ORPHANET BELGIUM DATABASE 2024 ACTIVITY REPORT

CONVENTION BETWEEN THE INSURANCE COMMITTEE OF THE NATIONAL INSTITUTE FOR HEALTH AND DISABILITY INSURANCE (NIHDI) AND SCIENSANO IN ORDER TO FINANCE STRATEGIC RESEARCH ON RARE DISEASES IN BELGIUM (CENTRAL REGISTRY OF RARE DISEASES – GENETIC TESTS DATABASE – GENETIC TEST RESULTS REGISTRY – ORPHANET)

CALOMME Annabelle

WHO WE ARE

Sciensano can count on more than 950 staff members who are committed to health every day.
As our name suggests, science and health are central to our mission. Sciensano's strength and uniqueness lie within the holistic and multidisciplinary approach to health. More particularly we focus on the close and indissoluble interconnection between human and animal health and their environment (the "One health" concept). By combining different research perspectives within this framework, Sciensano contributes in a unique way to everybody's health.
For this, Sciensano builds on the more than 100 years of scientific expertise.

Sciensano

Epidemiology and public health - Gezondheidszorgonderzoek . Étude des soins de santé

Rare Diseases Team

March 2025 • Brussels • Belgium

—

CALOMME Annabelle

•

- **Rare diseases accompanying committee:** a multistakeholder committee is in charge of reviewing the work carried out over the past year and approving new work plans at the start of each year covered by the "Central Registry of Rare Diseases - Genetic Tests Database - Genetic Test Results Registry - Orphanet Belgium " convention. To this end, two meetings per year are organised, to which the partners and sponsors of Orphanet Belgium are invited. This includes representatives of the NIHDI, the FPS Public Health, Safety of the Food Chain and Environment, the hospital Rare Diseases Functions and RaDiOrg, the Belgian umbrella organization for people living with a rare disease.

- **Sponsors and non-financial partnerships:**

SPONSORS & NON-FINANCIAL PARTNERSHIPS OF ORPHANET BELGIUM	
sciensano	The **Health services research service**, within the Scientific Directorate of Epidemiology and Public Health at Sciensano, hosts the Orphanet Belgium team. Within the **Rare Diseases Team**, Orphanet Belgium collaborates on various projects that are part of the Belgian Rare Diseases Plan, such as the **Central Registry of Rare Diseases** (CRRD) and other **national patient registries**, e.g. for cystic fibrosis, neuromuscular diseases and rare bleeding disorders. A collaboration has been established with the **Belgian Genetic Test Database (BGTD)** to improve the registration and updating of diagnostic tests carried out by the eight officially recognised human genetics centres. A collaboration with the **Quality of laboratories service** facilitates the identification of clinical biology analyses carried out in the context of rare diseases. A collaboration with the **Infectious Diseases Epidemiology service** facilitates the identification of national laboratories/reference centres carrying out tests relating to rare infectious diseases.
federal public service HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT	The **Federal Public Service for Public Health, Food Chain Safety and Environment** is a partner of the Orphanet Belgium team.
INAMI-RIZIV	The **National Institute for Health and Disability Insurance** (NIHDI) funds Sciensano through a convention for the implementation and management of various projects specific to rare diseases, including the Orphanet Belgium project. NIHDI provides information on specialized centres for certain rare conditions (centres working within the framework of a convention).
RaDiOrg	**Rare Diseases Belgium (RaDiOrg)**, the Belgian umbrella association for people living with a rare disease, plays a role in validating data relating to Belgian patient organisations registered in Orphanet.
COLLEGE GENETICS	The **Belgian College of Human Genetics and Rare Diseases**, which represents the eight officially recognized Belgian genetics centres, collaborates with the Orphanet team, in particular to improve the process of recording/updating data on genetic testing activities.

Contactperson: Annabelle Calomme • T+32 2 642 54 47 • orphanetbelgium@sciensano.be

EXECUTIVE SUMMARY

The **Orphanet portal** [1] **plays a key role in research and care spheres for the rare disease community.** Since its creation in 1997, Orphanet has become the international reference in collecting, integrating, producing and disseminating high-quality, manually curated expert-reviewed information and data on rare diseases and orphan drugs. Orphanet develops and maintains the nomenclature (**ORPHAcodes**) and classification of rare diseases, essential in improving the visibility and recognition of patients in health information systems.

In Belgium, participation in the Orphanet project is supported by the national health authorities. Sciensano [2], the Scientific Institute of Public Health, is endorsed by the Ministry of Health to host the Orphanet Belgium team [3]. An **accompanying committee** consisting of members of the Federal Public Service (FPS) Public Health [4] and the National Institute for Health and Disability Insurance (NIHDI) [5] oversees the project. The management of Belgian data registered in Orphanet is described in the successive conventions for the support of strategic research on rare diseases in Belgium (Central Registry of Rare Diseases – Genetic Tests Database - Genetic Test Results Registry - Orphanet) concluded between the NIHDI and Sciensano. These conventions are monitored by the accompanying committee to determine by consensus the priorities and actions to be undertaken to carry out the project.

