

orphanet

The international rare disease and
orphan drug database
bridging healthcare and research

2018



A global network improving visibility, awareness,
information and knowledge in the field of rare diseases

www.orpha.net

Orphanet in numbers

Database content and website

- A network of **38 countries in Europe and beyond**
- A freely accessible site available in **8 languages**
- **32 million pages viewed** in 2018
- **7.5 million PDF documents** downloaded in 2018
- Orphanet & ORDO - **IRDiRC Recognized Resources** and **HVP Recommended Systems**
- **Orphadata** – An **ELIXIR Core Data Resource**



Diseases

- 6,177** rare disorders with unique identifiers : ORPHA codes
- 5,340** genes linked to **3,832** rare disorders
- 3,312** disorders annotated with HPO terms
- 5,722** disorders annotated with point prevalence data

Rare disease summaries in 12 languages

5,574	English
3,736	French
3,484	Spanish
3,465	Italian
3,322	German
2,261	Dutch
1,173	Portuguese
1,088	Polish
422	Greek
255	Russian
166	Finnish
95	Slovak

Directory of expert resources in the Orphanet network

23,330	professionals
8,556	expert centres
2,636	patient organisations
1,648	medical laboratories
43,836	diagnostic tests
2,545	ongoing research projects
2,723	ongoing clinical trials
777	patient registries
270	mutation databases
161	biobanks

Data from Orphanet 2018 Activity Report, database content in January 2019



Around **1 million visitors per month** from **236 countries**

39 % health professionals

26 % patients, families and support groups

As well as **researchers, industry, policy makers, students**

Most appreciated products: **list of diseases, texts on diseases, epidemiological data** and **clinical guidelines** *

* Annual Orphanet Users' Survey January 2019

Users

Our mission statement

Orphanet was established in France in 1997 at the advent of the internet in order to gather scarce knowledge on rare diseases* so as to improve the diagnosis, care and treatment of patients with rare diseases. This initiative became a European endeavour from 2000, supported by grants from the European Commission (EC): Orphanet has gradually grown to a network of 38 countries, within Europe and across the globe.

Orphanet continues to face new challenges resulting from a rapidly evolving political, scientific, and informatics landscape. It is now crucial to help all audiences access quality information amongst the plethora of information available online, to provide the means to identify rare disease patients and to contribute to generating knowledge by producing massive, computable, re-usable scientific data.

* A rare disease in the Orphanet database is one with a prevalence of not more than 1 per 2000 inhabitants in Europe, as defined in Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products



Orphanet Network Members around the globe

Composition of Orphanet Network Members

- 50% University hospital/hospital
- 24% Ministry of Health
- 13% Research centre
- 5% Public health institute
- 8% Foundation/association other than patient organisation

OUR COMMITMENT TO THE RARE DISEASE COMMUNITY

- Contribute to improving knowledge on rare diseases
- Provide high-quality information on rare diseases, and ensure equal access to knowledge for all stakeholders
- Maintain the Orphanet rare disease nomenclature (ORPHA codes), essential in improving the visibility of rare diseases in health and research information systems

WORKING ACROSS BORDERS

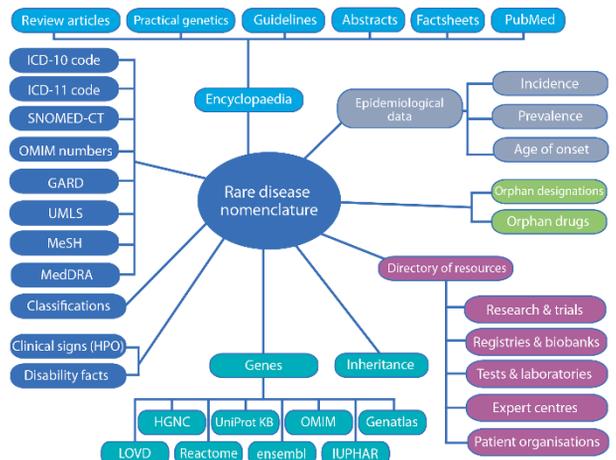
Orphanet is **a multi-stakeholder, global network of 38 countries**, coordinated by the INSERM (French National Institute for Health and Medical Research) in Paris.

The INSERM **coordinating team maintains the database** as well as core resources such as the Orphanet rare disease **nomenclature** (each with a unique ORPHA number), **classifications, encyclopaedia**, and the **Orphanet Ontology of Rare Diseases**. Countries in the network contribute to the database of **expert resources** in each country and to the **encyclopaedia**.

Orphanet and ORDO are IRDiRC Recognized Resources and HVP Recommended Systems. Orphadata is an ELIXIR Core Data Resource.

Orphanet's core activity is funded by the INSERM, the French Ministry of Health, and the EC. Orphanet's national activities are financed by the EC, national institutions and/or specific contracts.

