work together, and available to clinicians and scientists through commonly used software repositories. Additionally, the ecosystem will improve and streamline the interpretation of variants identified through exome and full genome sequencing by harmonising the way phenotypic information is collected.

Orphanet coordinates the project which includes partners from SickKids Toronto, La Charité Berlin, the European Bioinformatics Institute, and the Garvan Institute of Medical Research.

6. Funding

Orphanet's budget was approximately 3.1 million Euros in 2017, originating from 7 different contracts for the core activity funding and from various other contracts in some of the participating countries (Figure 26).

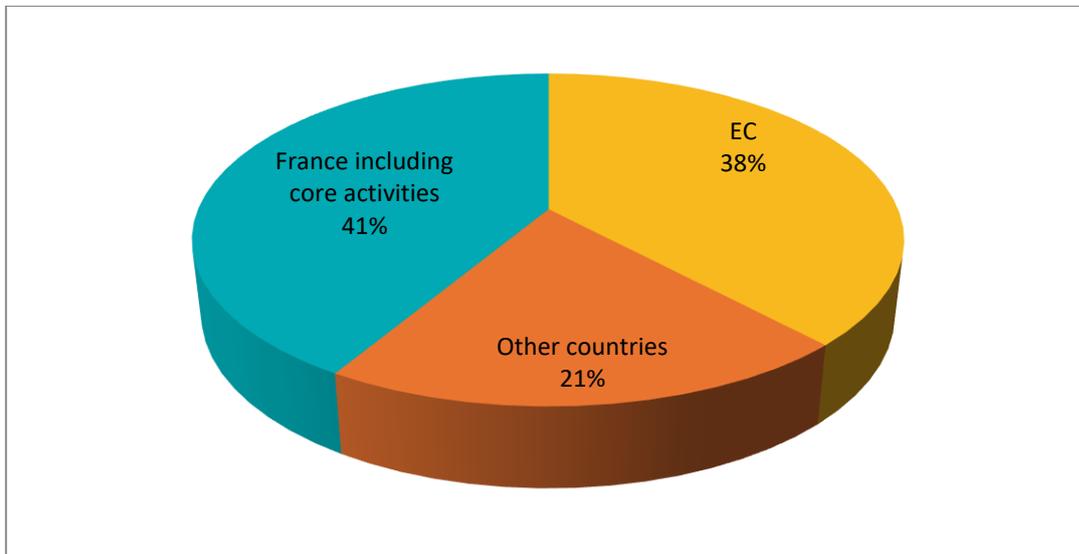


Figure 26 Orphanet's global budget 2017

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/partnerships. It excludes the collection of data on expert resources in the participating countries.

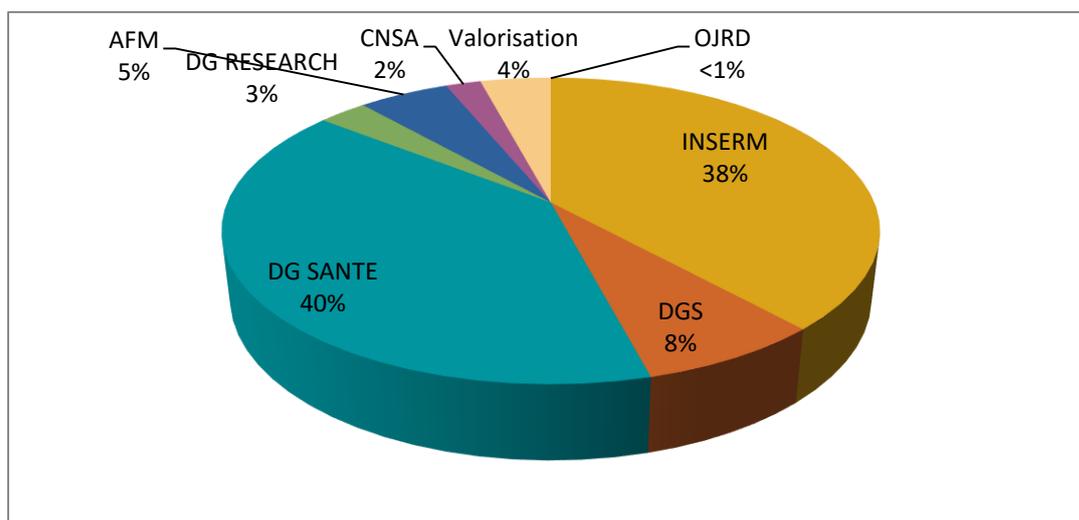


Figure 27 Orphanet core activities funding 2017

This budget (approx 1.7 million Euros) excludes the costs of infrastructure (office space and IT services) which are essentially covered by INSERM (Figure 27).

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 Health and Consumers Protection grant N°s S12.305098; S12.324970; SPC.2002269-2003220, 2006119, 20091215 and since 2004, DG Research and Innovation grant N°s LSSM-CT-2004-503246; LSHB-CT-2004-512148; LSHB-CT-2006-018933; Health-F2-2008-201230, HEALTH-F2-2009-223355, DG Santé grant 20133305-Operating Grant Orphanet). In 2014, the DG Santé grant 20102206 (Orphanet Europe Joint Action) was extended for one year without additional funding. In 2015, Orphanet participated in the ECRIN Integrating Activity (ECRIN-IA, 284395), funded by the European Union Framework Program 7. From 2016 Orphanet coordinates the HIPBI-RD project (E-Rare3 ERA-NET joint call). Orphanet is also involved in the ELIXIR-EXCELERATE Project (H2020 Project N° 676559). From 2018, Orphanet participates in the H2020 project Solve-RD (N° 779257).

The Orphanet consortium is funded by the DG Santé grant RD-ACTION Joint Action 677024 (2015-2018).