The objective of this report is to give **an overview of the main activities and challenges encountered during the year 2024 by the Orphanet Belgium team**. The recording and updating of Belgian activities carried out on rare diseases in the Orphanet database (information on expert centres, patient organizations and alliances/federations, medical laboratories and diagnostic tests, clinical trials, research projects and patient registries) remains the core of the Orphanet Belgium team's activity. The successful completion of these tasks requires the follow-up of numerous training sessions in order to be informed of the evolution of standard operating procedures and tools developed for this purpose by the Orphanet coordinating team (Orphanet-Inserm, France).

Part of our activities also involves **raising awareness about rare diseases**, in particular by participating in conferences, symposiums, congresses and events such as the Rare Disease Day which is held annually in February. We **offer assistance** to questions from people living with a rare disease as well as those from experts working in the field. During this year, we maintained a **close collaboration with many key players in the field of rare diseases in Belgium**, such as RaDiOrg [6], the eight rare disease functions [7], the College for Human Genetics and Rare Diseases [8] and the Terminology Centre of the FPS Public Health [9]. In 2024, we started a collaboration with the Belgian Health Care Knowledge Centre (KCE) [10] on the applicability of the NEED project to rare diseases.

The Orphanet Belgium team participates in a **European project called "Orphanet Data for Rare Disease" (OD4RD)** [11] launched in January 2022. The main objective of this international project is to promote the adoption of the Orphanet nomenclature (ORPHAcodes) within the different healthcare providers in the participating countries. Among the tasks to be accomplished by each national OD4RD team is the management of a **helpdesk** for end-users regarding the content of the Orphanet nomenclature and the correct implementation of ORPHAcodes in local Health Information Systems. Over the past years, we organized several **online and on-site trainings** dedicated to the use of the Orphanet nomenclature, developed and promoted new educational materials and advocated the implementation of ORPHAcodes towards national decision-makers (including the Ministry of Health and hospital managers).

For detailed information on Orphanet missions, services, quality commitment, general data management methodology and a description of the roles of the different team members, we refer to the previous activity reports of the Orphanet Belgium database [12] [13] [14] [15] [16], as well as to the activity reports [17] and procedures [18] published on the Orphanet website

TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

AISBL	Association internationale sans but lucratif
API	Application Programming Interface
BELAC	Belgian accreditation organisation
BfArM	The Federal Institute for Drugs and Medical Devices in Germany (Bundesinstitut für Arzneimittel und Medizinprodukte)
BGTD	Belgian Genetic Tests Database
CEGRD	European Commission Expert Group on Rare Diseases
CHU	Centre Hospitalier Universitaire
CRRD	Central Registry of Rare Diseases
EC	European Commission
EHR	Electronic Health Record
EQA	External Quality Assessment
ERICA	European Rare Disease Research Coordination and Support Action consortium
ERN	European Reference Network
EU	European Union
EUCERD	EU Committee of Experts on Rare Diseases
FAMHP	Federal Agency for Medicines and Health products
FAQ	Frequently Asked Questions
FPS	Federal Public Service
GDPR	General Data Protection Regulation
HCP	Health Care Provider
HIS	Health Information System
ICD	International Classification of Diseases
ICTRP	International Clinical Trials Registry Platform
INAMI	Institut national d'assurance maladie-invalidité
Inserm	The French National Institute of Health and Medical Research (Institut National de Santé et de Recherche Médicale, France)
IRDiRC	International Rare Diseases Research Consortium
IS	Information Scientist; member of an Orphanet national team, responsible for the data collection and registration of expert resources
MB	Management Board
MS	EU Member States (EU-27)
NIHDI	National Institute for Health and Disability Insurance
OD4RD	Orphanet Data for Rare Disease (European project)
ORPHAcode	A unique, time-stable and non-reusable numerical identifier generated randomly by the Orphanet database upon creation of a new entity in the nomenclature of rare diseases
OrphaNetWork	A website assigned to national teams and serving as a collection point for common tools and documents. This website is only accessible to Orphanet collaborators after entering a login and password
QAR	Quality Assurance Review
QC	Quality Control
RaDiOrg	Rare Diseases Organisation Belgium
RD	Rare Disease
RIZIV	Rijksinstituut voor ziekte- en invaliditeitsverzekering
SNOMED CT®	Systematized Nomenclature of Medicine Clinical Terms
SOP	Standard Operating Procedure
UZ	Universitair ziekenhuis
WP	Work Package; European projects work is organised into “work packages”. A work package can be thought of as a sub-project, which, when combined with other work packages, forms the completed project

INTRODUCTION

In Europe, the rarity of a disease is defined by an epidemiological threshold: **a rare disease is a medical condition with a specific pattern of clinical signs and symptoms that affects fewer than 1 in 2,000 people** [19]. For a long time, rare diseases remained a largely underestimated issue. However, in recent years, it has become more and more clear that they actually represent a **huge public health challenge**.

