orphanet

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

2019

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

www.orpha.net

Inserm
La science pour la santé
From science to health

Co-funded by the Health Programme of the European Union

elixir
Core Data Resource

IRDiRC
RECOGNIZED RESOURCES

THE HUMAN VARIOME PROJECT
RECOMMENDED SYSTEM

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

Orphanet in numbers

Database content and website

- A network of **41 countries in Europe and beyond**
- A freely accessible website available in **8 languages**
- **46 million pages viewed** in 2019
- **10.4 million PDF documents** downloaded in 2019
- Orphanet & ORDO - **IRDiRC Recognized Resources** and **HVP Recommended Systems**
- **Orphadata –** An **ELIXIR Core Data Resource**

Diseases

6,156 **rare disorders with unique identifiers : ORPHA codes**
5,544 **genes linked to 3,856 rare disorders**
3,842 **disorders annotated with HPO terms**
5, 804 **disorders annotated with point prevalence data**

Rare disease summaries in 13 languages*

5,899	English
4,072	French
5,091	Spanish
3,825	Italian
3,301	German
3,773	Dutch
1,163	Portuguese
1,252	Polish
421	Greek
245	Russian
166	Finnish
113	Japanese
103	Slovak

** Data from end of February 2020*

Directory of expert resources in the Orphanet network

27,337	professionals
8,508	expert centres
2,669	patient organisations
1,654	medical laboratories
45,274	diagnostic tests
3,926	ongoing research projects
3,385	ongoing clinical trials
785	patient registries
266	mutation databases
168	biobanks

Data unless stated differently from Orphanet 2019 Activity Report, database content in January 2020

Users

Around **1,5 million visitors per month** from **236 countries**

42 % health professionals
35 % patients, families and support groups
As well as **researchers, industry, policy makers, students**
Most appreciated products: **disease summaries, clinical signs, epidemiological data, classifications, and disability data***

* Annual Orphanet Users' Survey February 2020

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 41 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

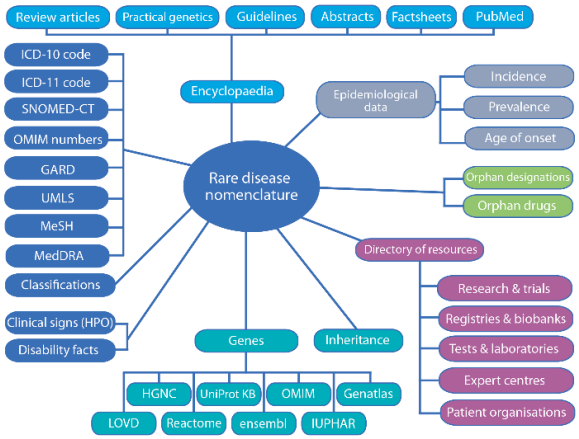
Orphanet is **a multi-stakeholder, global network of 41 countries**, coordinated by the INSERM (French National Institute for Health and Medical Research) in Paris.

The INSERM **coordinating team maintains the knowledge base** as well as core resources such as the Orphanet rare disease **nomenclature** (each with a unique ORPHA code), **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**. The website is available in 8 languages.

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 (see Activtiy Report).

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



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

2019 Highlights

COLLABORATION WITH EUROPEAN REFERENCE NETWORKS FOR RARE DISEASES

In order to improve rare disease knowledge generation and dissemination, **collaboration with the European Reference Networks (ERNs) for rare disease was further developed and formalised in 2019, in order to maximise the pool of expertise within the ERNs.** This common endeavour aims to improve rare diseases patients' lives by increasing knowledge and providing equal access to expertise. The Orphanet website can largely disseminate ERNs achievements, above all Clinical Practice Guidelines, and allows every European citizen to identify where ERNs' expertise is located.