6.1.2. OTHER CURRENT FINANCIAL PARTNERSHIPS FOR CORE ACTIVITY FUNDING

	<p>The “Institut National de la Santé et de la Recherche Médicale” finances Orphanet’s core activities.</p> <p><i>Inserm Transfert</i> is in charge of supporting Orphanet in providing access to its data to Industry and in providing advice concerning intellectual property.</p>
	<p>The French Directorate General for Health (DGS) finances Orphanet’s core activities.</p>
	<p>The European Commission finances the database of diseases and the encyclopaedia in English, as well as the coordination, communication (including OrphaNews International) and IT of the project through the EU Health Programme.</p>
	<p>The “Association Française contre les Myopathies” finances OrphaNews France and International, the scientific literature survey, as well as data collection on clinical trials.</p>

Table 9 Other current financial partnerships for core activity funding

6.1.3. CURRENT NON-FINANCIAL PARTNERSHIPS FOR CORE ACTIVITY

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

 <p>World Health Organization</p>	<p>Collaboration with the World Health Organisation (WHO) in the process of revising the International Classification of Diseases.</p>
 <p>hpo</p>	<p>HPO and Orphanet collaborate on disease-phenotype annotations.</p>
 <p>GENATLAS</p>	<p>Cross-referencing with Genatlas which collaborates in updating the data on genes involved in rare diseases.</p>
 <p>UniProt</p>	<p>Cross-referencing with UniProt KB which collaborates in updating the data on genes linked to proteins involved in rare diseases.</p>
 <p>HGNC HUGO Gene Nomenclature Committee</p>	<p>Cross-referencing with HGNC which collaborates in updating the data on genes involved in rare diseases.</p>
 <p>OMIM[®] Online Mendelian Inheritance in Man[®]</p>	<p>Cross-referencing with OMIM (The Online Mendelian Inheritance in Man).</p>
 <p>REACTOME A CURATED PATHWAY DATABASE</p>	<p>Cross-referencing with Reactome.</p>
 <p>e!Ensembl</p>	<p>Cross-referencing with Ensembl.</p>
 <p>IUPHAR International union of basic and clinical pharmacology</p>	<p>Cross-referencing with The International Union of Basic and Clinical Pharmacology DataBase (IUPHAR-DB).</p>
 <p>LOVD Leiden Open Variation Database</p>	<p>The LOVD (Leiden Open Variation Database) platform includes links to Orphanet's gene pages, and Orphanet cross-links to LOVD from gene pages.</p>
 <p>EuroGentest</p>	<p>EuroGentest financed the creation of a thesaurus of clinical signs to harmonise international phenotype nomenclatures. EuroGentest collaborates with Orphanet in the field of quality management of medical laboratories.</p>

	<p>Orphanet and RD-Connect share information on biobanks and patient registries. Orphanet provides RD-connect with the nomenclature of RD.</p>
	<p>Orphanet and EMBL-EBI have developed ORDO and in 2014, a new version of this ontology was launched (ORDO 2.0).</p>
	<p>Collaboration with Snomed International is ongoing in order to include RD lacking in SNOMED-CT, and to provide alignments between ORPHA codes and SNOMED-CT terms</p>
	<p>Orphanet is the 30th bioinformatics structure of the French Institute of Bioinformatics, which is the French node of ELIXIR. Orphanet participates in the ELIXIR Use Case on Rare Diseases in the framework of the H2020 EU Project ELIXIR-EXCELERATE project N°676559.</p>
	<p>Orphanet works with the Genetic and Rare Disease (GARD) Information Center, hosted by NIH-NCATS, in order to align their nomenclatures and improve the provision of textual information on rare diseases.</p>

Table 10 Current non-financial partnerships for core activity

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. Globally this budget reaches 1.4 million Euros. Please refer to Figure 28 for an overview of funding of national activities.

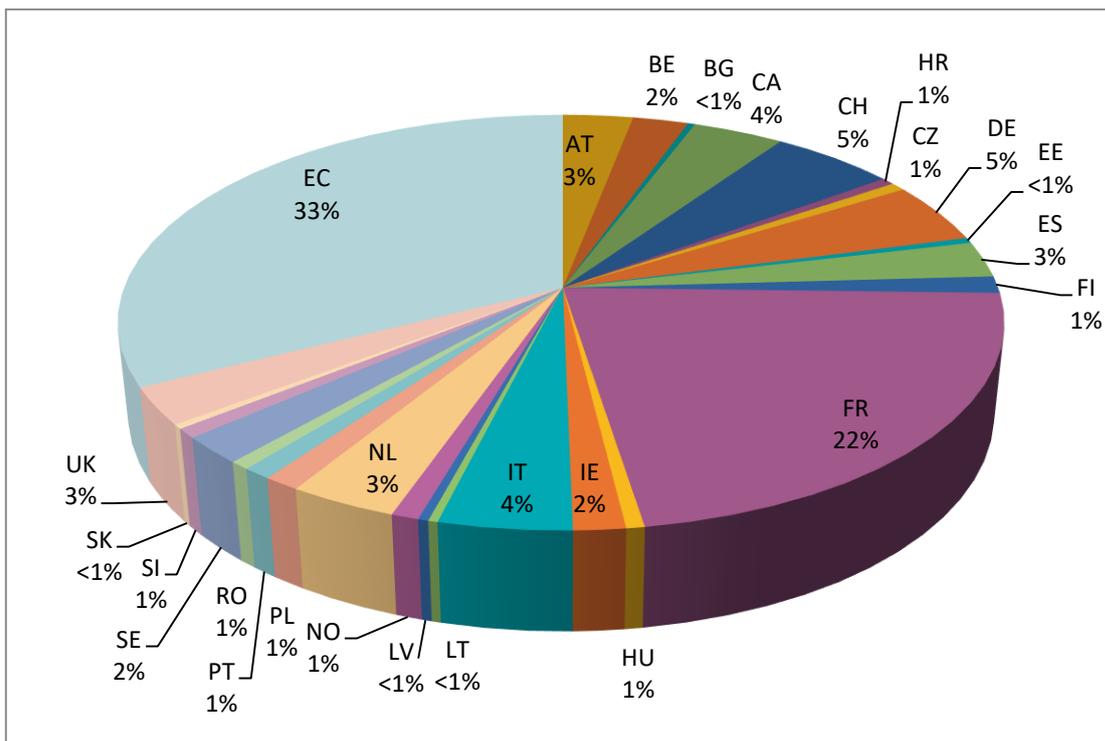


Figure 28 Funding sources for national activities in 2017

6.2.1. PARTNERSHIPS PROVIDING FUNDING FOR NATIONAL ACTIVITIES

Institutional partners host Orphanet’s national team activities and contribute to the project by allocating a budget and the time of some of their professionals.

