orphanet

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

GBC 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 **42 countries in Europe and beyond**
- A freely accessible website available in **9 languages**
- **33.8 million pages viewed** in 2022
- **3.9 million PDF documents** downloaded in 2022
- Orphanet & ORDO - **IRDiRC Recognized Resources** and **HVP Recommended Systems**
- **Orphadata Science –** A **Global Core Biodata Resource** & **ELIXIR Core Data Resource**

Diseases

6,258 **rare disorders with unique identifiers : ORPHAcodes**
4,440 **genes linked to 3,969 rare disorders**
4,348 **clinical entities annotated with HPO terms**
5,880 **disorders annotated with point prevalence data**

Rare disease summaries in 13 languages

6,688	English
5,361	French
6,617	Spanish
5,413	Italian
4,212	German
6,679	Dutch
1,241	Portuguese
1,946	Polish
419	Greek
180	Finnish
124	Japanese
103	Slovak
185	Hebrew
19	Czech

Directory of expert resources* in the Orphanet network

28,425 Professionals referenced in the database
2,915 Patient organisations and **31** National Alliances for Rare Diseases
8,814 Expert centres
1,622 Medical laboratories dedicated to diagnosis
44,972 Diagnostic tests
10,668 Research projects
8,561 Clinical trials
904 Patient registries
198 Variant databases
165 Biobanks

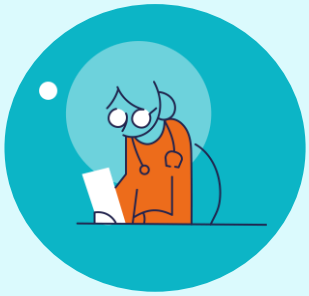
** individual resources outside of networks unless otherwise stated*

Data unless stated differently from Orphanet 2022 Activity Report (database content in December 2022-January 2023)

Users

Around **1,28 million visitors per month** from **238 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 2023

Know the rare for better care

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 42 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

42
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**
- **Maintain the Orphanet rare disease nomenclature (ORPHAcodes), essential in improving the visibility of rare diseases in health and research information systems**

WORKING ACROSS BORDERS

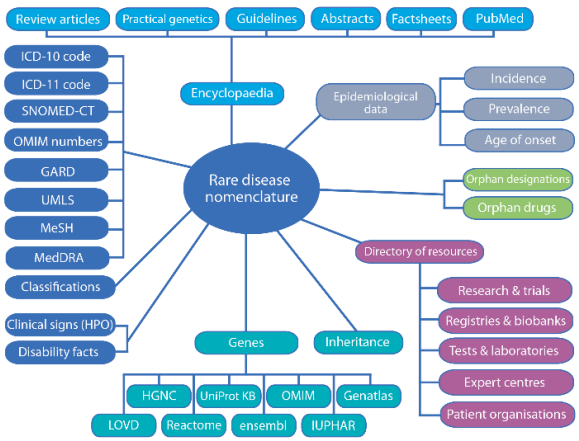
Orphanet is **a multi-stakeholder, global network of 42 countries**, coordinated by the INSERM (French National Institute for Health and Medical Research) in Paris.

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. **This cross-referencing is a key step towards the interoperability of databases.** A project, **RD-CODE**, was ran from 2019 to 2022 to support Member States in their implementation of the nomenclature in health information systems, followed by the **OD4RD and 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 Greek, Slovak, Japanese, 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.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

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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 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 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.
- 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 assumes 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**.

2022 Highlights

LAUNCH OF ORPHANET DATA FOR RARE DISEASES GRANT

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.

The aim of OD4RD was to **increase the visibility of rare diseases in Health Information Systems** by achieving the **implementation of ORPHAcodes in hospitals**, to increase the quality of data generated about RD patients by **disseminating best practices for coding with ORPHAcodes**, and to provide the means to generate accurate data for exploitation and analysis by European Reference Networks (ERNs), hospitals and decision makers, notably to improve their understanding of RD activities. The project also aimed to contribute to the **EU Health Data Strategy** by connecting the dots with structuring initiatives around EHR formats and health data spaces (EHDS) both for primary use in order to achieve better diagnosis and care of RD patients, (for example for the assessment of current practices and results against gold standards of care), as well as for secondary use, to inform policy decision-making and research.

