orphanet

September 2024

KNOW THE RARE

FOR BETTER CARE

The rare disease and orphan drug database bridging healthcare and research

www.orpha.net

RÉPUBLIQUE FRANÇAISE
Liberté
Égalité
Fraternité

Inserm
La science pour la santé
From science to health

Co-funded by the Health Programme of the European Union

GLOBAL CORE BIODATA RESOURCE

elixir
Core Data Resource

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

IRDiRC
RECOGNIZED RESOURCES

THE HUMAN VARIOME PROJECT
RECOMMENDED SYSTEM

Orphanet in numbers

Database content and website

- A network of **40 countries in Europe and beyond**
- A freely accessible website available in **9 languages**
- **35 million pages viewed** in 2023
- **2.9 million PDF documents** downloaded in 2023
- Orphanet & ORDO - **IRDiRC Recognized Resources** and **HVP Recommended Systems**
- **Orphadata Science –** A **Global Core Biodata Resource** & **ELIXIR Core Data Resource**

Diseases

6,345 **rare disorders with unique identifiers : ORPHAcodes**
4,496 **genes linked to 3,950 are disorders**
4,430 **disorders annotated with HPO terms**
5,878 **disorders annotated with point prevalence data**

Rare disease summaries in 14 languages

6,810	English
6,333	French
6,748	Spanish
5,816	Italian
5,114	German
6,761	Dutch
1,465	Portuguese
2,356	Polish
416	Greek*
179	Finnish*
153	Japanese*
103	Slovak*
185	Hebrew*
19	Czech*

Directory of expert resources* in the Orphanet network

30,645 Professionals referenced in the database
2,774 Patient organisations and **31** National Alliances for Rare Diseases
8,678 Expert centres
1,248 Medical laboratories dedicated to diagnosis
36,593 Diagnostic tests
3,970 Research projects
6,085 Clinical trials
853 Patient registries
177 Biobanks

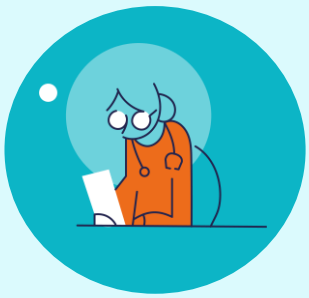
** individual resources outside of networks unless otherwise stated*

*Data unless stated differently from Orphanet 2023 Activity Report (database content in December 2023-January 2024). Data on *disease summaries from June 2024*

Users

Around **1.33 million visitors per month** from 236 **countries**

38 % health professionals
36,5 % patients, families and support groups
As well as **students, researchers, clinical coders, industry, policy makers.**
Most appreciated products: disease summary texts on diseases, clinical signs associated to a rare disease, classifications of rare diseases, functional consequences of rare diseases (disabilities), epidemiological data*
97% satisfaction rate



* Annual Orphanet Users' Survey (First Quarter 2023)

Know the rare for better care

Orphanet was established in France in 1997 at the advent of the internet to gather scarce knowledge on rare diseases* 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 40 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*

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

CREATION
1997

40
COUNTRIES

110
PEOPLE

KNOW THE RARE FOR BETTER CARE: OUR COMMITMENT TO THE COMMUNITY

- **Contribute to improving knowledge on rare diseases**
- **Provide high-quality information on rare diseases, and ensure equal access to knowledge for all stakeholders**
- **Deliver and support implementation of the Orphanet rare disease nomenclature (ORPHAcodes), essential in improving the visibility of rare diseases in health and research information systems, and facilitate its implementation in health information systems**

WORKING ACROSS BORDERS

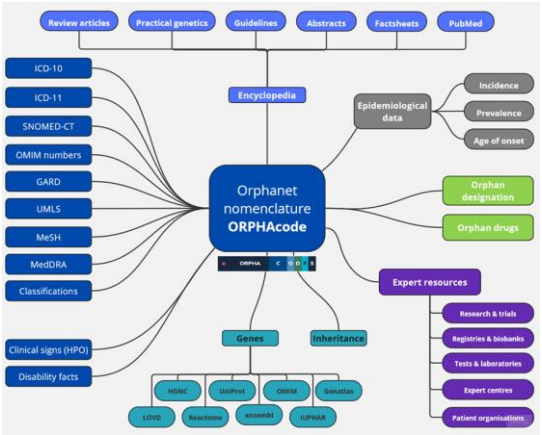
Orphanet is **a multi-stakeholder, global network of 40 countries**, coordinated by the INSERM (French National Institute for Health and Medical Research) in Paris.

The INSERM **coordinating team maintains the knowledge base** as well as core resources such as the Orphanet rare disease **nomenclature** (each with a unique ORPHAcode), **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 9 languages.