AUSTRIA	
	The Medical University of Vienna is a beneficiary in the RD-ACTION 677024 and hosts Orphanet Austria since 2004. It further provides part-time funding (in kind) for the work of the country coordinator.
	The Austrian Ministry of Health and Women’s Affairs provides funding to the RD-ACTION 677024 since June 2015.
BELGIUM	
	The Federal Public Service Health, Food Chain Safety and Environment is beneficiary in RD-ACTION 677024

 <p>WETENSCHAPPELIJK INSTITUUT VOLKSGEZONDHEID INSTITUT SCIENTIFIQUE DE SANTÉ PUBLIQUE</p>	<p>The “Wetenschappelijk Instituut Volksgezondheid – Institut Scientifique de Santé Publique” is a beneficiary in RD-ACTION 677024.</p>
	<p>For the period 2014-2016, a convention between the Scientific Institute of Public Health (hosting the Orphanet team) and the National Institute of Health and Disability Insurance (NIHDI) includes financial support for the Orphanet project.</p>
<p>BULGARIA</p>	
 <p>Bulgarian Association for Promotion of Education and Science BAPES</p>	<p>The Bulgarian Association for Promotion of Education and Science (BAPES) is a beneficiary in the RD-ACTION 677024 and hosts Orphanet Bulgaria’s activities.</p>
<p>CANADA</p>	
 <p>CIHR IRSC Canadian Institutes of Health Research / Institut de recherche en santé du Canada</p>	<p>The Canadian Institute of Health Research is the host institution of Orphanet Canada, finances a position for an information scientist and provides additional administrative support for the project.</p>
 <p>Santé et Services sociaux Québec</p>	<p>The Québec “Ministère de la Santé et des Services sociaux” finances a project manager position in Quebec and some administrative support.</p>
 <p>Centre universitaire de santé McGill McGill University Health Centre</p>	<p>The Department of Medical Genetics of the McGill University Health Centre is the host institution of Orphanet-Quebec and provides the medical coordinator.</p>
 <p>RQMO REGROUPEMENT QUÉBÉCOIS DES MALADIES ORPHELINES</p>	<p>Le “Regroupement québécois des maladies orphelines” provides the project coordinator and administrative support.</p>
	<p>Pfizer Canada finances different Orphanet-Canada outreach events (Café Scientifique, Booth, Presentation) and helps distribute Orphanet-Canada information through their network.</p>
 <p>CARE for RARE</p>	<p>Care4Rare finances a part-time position for an information scientist.</p>
<p>CROATIA</p>	
 <p>Hrvatski savez za rijetke bolesti</p>	<p>Rare Diseases Croatia is a beneficiary in RD-ACTION 677024.</p>
<p>CZECH REPUBLIC</p>	
 <p>CHARLES UNIVERSITY</p>	<p>The Charles University Prague - 2nd School of Medicine is beneficiary in RD-ACTION 677024.</p>
 <p>Česká asociace pro vzácná onemocnění</p>	<p>The Czech Association of rare diseases finances the activity of the Czech team since April 2012.</p>

	<p>The Czech Medical Genetics and Genomics Society (www.slg.cz) helps Orphanet CZ in the collection of information on DNA diagnostic laboratories in the country, information on rare diseases clinics - dysmorphology, genetic counseling and information on patient support groups. Genetics professionals work with the overarching Czech rare disease patient association (www.vzacna-onemocneni.cz) which represents more than 30 individual associations. They have a joint partnership for the development of the Czech National Plans for rare diseases following the Czech National Strategy from 2010. The first, second and third Czech National Plans (2012-2014, 2015-2017 and 2018-2020) have been developed under the auspices of the Ministry of Health - Department of Medical Services and in collaboration with the National Coordination Centre for Rare Diseases at UH Motol (www.nkcvo.cz).</p>
ESTONIA	
	<p>The University of Tartu is a beneficiary in RD-ACTION 677024.</p>
FINLAND	
	<p>Rinnekoti Foundation is a beneficiary in RD-ACTION 677024.</p>
FRANCE	
	<p>The French Directorate General for Health (DGS) finances the collection of data in France for the expert resources catalogue.</p>
	<p>The “Association Française contre les Myopathies” finances OrphaNews France.</p>
	<p>The “Fondation Groupama pour la santé” contributes to the development of the mobile application.</p>
	<p>The “LFB Biomédicaments” helps finance the development and update of emergency guidelines and the French encyclopaedia for the general public. LFB also helped Orphanet fund its 20th anniversary celebrations.</p>
	<p>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.</p>
	<p>The “Caisse nationale de solidarité pour l'autonomie” supports the annotation of rare diseases with the International Classification of Functioning, Disability and Health (ICF) and the Orphanet encyclopaedia of disabilities.</p>