Orphanet is governed by a Management Board of Network members, overseen by a multi-stakeholder International Scientific Advisory Board.



A relational database centred around a unique, clinical rare disease nomenclature, cross-referenced with other resources

2018 Highlights

END OF RD-ACTION & KICK-OFF OF THE ORPHANETWORK DIRECT GRANT

RD-Action (www.rd-action.eu), the 3 year Joint Action funded by the EU's 3rd Health Programme and coordinated by Orphanet, ended in 2018. This Joint Action brought together 40 countries **to support the development and sustainability of the Orphanet database, and conduct political actions at the European level**, in particular regarding the **codification of rare diseases in health information systems**. RD-Action also had the role of ensuring the **communication between the Member States** and the European Commission by coordinating priority actions, such as the elaboration and implementation of **European Reference Networks (ERNs)**. This Joint Action was unique in its kind, as it for the first time **integrated data and policy support** in the field of rare diseases.

The past three years have seen the emergence of a real multi-stakeholder consortium spanning the whole spectrum of fields, from data to policy, implicated in meeting the challenges of rare diseases, demonstrating the **high added value of a transverse approach**. Many key questions, notably concerning **the sustainability of resources and policies**, will continue to be addressed within the newly constituted Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases, and in the context of the Orphanetwork Direct Grant, the RD-CODE project, and the Rare 2030 Participatory Foresight Study. A [leaflet outlining the achievements](#) has been produced.

The European Commission decided in 2018 to allocate a Direct Grant within the 3rd Health Programme to Orphanet: the **Orphanetwork Direct Grant**, running from 1st June 2018 to 31 December 2020. **The objectives of the project are:**

- To provide the RD community with **interoperability tools**, in particular around an inventory of RD, to allow for semantic interoperability between countries and between domains (health, research);
- To provide **high-quality information** on RD, in particular through an encyclopedia in several languages;
- To provide a **directory of expert services** in order to help patients, physicians and stakeholders find the expertise on a particular disease in Europe and beyond, and to produce data needed to support policy actions;
- To further **develop and sustain Orphanet as the reference knowledge base on RD**, by establishing and consolidating **collaboration within the Orphanet pan-European network and with European Reference Networks (ERNs)** for the production, improvement and dissemination of knowledge on rare diseases. It will allow for the creation of a consistent expertise ecosystem for rare diseases in Europe.

The main expected outcome of this project is to **consolidate Orphanet as the European database for rare diseases**, achieving a position of the **international reference for information and data on rare diseases** in a steady RD ecosystem as the result of the **close cooperation between Orphanet and European Reference Networks**.

EUROPEAN JOINT PROGRAMME CO-FUND ON RARE DISEASES



The European Joint Programme on Rare Diseases (EJP RD; <http://www.ejprarediseases.org/>) brings over 130 institutions from 35 countries: to create a **comprehensive, sustainable ecosystem** allowing a virtuous circle **between research, care and medical innovation** to **improve the impact, reuse and funding of RD research**.

The EJP RD actions are organised within four major Pillars assisted by the **central coordination and transversal activities**:

- Pillar 1: **Funding of research**;
- Pillar 2: **Coordinated access to data and resources**;
- Pillar 3: **Capacity building**;
- Pillar 4: **Accelerated translation of research projects and improvement outcomes of clinical studies**.

Orphanet as a network is a partner, and co-leads the Pillar 2 of the EJP. Orphanet will develop its collection of research data, and provide training on the Orphanet nomenclature and ORDO.

2018 Highlights

RD-CODE: SUPPORTING THE IMPLEMENTATION OF ORPHA CODES IN HEALTH INFORMATION SYSTEMS

RD-CODE (www.rd-code.eu/), co-funded by the Third Health Programme, started on January 2019 and will end in June 2021. The objective of this project is to **support Member States in improving gathering information on rare diseases by implementation of ORPHA codes.**

The implementation process will be guided by the "Standard procedure and guide for the coding with Orphacodes" and the "Specification and implementation manual of the Master file" both developed in the framework of the previous Joint Action on Rare Diseases RD-ACTION (2015-2018).

The aim of the RD-CODE project is to **promote the use of the Orphanet nomenclature for implementation into routine coding systems.** This enables a **standardised and consistent level of information** to be shared at European level. Starting with countries that have no systematic implementation of ORPHA codification yet, but that are already actively committed to doing so, **this project will demonstrate real-world implementation to guide other countries** in the future.



ORPHADATA BECOMES AN ELIXIR CORE DATA RESOURCE

Orphadata download platform was designated as an **ELIXIR Core Data Resource** at the end of 2018.

The **ELIXIR Core Data Resources** are a set of European data resources of fundamental importance to the wider life-science community and the long-term preservation of biological data.