Orphanet and ORDO are IRDiRC Recognized Resources and HVP Recommended Systems. Orphadata Science is an ELIXIR Core Data Resource and a Global Core Biodata 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 Activity 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

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 **ORPHAcode**: 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-10, ICD-11, SNOMED-CT, MedDRA, UMLS, MeSH, GARD. **These alignments are a key step towards the interoperability of databases.** A project, **RD-CODE**, ran from 2019 to 2022 to support Member States in their implementation of the nomenclature in health information systems, followed by the **OD4RD/OD4RD2** projects to promote ORPHAcode implementation. In 2021 the **first human readable mapping of SNOMED CT to Orphanet** was released on Orphadata, thanks to a 7-year collaboration with SNOMED International and in 2022 **Orphanet was integrated into UMLS' Metathesaurus**.

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 **9 languages** of the database (English, French, Spanish, Italian, German, Dutch, Czech, Portuguese, Polish) with texts also freely available in 5 other languages.

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.com platform and as a **structured vocabulary for rare diseases, the Orphanet Ontology of Rare Diseases** (ORDO). **Orphadata Science is an ELIXIR Core Resource** and a **Global Core Biodata 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.

ordo Orphanet Rare Disease Ontology

HOOM HPO & ORDO Ontological Module

orphadata

GBC GLOBAL CORE BIODATA RESOURCE

elixir Core Data Resource

IRDiRC RECOGNIZED RESOURCES

THE HUMAN VARIOME PROJECT RECOMMENDED SYSTEM

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**.

Informing policy & research

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 has co-led 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, Orphadata) for analysis: Orphanet delivers analysis on RD coverage and gaps in expert centre organisation, and in research funding.
- 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 has served as one of the core sources for the Rare2030 Participatory Foresight study, to **inform future policy scenarii** in the field of rare diseases and craft recommendations to reach community-agreed goals.
- 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, and has received Direct Grant funding from the European Commission in recent years.
- ORPHAcodes are recognised as a **best practice** by the EC Steering Group on Promotion and Prevention (SGPP).
- In 2021, the **Rare2030 Policy Foresight project** included in its final recommendations support to Orphanet and use of Orphanet resources in a number of the different themes and associated recommendations.
- In 2021, the first **Resolution of the United Nations** on Persons Living with a RD encouraged, amongst other priorities, Member States and UN Agencies to collect, analyse and disseminated data on RD. ORPHAcodes are essential to achieving this goal.

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 has take, on this role in the **European Joint Programme Co-Fund on Rare Diseases**, coordinated by INSERM, in which it co-coordinated Pilar 2, aimed at improving **coordinated access to data and services** for the research community, as well as in EU structuring projects on health data, including **X-eHealth**, **TEHDAS Joint Action** and the European Health Data Space Pilot 2.

2023 Highlights

LAUNCH OF ORPHANET DATA FOR RARE DISEASES GRANT 2

The Orphanet Data for Rare Diseases Direct Grant (OD4RD) was a one-year project co-funded by the European Commision's EU4Health programme that started in 2022 which was followed up in 2023 by the OD4RD2 Direct Grant for a three-year period.

OD4RD was followed in mid-2023 by the Orphanet Data for Rare Diseases 2 (OD4RD2) 3-year Direct Grant. This project builds and expands on the achievements of the previous OD4RD project, taking advantage of Orphanet's specific expertise and its organisation as a long-lasting, well-established network, to fulfil the following general objectives:

• To contribute to the generation of standardised, interoperable data on RD diagnosis for primary and secondary use, by maintaining and supporting the implementation of the Orphanet nomenclature of RD, in collaboration with the ERNs.

• To contribute to the harmonisation of data collection across settings (health records, registries) and amongst countries, by the dissemination of coding good practices at the data source level.

•To contribute to supporting evidence-based decision-making in the frame of the European strategy around ERNs, by supporting the exploitation of reference corpuses of data and information on RD.

NEWBORN SCREENING KNOWLEDGEBASE

Launched in 2023 this new knowledgebase indexes scientific articles and reglementary texts on newborn screening across the world, based on an ongoing literature review.

Users can filter results by a range of features, such as the name of the disease, ORPHAcode, type of text, language, geographical region, and more. A search function is also available.

This resource was developed thanks to support from the AFM-Téléthon.

COLLABORATION WITH EUROPEAN REFERENCE NETWORKS FOR RARE DISEASES

In order to improve rare disease knowledge generation and dissemination, Orphanet collaborates with European Reference Networks (ERNs) for rare diseases. This common endeavour aims to improve rare diseases patients' lives by increasing knowledge and providing equal access to the pool of expertise provided by the ERNs. The coordination of complementary activities was a key action of the EC Direct Grant supporting Orphanet and will be a core component of the Orphanet Direct Grant OD4RD2. Work in 2023 focused on the following key areas:

European Reference Networks

Share. Care. Cure.