The project aimed to maintain the update of the Orphanet nomenclature and classification of RD, the development of the Orphanet knowledge and information base around RD in collaboration with ERNs, the development of national Orphanet nomenclature hubs to ensure optimal implementation at national level, and support to the EC in its ERN strategy through dedicated IT systems. Training sessions and a help desk have been provided.

OD4RD
Orphanet Data For Rare Diseases

CODING THE UNDIAGNOSED

ORPHA: 616874

In 2022, in order to allow for efficient coding of patients with a suspected rare disease but without a determined diagnosis after full investigation, the ORPHAcode ORPHA:616874 was introduced in the Orphanet nomenclature of rare diseases.

This has been accompanied by guidance for coding undiagnosed patients including a video.

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 was a core component of the Orphanet Direct Grant OD4RD (start 2022). Work in 2022 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, including the Orphanet classifications of rare eye diseases (ERN-EYE), primary lymphedema (VASCERN), rare kidney diseases – renal tubular diseases and ciliopathies (ERKNet), inherited epidermolysis bullosas (ERNSKIN), cranial malformations (ERN CRANIO), as well as anorectal malformations (eUROGEN). Collaborations are also underway with other ERNs, including ERN BOND, ERN-ITHACA, ERN-EUROGEN, ENDO-ERN, , MetabERN, EpiCARE, VASCERN.
- **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 2022, texts on 99 diseases 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.
- **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.

2022 Highlights

ORPHADATA SCIENCE AWARDED GLOBAL CORE BIODATA RESOURCE STATUS

On 15 December 2022, the **Global Biodata Coalition announced its first list of Global Core Biodata Resources** (GCBRs). Amongst the 37 resources whose long-term funding and sustainability is deemed to be critical to life science and biomedical research worldwide figures **Orphadata Science**, which includes Orphanet's scientific knowledge base, nomenclature (ORPHAcodes) and ontologies.

This status comes 4 years after Orphadata Science received **ELIXIR Core Data Resource** in 2019, and makes Orphadata Science one of the 12 European resources to have been designated at international level by the Coalition and is the only resource based in France.

The selected resources are deemed to be essential to the management curation and access of research data, and are either deposition databases, or knowledge bases such as Orphanet, that draw together data and add value through expert curation and annotation. The Coalition frames these open resources such as *"keystone species in an ecosystem.... whose failure would have a critical impact on the global research endeavour".*

The Coalition's partner funders will now work actively with the selected resources in order to determine the funding models that would assure the long-term sustainability of these resources so that they can develop and continue to serve the global research community.

In 2022 the Orphadata platform was reorganised to make the site more user-friendly and to make services more easily identifiable. The site has now moved to www.orphadata.com.

25 YEARS OF ORPHANET A VIRTUAL CELEBRATION

2022 marked the 25th anniversary of Orphanet. To mark the occasion a social media campaign featuring the opinions of key opinion leaders from around the rare disease community on how Orphanet has helped change the rare disease landscape over the past 25 years by helping to 'know the rare'. We also included input from Orphanet country coordinators, project managers and information scientists on why they work for Orphanet. A dedicated hashtag #Orphanet25 was also launched to collect the views of Orphanet's end users.

The testimonies provided have been compiled into a **celebratory document**.

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 co-leads activities around **coordinated access to data and services** within this programme. Orphanet is developing its catalogue 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 in 2021 and 2022. The first version of a **web-based RD research analysis platform** open to Orphanet partners and IRDiRC funders has also been made available.

ORPHANET IN EU HEALTH DATA PROJECTS

Orphanet participates in EU structuring projects on health data, including **X-eHealth**, **TEHDAS Joint Action** and the **European Health Data Space Pilot 2.**

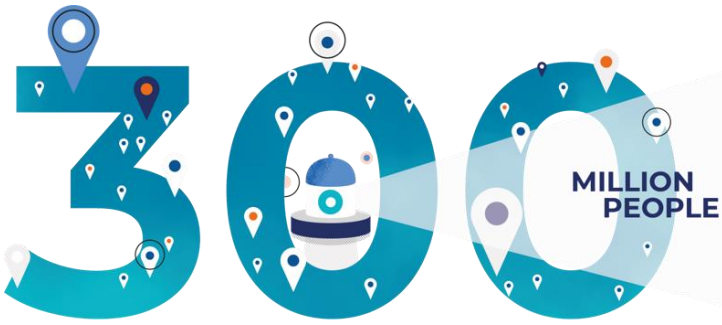
Our commitment to the global RD community

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 by registering them with Orphanet
- **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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