Rare diseases are **very heterogeneous, in terms of causes, symptoms and prevalence.** The number of people affected can vary considerably from one rare disease to another, ranging from hundreds of thousands of people to only a few worldwide. However, **when considered globally, rare diseases affect a large number of people**. A study [20] published in 2019 by Orphanet in the *European Journal of Human Genetics* estimates the number of people living with a rare disease at 3.5-5.9%, which equates to 263-446 million persons affected worldwide. If we transpose this figure on the Belgian population, it is equivalent to a **conservative estimate of at least 500,000 people suffering from a rare disease in our country** (not taking into account rare tumours, rare infectious diseases and poisonings). The large number of rare diseases, their rarity when taken individually, but also the different medical disciplines that should be involved in ensuring appropriate medical care make the organization of health policy in this area particularly complex.

More than 6,400 rare disorders[1] have been clinically defined to date [21] and new pathologies are regularly described in the scientific literature. Many rare diseases present with **complex constellation of symptoms** and are **multisystemic**: they affect several systems and organs of the human body and therefore require close collaboration between different medical specialities for adequate care. 72% of rare diseases have a genetic origin. About 70% of rare diseases start in childhood and around 30% of affected children will not reach the age of 5 [20]. Few rare diseases are preventable or curable and most often, they are severe, chronic, progressive and significantly affecting the quality of life.

People living with a rare disease face common difficulties in their daily life that arise from the rarity of their medical conditions. Among them is the **diagnostic odyssey** very frequently encountered by patients. An international survey on the journey to diagnosis for people living with a rare disease [22] was launched in June 2022 by EURORDIS [23]. It gathered 13,300 responses from 107 countries worldwide and more than 1900 rare diseases were represented. The survey's findings reveal an average diagnostic journey of nearly five years, with marked variations depending on demographic and geographic factors. **For Belgium, the EURORDIS study shows that it takes an average of 4.9 years from the onset of the first symptoms to receive a confirmed diagnosis of rare disease.** This delay has a significant impact on people's health, with preventable complications and missed opportunities for a better quality of life. It also generates significant expenses, with a high number of medical consultations and tests carried out before finally making an accurate diagnosis.

Once the diagnosis is made, other difficulties follow throughout life: struggle to identify where to find adequate clinical care, absence or limited access to an effective and affordable treatment, lack of relevant and validated information on the disease, misunderstanding of relatives and sometimes even of the medical profession and feelings of isolation due to the challenge of identifying companions in misfortune with whom to share the many difficulties encountered.

[1]The number of rare disorders listed in Orphanet is available at the bottom of the Orphanet website homepage. It is based on the content of the Orphanet nomenclature pack (version 07/2024).

The burden of rare diseases on patients, but also on their families, carers, healthcare systems and society overall merits greater attention and visibility. Among the key players seeking to provide a better understanding and recognition of rare diseases and therefore, ultimately, to guarantee better care, is the Orphanet network. **Orphanet is the reference knowledge base on rare diseases** [1]. It contains scientific information on each of the rare diseases identified to date and on the activities carried out in the countries belonging to its network. **Orphanet was co-created in 1997** by the French Ministry of Health and Inserm (French National Institute for Health and Medical Research). This initiative became a European endeavour from 2000 onwards, supported by grants from the European Commission and has gradually grown into a **consortium of around 40 countries**[2] within Europe and across the globe. The Network members are institutions endorsed by the Ministry of Health or Ministry of Research of the member country. **Belgium was one of the first countries to join the Orphanet consortium in 2001**.

Since 2007, in addition to its role as a knowledge base on rare diseases, **Orphanet has been developing the nomenclature of rare diseases (ORPHAcodes)**. Rare diseases are not correctly represented in generic medical terminologies, and as a result, these diseases are invisible or poorly documented in health systems and in the databases used to advance research. Orphanet therefore plays a central role in providing the only specific nomenclature for rare diseases, which ensures interoperability between hospital patient files and international databases and registries.