GERMANY	
 MHH Medizinische Hochschule Hannover	The Medical School of Hanover (MHH) supports data collection, and is a beneficiary in RD-ACTION 677024.
 amedes integrated diagnostics	Amedes Medizinische Dienstleistungen GmbH is a private company who supported Orphanet Germany financially.
	Förderverein Orphanet Deutschland e.V., a charity founded by Orphanet Germany to support national activities, provides funding to the team.
 Humangenetik Freiburg	Humangenetik Freiburg, a private company, provides funding to support national activities.
 MERCK Family Foundation	Merck Family Foundation, a charitable limited company founded by the Merck Group, is supporting national data collection.
 SANOFI GENZYME	Sanofi Genzyme, a pharmaceutical company, supports the German team by funding the team work within the frame of the Rare Disease Day 2017.
 B. BRAUN-STIFTUNG DER GESUNDHEIT NEUE WEGE BEREITEN	B.Braun Stiftung, a charity, is supporting the overall knowledge of the database by funding national training sessions for teaching experts on how to use the Orphanet database.
HUNGARY	
 ANTSZ	Országos tisztifőorvosi hivatal - OTH is a beneficiary in RD-ACTION 677024.
	Semmelweis Egyetem is a beneficiary in RD-ACTION 677024.
ITALY	
 Ministero della Salute	The Italian Health Ministry finances Orphanet-Italy activities through current research funding.
 Bambino Gesù OSPEDALE PEDIATRICO	The Bambino Gesù Children's Hospital is a beneficiary in RD-ACTION 677024.
 SANOFI GENZYME	Genzyme, a Sanofi Company, finances OrphaNews Italia.

IRELAND	
 <p>Feidhmeannacht na Seirbhíse Sláinte Health Service Executive</p>	The Health Service Executive jointly funds Orphanet Ireland with RD-Action for the provision of a project manager, 0.5 information scientist, and part time administrative support.
LATVIA	
 <p>Centre for Disease Prevention and Control of the Republic of Latvia</p>	"Centre for Disease Prevention and Control of Latvia" (Slimību profilakses un kontroles centrs) is a beneficiary in RD-ACTION 677024.
LITHUANIA	
 <p>VILNIUS UNIVERSITETAS 1579 UNIVERSITAS VILNENSIS</p>	The Vilnius University Hospital, "Santariškių Klinikos" Centre for Medical Genetics is a beneficiary in RD-ACTION 677024.
NETHERLANDS	
 <p>Leiden University Medical Center</p>	The LUMC is a beneficiary in RD-ACTION 677024. It hosts Orphanet Netherlands and co-funds the work of Prof van Ommen.
 <p>CENTRE FOR Medical Systems Biology</p>	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 project manager Dr Petra van Overveld and of the chair of the Dutch Scientific Advisory Board, Prof Cornel.
NORWAY	
 <p>Helsedirektoratet</p>	The Norwegian Directorate of Health hosts part of Orphanet Norway's activities and contributes to the project by allocating the time of some professionals. It is beneficiary in RD-ACTION 677024.
 <p>Norwegian National Advisory Unit on RARE DISORDERS</p>	The Norwegian National Advisory Unit for Rare diseases hosts part of Orphanet Norway's activities and contributes to the project by allocating the time of some professionals. It is beneficiary in RD-ACTION 677024.
POLAND	
	The "Instytut Pomnik Centrum Zdrowia Dziecka" (Children's Memorial Health Institute) is beneficiary in RD-ACTION 677024. 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.
 <p>Ministerstwo Zdrowia</p>	The Polish Ministry of Health contributes to the translation of the Orphanet encyclopaedia in Polish and contributes to translation of the Orphanet international website.

PORTUGAL	
	<p>IBMC - Institute for Molecular and Cell Biology hosted Orphanet-Portugal from 2009 to June 2015.</p>
	<p>ICBAS - Instituto de Ciências Biomédicas Abel Salazar, the Biomedical Sciences Institute at the University of Porto, funded Orphanet Portugal activities from 2009 till June 2015.</p>
	<p>DGS - The Directorate-General of Health, at the Portuguese Ministry of Health, is beneficiary in RD-ACTION 677024 and hosts the Orphanet Portugal team since June 2015.</p>
ROMANIA	
	<p>The “Universitatea de Medicina si Farmacie “Gr.T.Popa” Iasi” is a beneficiary in RD-ACTION 677024.</p>
SLOVAKIA	
	<p>CUMS (UNIVERZITA KOMENSKÉHO V BRATISLAVE) is a beneficiary in RD-ACTION 677024.</p>
SLOVENIA	
	<p>The University Medical Centre Ljubljana is a beneficiary in RD-ACTION 677024.</p>
SPAIN	
 	<p>The Centre for Biomedical Network Research (CIBER), Area on Rare Diseases (formerly known as CIBERER), has been the partner for Orphanet in Spain since April 2010 and is beneficiary in the RD-ACTION 677024. CIBER (Institute of Health Carlos III, Ministry of Economy, Industry and Competitiveness) finances the salary of one full-time information scientist as well as the main activities of the Spanish team. CIBER financed in 2017 the different expenses associated to Orphanet Spain activities, such as the production of fliers and attending meetings where the Orphanet team’s activities were disseminated.</p>
SWEDEN	
	<p>Karolinska University Hospital, Department of Clinical Genetics, Centre for Rare Disease is a beneficiary in RD-Action 677024.</p>

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. In 2015, the support financed an information scientist part time position.
TURKEY	
	The Association of Research-Based Pharmaceutical Companies gives non-restricted support for the Turkish translation of the Orphanet webpage and the documents. They supported the creation of the Orphanet-Turkey website and help Orphanet Turkey to prepare and print leaflets for health care professionals and the general public.
UNITED KINGDOM	
	The National Congenital Anomaly and Rare Disease Reg. Service (Public Health England) hosts Orphanet UK activities and contributes to the project by allocating the time of some professionals since August 2014. It is a beneficiary in RD-ACTION 677024.

Table 11 Partnerships providing funding for national activities

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.

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.
AUSTRIA	
	The "Gesundheit Österreich GmbH" (GÖG) is a collaborating stakeholder in the RD-ACTION.
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.