These resources include services such as data platforms and knowledge bases that are authoritative in their field of expertise. **Orphadata was added to this list after a detailed study conducted by an independent panel of reviewers following Orphanet's decision to adopt a more open licence,** compatible with Open Science principles (Creative Commons BY-4.0, compatible with the French Licence LOV2). The knowledge bases singled out as Core Resources, to which Orphanet now belongs, work as "conceptual authorities" with a **clear role in the standardisation of evolving concepts.**

Orphanet will play this role for rare diseases within the scientific community. The **Core Data Resources are also at the core of ELIXIR's long-term sustainability strategy** as a European infrastructure for information and life sciences data. **ELIXIR aims to ensure that these resources are available long-term** and that the life-cycles of these resources are managed such that they support the scientific needs of the life-sciences, including biological research.



ORPHANET BECOMES A PARTNER IN SOLVE-RD: HORIZON 2020 PROJECT TO SOLVE UNSOLVED RARE DISEASES

Led by the University of Tübingen, the Solve-RD consortium (www.solve-rd.eu), allocated €15 million by the European Commission Horizon 2020 programme, works from 2018 to **improve the diagnosis of rare diseases**, hand in hand with the European Reference Networks (ERN) on rare diseases.

The Orphanet coordinating team leads the work package in charge of **collecting standardised genetic and phenotypic information** concerning unsolved rare diseases cases from ERN cohorts and the RD-Connect GPAP, and **developing an ontology of unsolved cases (RDCO)** that will work alongside the Orphanet Rare Disease Ontology (ORDO) and the HPO-ORDO Ontological Module (HOOM) in order to make **new diagnostic hypotheses.**

In 2018 the project kicked-off, and the Orphanet team is currently developing the **Rare Disease Case Ontology** in order to reach the goals of the project.



RARE2030 PARTICIPATORY FORESIGHT PROJECT



Rare 2030 (www.rare2030.eu) is a EU-funded **foresight study** that gathers the input of a large group of patients, practitioners and key opinion leaders to **propose policy recommendations** that will answer leading us for a better future for people living with a rare disease in Europe.

Since the adoption of the Council Recommendation on European Action in the field of Rare Diseases in 2009, the European Union has fostered tremendous progress to improve the lives of people living with rare diseases. **Rare 2030 will guide a reflection on rare disease policy in Europe through the next ten years and beyond.**

In order to propose future policy scenarios and recommendations, an **extensive literature review is conducted to build a knowledge base, using sources including OrphaNews and the Orphanet database,** in order to identify trends and drivers of change that affect the future of rare diseases and inform policy options. This knowledge base will inform structured stakeholder dialogue that will identify trends and drivers of change of most relevance for policy recommendations. The Orphanet coordinating team is playing a leading role in this process.

Our key objectives

IMPROVING VISIBILITY

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 our relational database is structured. Each disease is assigned a unique **ORPHA number** (or ORPHA code): integrating these codes in health and research information systems is essential in ensuring rare diseases are visible and that different systems can work together. This nomenclature is aligned with other terminologies: OMIM, ICD, SNOMED-CT, MedDRA, UMLS, MeSH, GARD. **This cross-referencing is a key step towards the interoperability of databases.** A project, **RD-CODE**, was launched in 2019 to support Member States in their implementation of the nomenclature in health information systems.

Rare diseases patients are scattered across the globe, as are rare disease experts. Orphanet **provides visibility to experts and patients by providing access to a directory of expert services in 32 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.**

PROVIDING INFORMATION

To serve the needs of a global audience, Orphanet draws on the **expertise of professionals from across the world**, Orphanet produces an **encyclopaedia of rare diseases**, progressively translated into the **8 languages** of the database (English, French, Spanish, Italian, German, Dutch, Portuguese, Polish) with texts also freely available in Greek, Slovak, Finnish and Russian online.

Orphanet **integrates and provides access to quality information produced around the world**, such as clinical practice guidelines and information tailored to the general public.

GENERATING KNOWLEDGE

To develop and curate the scientific data in the Orphanet database, Orphanet works with **experts from around the globe**, from health care 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 can sometimes seem like pieces of an irresolvable puzzle. **Integration of 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)**. This has recently been **designated as an ELIXIR Core Resource** for the life science data community; In the context of the HIPBI-RD (www.hipbi-rd.net) E-Rare3 ERA-NET project aimed at the harmonisation of phenomics information for a better interoperability in the RD field, the **HPO-ORDO Ontological Module (HOOM)** provides a bridge between the Human Phenotype Ontology and ORDO.



These key 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 order to help **piece together the parts of this puzzle**.