The coordination of complementary activities is a key action of the current EC Direct Grant supporting Orphanet, continuing work started under the Joint Action on Rare Diseases, RD-Action. These activities are centred around the **improvement and maintenance of the standard Orphanet nomenclature of rare diseases** (ORPHA codes), the **scientific annotations** in the Orphanet, as well as the **production and dissemination of textual information** on rare diseases, including abstracts co-produced by Orphanet and ERNs. In addition, Orphanet and ERNs are working to ensure that all stakeholders have access to a **directory of healthcare, patient support and research activities** related to RD in Member States, in particular the activities of ERNs. Finally, a dedicated ERN section in OrphaNews International, Orphanet's twice-monthly newsletter, provides a **showcase for ERN activities**.

Orphanet's expertise in standardising clinical information has been associated with the rare disease and scientific expertise of ERNs to ensure that the nomenclature and classifications reflect current scientific and clinical knowledge. This work provides stakeholders with a **common, controlled language as a basis to improve the identification of patients and aid access to diagnosis and care, to better structure and optimise rare disease data, and to improve the interoperability between health information systems and research data**. Several groups of diseases have been revised and finalised so far, including the Orphanet classifications of rare eye diseases (ERN-EYE), primary lymphedema (VASCERN), as well as rare kidney diseases (ERKNet). Collaborations are also underway with other ERNs, including ERN BOND, ERN CRANIO, ERN Skin, MetabERN, EpiCARE, TransplantChild, and eUROGEN.

Collaborations are ongoing to produce information for doctors and patients in a coordinated way together with ERKnet, ITHACA and EpiCare, and others will follow.

European Reference Networks

EUROPEAN JOINT PROGRAMME CO-FUND ON RARE DISEASES

EUROPEAN JOINT PROGRAMME 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**.

Orphanet as a network is a partner, and co-leads activities around coordinated access to data and services within this programme. Orphanet is developping its collection of research data, and is working to provide training modules on the Orphanet nomenclature and ORDO.

2019 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 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.

The reference documents **"Standard procedure and guide for the coding with ORPHA codes"** 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) are being updated according to the field's needs and are freely available on the project website.

Within the project, a direct link with ERNs is established as it is foreseen that ERNs will use ORPHAcodes in their clinical patient management system (CPMS). The **ORPHAcode helpdesk is available and it is dedicated to answering questions related to the Orphanet nomenclature and the implementation of ORPHAcodes in Health Information Systems**. This is of particular importance in HCPs hosting ERNs.

NEW ESTIMATE OF WORLDWIDE POPULATION AFFECTED BY A RARE DISEASE

An article published in the *European Journal of Human Genetics* in September 2019, and co-authored by Orphanet, Orphanet Ireland and EURORDIS, presents an analysis of the prevalence data in the Orphanet database and estimates that **the number of people living with rare diseases between 263–446 million people in the world**. The publicly available epidemiological data in the Orphanet database was used to carry out this analysis and the figures are derived from data from 67.6% of the prevalent rare diseases; the diseases analysed are rare according to the European definition and exclude rare cancers, infectious diseases, and poisonings.

The analysis of this dataset provides **an estimation of the population prevalence of rare diseases of 3.5–5.9% of the population affected globally at any point in time**. The paper highlights the policy implications of these estimates. Indeed, it strengthens the rare disease community's current discourse, that **rare diseases affect millions of people and are thus a global health priority**. Future registry research and the implementation of rare disease codification, notably through the introduction of ORPHA codes, in healthcare systems will further refine the estimates.

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 scenarii and recommendations, an **extensive literature review has been conducted to build a knowledge base, using sources including OrphaNews and the Orphanet database**. This is used to identify trends and drivers of change that affect the future of rare diseases and inform policy options through structured stakeholder dialogue. Policy recommendations will be issued to the European Parliament in 2021. 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 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 36 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 including ERNs, 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. Orphanet also provides **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**, 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

CONTACT DETAILS

INSERM US14 – Orphanet
Plateforme Maladies Rares
96, rue Didot
75014 Paris, FRANCE
+33 1 56 53 81 37
contact.orphanet@inserm.fr
www.orpha.net
@Orphanet

This leaflet is part of the Direct Grant N°831390 which has received funding from the European Union's Health Programme (2014-2020). The content of leaflet represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.
Photo credits: Cover - © Everything possible/Fotolia-Adobe Stock, Backpage - ©Sergey Nivens / Fotolia - Adobe Stock