CYPRUS	
	The Department of Medical and Public Health Services is an associated partner in the Orphanet Europe Joint Action as of April 2011.
CROATIA	
	The Zagreb Children's Hospital contributes to the project by allocating the time of the country coordinator
IRELAND	
	The Mater Misericordiae University Hospital (MMUH) supports Orphanet Ireland by housing the National Rare Disease Office and Orphanet Ireland. The MMUH provides Clinical Geneticist hours to Orphanet Ireland, and provides Human Resources and IT support.
ISRAEL	
	Sheba Medical Center, Tel Hashomer of Israel hosts Orphanet Israel's activities and contributes to the project by allocating the time of some professionals since June 2014.
MOROCCO	
	The National Institute of Hygiene hosts Orphanet Morocco'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.
SPAIN	
	The Príncipe Felipe Research Center (CIPF) hosts Orphanet Spain's activities.
	The Foundation for the Promotion of Health and Biomedical Research of Valencia Region (FISABIO) hosts Orphanet Spain's activities.
TURKEY	
	The Istanbul University hosts Orphanet Turkey's activities and contributes to the project by allocating the time of some professionals.

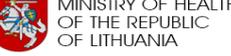
Table 12 Institutional partnerships providing services in kind for national activities

6.2.3. NON-FINANCIAL PARTNERSHIPS FOR NATIONAL ACTIVITIES

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, is 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 AMS-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 disease patients in Bulgaria, as well as to list the Bulgarian patient associations on the Orphanet database.
CZECH REPUBLIC	
	The Ministry of Health of the Czech Republic officially supports Orphanet.
CROATIA	
	Rare Diseases Croatia cooperates with its member organisations and with the Medical Faculty of the University of Zagreb.
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 in the online publication of the 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 a quota of airline tickets for patients to travel to medical experts or for experts to travel to patients with rare diseases. Orphanet provides expertise on the merits of applications when needed.
	Orphanet has delegated to "Maladies Rares Info Services", the French helpline for information on rare diseases - 0156538136, the role of replying to unsolicited electronic messages received by Orphanet.
GERMANY	
	The "Allianz Chronischer Seltener Erkrankungen e.V." (ACHSE) works together with Orphanet Germany on information 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.

 <p>AWMF Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V.</p>	<p>The AWMF (Association of the Scientific Medical Societies in Germany) cooperates with Orphanet DE by supplying the web links of their clinical practice guidelines to the Orphanet encyclopaedia.</p>
 <p>DIMDI Deutsches Institut für Medizinische Dokumentation und Information</p>	<p>DIMDI cooperates with Orphanet DE in including the disease terms from the German Orphanet nomenclature into the alpha-code of the ICD-10GM.</p>
<p>HUNGARY</p>	
 <p>EMBERI ERŐFORRÁSOK MINISZTERIUMA</p>	<p>The State Secretary of Health within the Ministry of Human Resources officially supports Orphanet.</p>
<p>IRELAND</p>	
 <p>An Roinn Sláinte DEPARTMENT OF HEALTH</p>	<p>The Department of Health officially supports Orphanet and provides governance of Orphanet Ireland.</p>
 <p>NRDO National Rare Diseases Office</p>	<p>The National Rare Disease Office (NRDO) hosts the Orphanet Ireland team. Orphanet is the main source of rare disease resource information for the NRDO Information Line.</p>
 <p>ROYAL COLLEGE OF PHYSICIANS OF IRELAND</p>	<p>The Royal College of Physicians National Clinical Programme for Rare Diseases Clinical Advisory Group (Chair: Prof. Andrew Green) acts as Scientific Advisory Group for Orphanet Ireland.</p>
	<p>Rare Diseases Ireland (RDI) (who together with MRCG and IPPOSI form the Irish National Alliance for Rare Disease) collaborate in the promotion of Orphanet and Rare Disease activities in Ireland. The Orphanet Country Coordinator is a board member.</p>
 <p>Medical Research Charities Group Unity is our Strength</p>	<p>The Medical Research Charities Group (MRCG) collaborates in the endorsement and promotion of Orphanet and Irish Rare Disease activities.</p>
 <p>IPPOSI Irish Platform for Patients' Organisations, Science and Industry</p>	<p>The Irish Platform for Patient Organizations, Science and Industry (IPPOSI) collaborate in the promotion of Orphanet and Rare Disease activities in Ireland. IPPOSI is also actively engaged in implementation of the RD-action WP5 in Ireland by providing links between the Orphanet Ireland team and eHealth and software developers.</p>
<p>ISRAEL</p>	
 <p>State of Israel Ministry of Health מדינת ישראל משרד הבריאות</p>	<p>The Israeli Ministry of Health officially supports Orphanet.</p>
<p>ITALY</p>	
 <p>ISTITUTO SUPERIORE DI SANITÀ</p>	<p>The "Istituto Superiore di Sanità" officially supports Orphanet.</p>
 <p>teleThon</p>	<p>Telethon collaborates with Orphanet for the collection of data concerning research projects.</p>

	<p>Uniamo, the Italian Federation of support groups on rare diseases, collaborates with Orphanet in the organisation and promotion of events dedicated to rare diseases, in order to increase public awareness on this particular issue.</p>
	<p>Netgene collaborates with Orphanet for the diffusion of information on rare diseases.</p>
	<p>Farmindustria promotes Orphanet publications.</p>
	<p>Osservatorio Malattie Rare (O.Ma.R.) collaborates with Orphanet in disseminating information rare diseases and the promotion of events.</p>
	<p>The Italian Inter-regional Technical Board for Rare Disorders collaborates with Orphanet in collecting data concerning the Centres of Reference officially recognised in Italy.</p>
<p>LATVIA</p>	
	<p>The Ministry of Health of the Republic of Latvia officially supports Orphanet.</p>
	<p>The Rare Diseases Society in Latvia aims to promote equal rights and opportunities for patients with rare diseases.</p>
	<p>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.</p>
<p>LITHUANIA</p>	
	<p>The Ministry of Health of the Republic of Lithuania officially supports Orphanet.</p>
<p>NETHERLANDS</p>	
	<p>The Ministry of Health, Welfare and Sport of the Netherlands officially supports Orphanet Netherlands.</p>
	<p>The Erfocentrum provides information to the general public on mainly rare, genetic disorders. Collaboration has been established to increase the number of Dutch texts available on Orphanet and to list the Dutch designated centers of expertise for rare diseases for the public and for experts.</p>
	<p>The VSOP (umbrella organisation of parent and patient organisations for genetic, congenital and rare disorders) provides information regarding patient organisations dedicated to rare disease and participates in the designation of Dutch centers of expertise for rare diseases.</p>