A key policy resource

ORPHANET DATA INFORMING RARE DISEASE POLICY - ORPHANET DATA RESPONDING TO POLICY NEEDS

Orphanet plays a key role in informing rare disease policy and responding to policy needs. Between 2015-2018 Orphanet coordinated the European Joint Action on Rare Diseases (RD-Action) www.rd-action.eu, and currently co-leads a pillar of the European Joint Programme Co-fund on Rare Diseases: as such **Orphanet and its data is key to informing healthcare and research policy**. The presence of Orphanet in our partner countries has also proved to be an important catalyst in the improving the awareness of rare diseases, in particular as regards the national political agenda.

A virtuous, symbiotic cycle has evolved, connecting Orphanet's data and rare diseases policy:

- Orphanet **informs policy** by providing aggregated data (Orphanet Report Series), and data for annual **reports on the State of the Art of rare disease policies in Europe**, and the **State of Play of rare disease research**. Orphanet data has proved indispensable in **implementing policy measures**, such as the official designation of centres of expertise for rare diseases at national level by identifying where experts and expertise is located in a country.
- Orphanet's data can **respond to policy needs**: for example, data on laboratories carrying out diagnostic tests for rare diseases in Orphanet has evolved in order to facilitate cross-border testing. It is also being used in the context of the Rare2030 Participatory Foresight study to **inform future policy scenarii** in the field of rare diseases.

- In 2009, the Council of the European Union recommended that all EU Member States develop **national plans or strategies** to structure their response to the challenges presented by rare diseases. National contribution to the Orphanet network was recommended, and as a result many **national plans or strategies developed to date mention Orphanet and Orpha codification as key measures**.

- Orphanet is also cited in the **EU Cross-Border Healthcare Directive (2011)** as a key resource to assist « *health professionals [...] in correct diagnosis of rare diseases*».

- **Orphanet's activities and resources are also supported by a number of key policy recommendations** issued by expert committees at the European Commission, on topics such as codification of rare diseases, centres of expertise, European Reference Networks and cross-border genetic testing.

- In 2017, Orphanet was recognised as having a **de facto monopoly** in its field in the 2018 Work Plan of the European Union's Third Health Programme (2014-2020), notably for its unique nomenclature of rare diseases. From 2018 it is the recipient of a Direct Grant from CHAFEA, the executive body of DG Santé.

- A solution to assure the **sustainability of Orphanet** is currently under discussion at the Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases.

AT THE CROSSROADS OF THE RARE DISEASES WORLD: ORPHANET AS AN INTEGRATED PLATFORM

Orphanet is at the crossroads of multiple spheres implicated in issues arising from the rare disease challenge. Its role as an integrated, global platform is to **build the bridges necessary to help advance policy, healthcare and research by delivering global information, data and knowledge**. As such, Orphanet's networking capacity is key in **bringing together different countries and different languages**, as well as the **different types of expertise** emanating from different domains (healthcare, research, genetics, medical – social sector, patient organisations).

The scientific and informatics revolution underway offers **possibilities to further integrate data in Orphanet to facilitate the connection between the worlds of healthcare and research**: it is in this context that Orphadata has been designated an ELIXIR Core Data Resource. This same revolution also offers opportunities for Orphanet to become truly global and better respond to needs of users' across the world and across stakeholder groups.

Orphanet assumes this role in the **European Joint Programme Co-Fund on Rare Diseases**, that started in 2019, coordinated by INSERM.

Our commitment to the global rare disease community

Rare diseases know no borders, and the challenges faced by people living with rare diseases share commonalities across many different diseases and regions of the world. No nation, no continent can tackle the challenges around the diagnosis, treatment and care of people living with rare diseases alone. This challenge is a global one, and all stakeholders must cooperate at a global level in order to address the challenge and provide answers. The synergies resulting from cooperation across all stakeholder groups and across all continents are essential in this effort.

Global data is essential for global policies. Orphanet will continue to fulfil its missions at the service of the global community by:

- Ensuring equality of access to high quality information, essential in the empowerment of people living with rare diseases, and in the generation and improvement of scientific knowledge on rare diseases
- Promoting a common language and the means to integrate data on rare diseases in order to tackle the fragmentation of research into rare diseases
- Providing data essential for rare disease policy development, and remaining attentive to the needs of stakeholders in terms of rare disease data

“The Orphanet Consortium supports the work of the NGO Committee for Rare Diseases, and will, to the best of its ability, support the endeavour to improve the recognition and inclusion of rare diseases into the UN Sustainable Development Goals, and to strengthen the voice of research and medical institutions in all subsequent UN policy discussions around rare diseases.”

Orphanet Management Board, 4 November 2016



For more information about our objectives, achievements and partnerships, consult the annual Orphanet Activity Report at www.orpha.net

Get involved!

There are different ways you can help Orphanet improve its services for the rare disease community:

- **Contribute:** make your activities related to RD visible and register via Orphanet's homepage
- **Curate:** experts are encouraged to give their feedback on our data through the suggest an update button
- **Sustain:** sponsor one of Orphanet's activities
- **Give your feedback:** participate in our annual users' survey

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