- **Improve the Orphanet nomenclature of rare diseases to provide 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: a full list of the status of ongoing collaborations with ERNs is available in our GitHub (updated every six months).
- **OrphaID platform** (https://id-genes.orphanet.app/ithaca/): launched in 2022 to provide access to curated intellectual disability related genes and phenotypes, resulting from a collaboration between ITHACA and Orphanet.
- **Revise and enlarge the Orphanet encyclopedia of rare diseases:** in 2023, 74 texts have been revised in collaboration with ERNs.
- **Prove a directory of healthcare, patient support and research activities related to RD**: work continued to represent all ERNs' activities. In particular, to build a repository of clinical research conducted by ERNs in the framework of the ERICA project.
- **Communicate on ERN activities to the RD community**: a dedicated section of OrphaNews International provides a showcase, with an edition dedicated to resources provided by ERNs concerning COVID-19 and RD and resources provided by the ERNs for refugees/displaced persons.

2023 Highlights

RARE DISEASE KNOWLEDGE
A MOBILE APP TO REDUCE THE DIAGNOSTIC ODYSSEY

Orphanet, Tekkare® and As We Know® launched RDK Rare Disease Knowledge™, a one-of-a-kind application designed to combat the diagnostic odyssey for people living with rare diseases. RDK allows primary care practitioners to search for rare diseases by name, or by a combination of clinical signs. Patients can also be directed to expert centres in France that manage specific diseases, overall helping to shorten the diagnostic process. Orphanet's rare disease data and expertise, coupled with Tekkare's technical know-how, make RDK a veritable fount of knowledge, putting the power of information on more than 6200 rare diseases right at hand.

While primarily dedicated to healthcare professionals, this Class 1 medical device is freely available to all in both French and English, without the need for prior registration. When performing a search based on clinical signs, the application yields a list of possible diseases, ranked based on a weighted score which considers the clinical features of each disease. The user can then access information on each disease. This includes data from Orphanet, as well as best practice tools such as emergency guidelines and national diagnostic and care protocols.

RDK can be accessed on the web, or downloaded to mobile devices and is available in French and English.

ERICA PROMS REPOSITORY

The overarching goal of the project is to is to build on the strength of the individual ERNs and create a platform that integrates all ERNs research and innovation capacity. In this project Orphanet co-leads WP3 which has the general aim of facilitating the Europe-wide implementation of standardised Patient-Centred Outcome Measures (PCOMs) and Patient Reported Outcome Measures (PROMs) for rare diseases while ensuring the involvement of the patient community in their development and validation process.

The PROMs Repository is an open-access tool which provides a centralised point of access for information on patient-centred outcome measures of relevance for rare disease research. The repository was updated in 2023 and can be accessed on ERICA's website.

A NEW LOOK FOR ORPHANEWS

OrphaNews launched a new look and feel in 2023 in line with the new graphic identity of Orphanet. The new format is easier to read and navigate and it is hoped will make the information provided more accessible.

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 Orphanet Network is a partner, and has co-led activities around **coordinated access to data and services** within this programme. Orphanet has augmented its collection of research data, and provides **training modules on the Orphanet nomenclature and ORDO**. A series of **national training sessions** were organised and led by Orphanet national teams since 2021. The first version of a **web-based RD research analysis platform** open to Orphanet partners and IRDiRC funders has also been made available.

AWARD FOR UNDIAGNOSED ORPHACODE

On 16 March 2023, Orphanet was honoured by the Spanish Federation for Rare Diseases (FEDER) with an award for the creation of a specific ORPHAcode for undiagnosed patients.

The ORPHAcode in question, 616874, is assigned to patients left without a definitive diagnosis following a full investigation by rare disease experts.

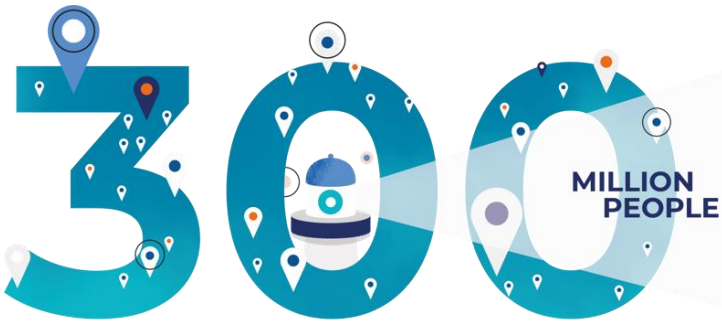
Our commitment to the global RD community

Rare diseases know no borders, and the challenges faced by over 300 million 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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