	<p>The Dutch Federation of University Medical Centers (NFU) is, in collaboration with Orphanet NL and the VSOP, responsible for the inventorying and documentation of Dutch centers of expertise for rare diseases.</p>
POLAND	
	<p>The patient organisation, Ars Vivendi, provides patients and parents with information about Orphanet services and cooperates with Orphanet Poland.</p>
	<p>The Polish Association of Patients with Muchopolysaccharidosis and Rare Diseases provides patients and parents with information about Orphanet services and cooperates with Orphanet Poland.</p>
ROMANIA	
	<p>The Ministry of Health collaborates with Orphanet Romania in updating data on the Romanian medical system. It officially supports Orphanet.</p>
	<p>Orphanet Romania collaborates with the Romanian Medical Association in updating data on health professionals.</p>
	<p>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.</p>
	<p>Orphanet Romania collaborates with the 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.</p>
SLOVAKIA	
	<p>The Ministry of Health of the Slovak Republic officially supports Orphanet.</p>
SLOVENIA	
	<p>The Ministry of Health of Slovenia officially supports Orphanet.</p>
SPAIN	
	<p>The Spanish Ministry of Health, Social Services and Equality - Office for Health Planning and Quality officially supports Orphanet.</p>
	<p>The Institute of Health Carlos III (ISCIII) provides Orphanet with data on national research projects funded through the Health Strategic Action Calls.</p>

	<p>The Spanish Federation for Rare Diseases (FEDER) collaborates with Orphanet with the updating of Patient Organizations' information, the revision of some texts included in the disability factsheets and articles for the general public, and Orphanet resources dissemination.</p>
<p>SWEDEN</p>	
	<p>The Ministry of Health and Social Affairs of Sweden officially supports Orphanet.</p>
<p>SWITZERLAND</p>	
	<p>The Health On the Net Foundation owns the domain www.orphanet.ch and supports the technical aspect of the Orphanet Switzerland online forms to collect data.</p>
	<p>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 professionals and in the organisation and promotion of events dedicated to rare diseases, in order to increase public awareness on this particular issue.</p>
	<p>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 support the adoption and the implementation measures of the National Concept on Rare Diseases by the Swiss federal Office of Public Health.</p>
<p>TURKEY</p>	
	<p>The Turkish Ministry of Health officially supports Orphanet. It collaborates with Orphanet Turkey for data collection and the dissemination of Orphanet in Turkey.</p>
<p>UNITED KINGDOM</p>	
	<p>The Department of Health officially supports Orphanet.</p>
	<p>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.</p>
	<p>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 concerning UK PO.</p>
	<p>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</p>

	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 UK PO.
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Table 13 Non-financial partnerships for national activities

7. Communication

7.1. Communication documents

In 2017, A5-size flyers to present Orphanet and Orphanet services were updated when necessary and distributed:

- Orphanet in 4 languages (English, French, Spanish and German)
- Orphadata (English)
- Orphanet application for iPhone and iPad (English)
- ORPHA codes (English)
- Orphanet database structure and main products (English)
- Orphanet rare disease ontology (English)
- Registering your activity as a professional with Orphanet (English)
- Resources for ERNs (English)

An A4 leaflet about Orphanet global positioning and achievements in 2016 was also printed and distributed at congresses.

7.2. Invitations to give lectures at conferences in 2017

Orphanet representatives, as specialists in the field of rare diseases, were invited to give lectures and to participate with poster presentations in more than 31 conferences worldwide in 2017. These lectures were mostly focused on presenting the Orphanet database (27), public health policies (2), and RD research (2). In addition to this, Orphanet was also represented in a range of national and international workshops and training sessions in raise awareness of Orphanet data and tools, and to liaise with other rare-disease focused projects.

7.3. Booths at conferences in 2017

Orphanet booths were held in 11 different congresses in 2017 as indicated in the list below:

- The Finnish Medical Convention, 11 -13 January 2017, Helsinki
- IRDiRC 3rd Conference, 8-9 February 2017, Paris
- 61st Annual Meeting of the Society of Thrombosis and Hemostasis Research –Basel – February 15-18, 2017
- Rare Disease Day, International School of Geneva, 18 February 2017, Geneva
- Rare Disease Day, CHUV, 4 March 2017, Lausanne
- GfH2017, 29 -31 March 2017, Bochum

- Congress of the French Paediatrics Society, 19 May, Marseille
- Irish Society for Human Genetics Annual Conference, 15 September 2017, Dublin
- Conference of the American Society of Human Genetics, 18-20 October 2017, Orlando
- RARE 2018, 20-21 November, Paris
- Disability Awareness day, Mater Misericordiae University Hospital, 28 November 2017, Dublin

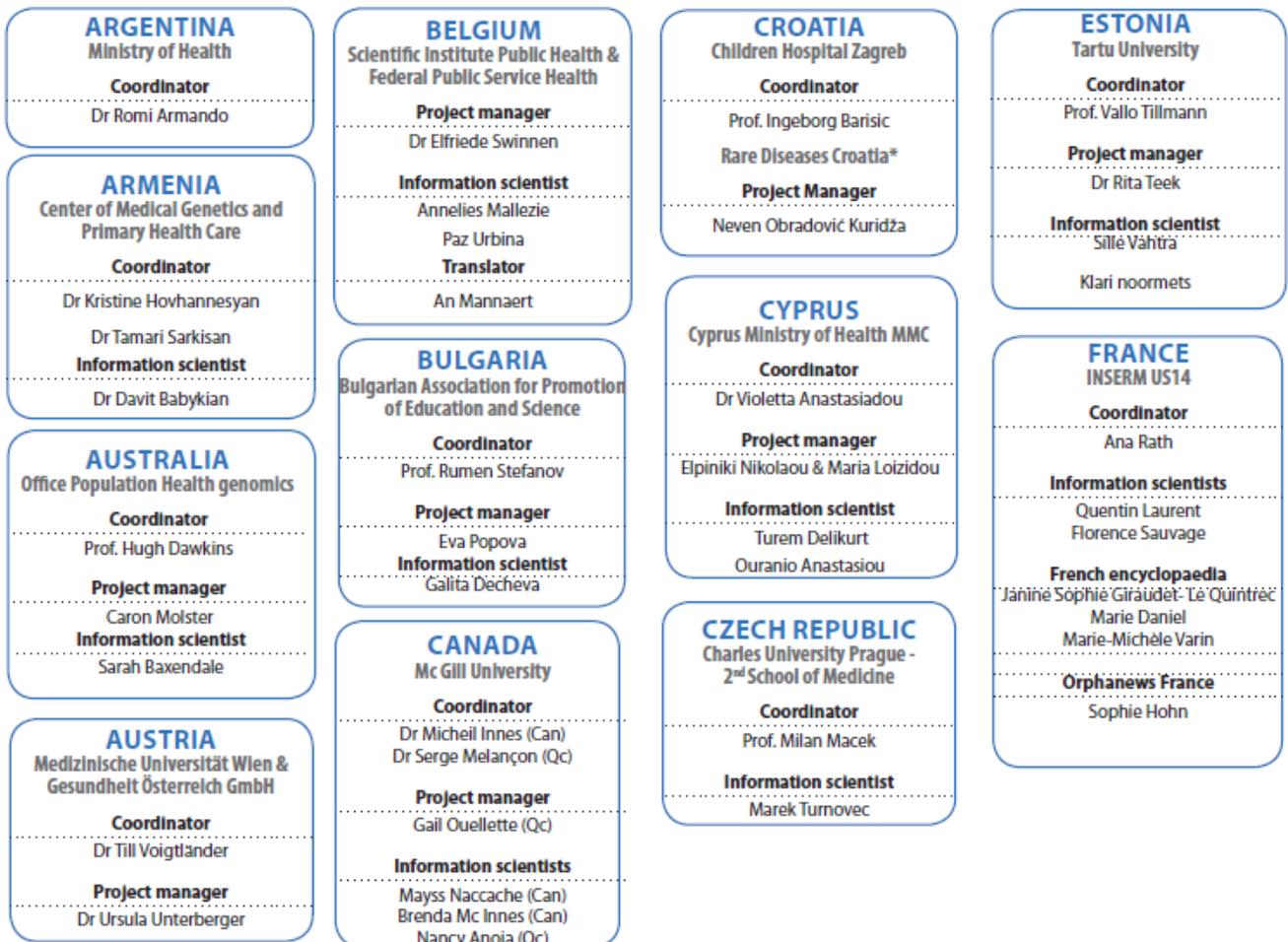
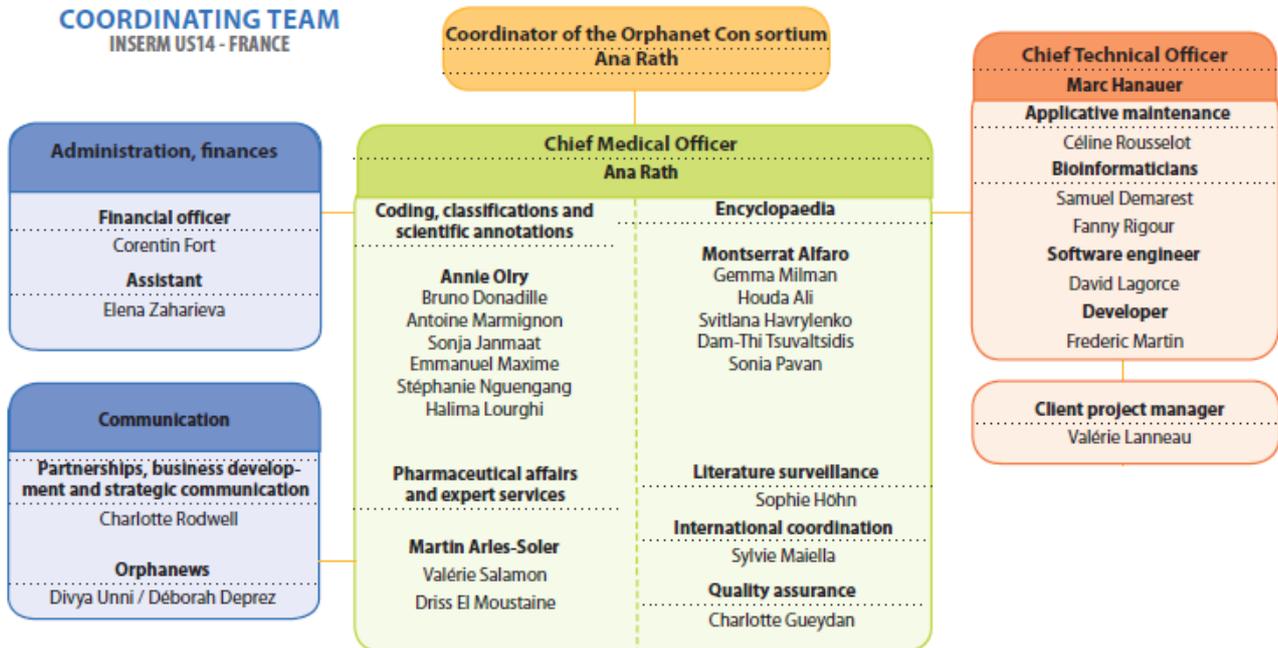
7.4. Social media

The Orphanet coordinating team maintains a [Facebook page](#) (3,780 followers) and a [Twitter account](#) (@orphanet : 2'870 followers) as well as the [Orphanet Tutorials](#) Youtube channel.

The Orphanet Italy team also maintains a [Facebook page](#) (2,700 followers) and a [YouTube channel](#).
The Orphanet Germany team maintains a [Facebook page](#) (200 followers)

8. The Orphanet team in 2017

COORDINATING TEAM INSERM US14 - FRANCE



<p>FINLAND Rinnekehti Foundation</p> <p>Coordinator Prof. Helena Käriäinen</p> <p>Information scientist Leena Toivanen</p>	<p>LATVIA Centre for Disease Prevention and Control of Latvia</p> <p>Coordinator Jana Lepikšone</p> <p>Information scientist Santa Pildava Irisa Zile</p>	<p>PORTUGAL Directorate General of Health</p> <p>Coordinator Dr Mario Carrera</p> <p>Project manager Dr Carla Pereira</p> <p>Medical translator Dr Rui Gonçalves</p>	<p>SWEDEN Karolinska University Hospital</p> <p>Coordinator Prof. Désirée Gavhed</p> <p>Ass. Prof. Rula Zain</p>
<p>GERMANY Medizinische Hochschule Hannover</p> <p>Coordinator Prof. Thomas Illig</p> <p>Project manager Dr Kathrin Rommel</p> <p>Information scientists Elisabeth Nyoungui</p>	<p>LITHUANIA Vilnius University Hospital</p> <p>Coordinator Prof. Vaidutis Kucinskis</p> <p>Information scientist Birute Burnyte Birute Tumiene</p>	<p>ROMANIA Universitatea de Medicina si Farmacie «Gr.T.Popa» Iasi</p> <p>Coordinator Ass. Prof. Cristina Rusu</p> <p>Information scientists Monica Panzariu Elena Braha</p>	<p>SWITZERLAND Service of Genetic Medicine - Geneva University Hospitals</p> <p>Coordinator Dr Loredana D'Amato Sizonenko</p> <p>Project Manager Philippe Suarez</p> <p>Information scientist Beatrice Geissbuhler</p>
<p>HUNGARY Országos Tisztifőorvosi Hivatal</p> <p>Coordinator Dr Melinda Csaky-Szunyogh</p> <p>Assistant Anita Szilagyi</p> <p>Semmelweis University</p> <p>Project manager Dr Maria Judit Molnar</p> <p>Information scientist Dr Marta Szegedi/ Dr. Gyorgy Milley</p>	<p>MOROCCO Institut National d'Hygiène</p> <p>Coordinator Prof. Abdelaziz Sefiani</p> <p>Information scientist Imane Cherkaoui-Jaouad</p>	<p>SERBIA Institute of Molecular Genetics and Genetic Engineering</p> <p>Coordinator Dr Dragica Radojkovic</p> <p>Project manager Dr Maja Stojiljkovic</p> <p>Information scientists Kriszta Klaassen</p>	<p>TUNISIA CHU Farhat Hached</p> <p>Coordinator Dr Dorra H'rida Ben Brahim</p>
<p>IRELAND National Rare Disease Office</p> <p>Coordinator Prof. Eileen Tracey</p> <p>Project manager Debby Lambert</p> <p>Information scientist Jackie Turner</p> <p>Medical writer Daniel Murphy</p>	<p>NETHERLANDS Leiden University Medical Center</p> <p>Coordinator Prof. Gert-Jan van Ommen</p> <p>Project manager Dr Petra van Overveld</p> <p>Information scientist Dr Judith Carlier - de Leeuw van Weenen</p> <p>Chairperson scientific advisory board Prof. Martina Cornel</p>	<p>SLOVAKIA Comenius University Bratislava</p> <p>Coordinator Prof. László Kovács</p> <p>Information scientist Gabriela Nagyova</p> <p>Medical Writer Veronika Urbán</p>	<p>TURKEY University of Istanbul</p> <p>Coordinator Prof. Ugur Ozbek</p>
<p>ISRAEL Chaim Sheba Medical center</p> <p>Coordinator Dr Annick Raas-Rothschild</p> <p>Project manager Vivi Einy</p>	<p>NORWAY Norwegian National Advisory Unit on RD</p> <p>Coordinator Lena Lande Wekre</p> <p>The Norwegian Directorate of Health</p> <p>Coordinator Bodil Stokke</p>	<p>SLOVENIA University Medical Centre Ljubljana</p> <p>Coordinator Dr Luca Lovrecic</p> <p>Information scientist Ales Maver Esada Kedric</p>	<p>UNITED KINGDOM National Disease Registration Division at Public Health England</p> <p>Coordinator Sarah Stevens</p> <p>Project Manager Ayomikun Ilevbare</p>
<p>ITALY Bambino Gesù Children's Hospital</p> <p>Coordinator Prof. Bruno Dallapiccola</p> <p>Project manager Dr Rita Mingarelli</p> <p>Information scientists Martina Di Giacinto Francesca Clementina Radio Michele Nutini Laura Barberito Fabiana Battisti</p>	<p>POLAND Instytut Pomnik Centrum Zdrowia Dziecka</p> <p>Coordinator Prof. Malgorzata Krajewska-Walasek Prof. Krystyna Chrzanowska</p> <p>Information scientists Dorota Karczarewicz Aleksandra Jezela-Stanek</p>	<p>SPAIN CIBER</p> <p>Coordinator Dr Francesc Palau</p> <p>Project manager Dr Virginia Corrochano</p> <p>Information scientists María Elena Mateo Estrella Rubio Cristina Aroca</p>	<p>ORPHANET CONTACT POINTS**</p> <p>Denmark Dr John Ostergard</p> <p>Georgia Dr Tamarl Rukhadze</p> <p>Lebanon Prof André Megarbane</p> <p>Luxembourg Dr Yolande Wagener</p> <p>Malta Dr Neville Calleja</p>

Figure 8 Organisational chart

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

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