Orphanet ensures **equal access to knowledge for all stakeholders** and serves the following communities: health care professionals, patients and their relatives, patient organisations, researchers, biotech and pharmaceutical companies, public health and research institutions and public authorities. The information on the Orphanet website is currently available in nine languages including French, Dutch and German, the three official languages in Belgium. In 2023 around 16 million users consulted the Orphanet website with around 34 million pages viewed. The users come from 236 countries and Belgium is among the top ten countries of the website's audience [24].

Belgium's contribution to the international database Orphanet makes it possible to collect data related to the clinical and research activities carried out in our country in the field of rare diseases (directories of patient organisations, expert centres, diagnostic test laboratories, research projects, clinical studies, patient registries, biobanks), and thus gives them visibility both nationally and internationally. Structural and financial support for the creation and management of a national Orphanet portal stems from one of the 20 actions defined in the first **Belgian Plan for Rare Diseases** [25] [26] launched at the end of 2013. The Orphanet Belgium management is listed in the Plan as "Action 17" which focuses on sharing knowledge and information on rare diseases.

In addition to its data identification, validation and publication activities in the Orphanet platform, **the Orphanet Belgium team participates actively in the "Orphanet Data for Rare Disease" project (OD4RD)** [11], co-funded by the European Union (EU4Health funding). The OD4RD project was launched in January 2022 for a 15 months period (OD4RD1). Belgium was one of the participating countries in this pilot-phase. The project has been renewed until the end of 2025 (OD4RD2) and is operational in 20 European countries. The main objectives are to tackle the lack of visibility of rare diseases in European Member States health systems, promote harmonisation in the coding practices and facilitate generation of standardised interoperable data around rare diseases. The Orphanet Belgium team participates in Work Package 4 which intends to **provide support for the local implementation of ORPHAcodes** - recognised as best practice by the European Commission [27] - by Belgian healthcare providers through the establishment of national support hubs for the use of the Orphanet nomenclature and classification.

[2] This number evolves as countries join the consortium or are (temporarily) suspended. To have access to the most up to date figure, please refer to this document.

COMPOSITION OF THE ORPHANET BELGIUM TEAM IN 2024

Since November 2023, Prof. Dr. Olivier Devuyst is the Orphanet Belgium country coordinator. He is a nephrologist, head of clinic and head of the Institute of Rare Diseases at the Cliniques universitaires Saint-Luc (CUSL). He is Full Professor of Medicine at the UCLouvain Medical School (Belgium) and teaches nephrology at the University of Zurich (Switzerland) where he co-directs the university program on RDs. Prof. Dr. Devuyst has coordinated several RD European programs and is one of the founding members of the European Reference Network on Rare Kidney Diseases (ERKNet).

What are the roles of an Orphanet country coordinator?

In each country participating in the Orphanet network, a national coordinator is appointed in agreement with the Orphanet Board of Directors. Each national coordinator undertakes to promote the objectives of the project and to be responsible for the content and quality of the data collected on expert resources at national level. He/she organizes the governance of the project at national level, including liaison with learned societies, health authorities and patient organisations, and the build-up of the Orphanet team if applicable. The country coordinator is responsible for data quality management about expert resources in the country. He/she acts as the national contact point for the health authorities on RDs. He/she is a professional well established in the field of RDs, with a strong interest for public health and research issues. The country coordinator participates in the Orphanet Management Board meetings where decisions relating to the strategy developed by Orphanet are voted on (6 times a year on average), edits the national web pages of Orphanet, contributes to the dissemination of national initiatives in the field of RDs via Orphanews and the OrphaNetWork internal newsletter, and takes part in the annual Orphanet consortium meeting organized by the coordination team and attended by all national coordinators.

Annabelle Calomme has been part of the Orphanet Belgium team since 2017. She is senior Orphanet Information Scientist (IS) and Project Manager (PM), in charge of the Belgian rare disease data in the Orphanet database (collection, validation, publication and update of expert centres, patient associations, laboratories and their offer of diagnostic tests, clinical trials, research projects and registries). She also manages the Orphanet Belgium site (French version). She is the Project Manager of the OD4RD European project in Belgium.

Kim Van Roey is responsible for activities related to data translation of the Orphanet content into Dutch: Orphanet nomenclature and encyclopedia of rare diseases and content of international and national Orphanet sites. He also manages the Orphanet Belgium site (Dutch version). A separate annual activity report is available for this part of the activities.

MAIN ACTIVITIES CARRIED OUT IN 2024

1. Belgian contribution to the Orphanet database [January – December 2024]

1.1. CONTENT OF THE ORPHANET BELGIUM DATABASE

The management of the Orphanet database (Figure 1) is **a continuous and constantly evolving task**.

Orphanet data is **processed manually** by the national teams and **validated by rare disease experts**, in accordance with **standard operating procedures** (SOPs) which include the methodology to be adopted, the workflow to be followed and the inclusion/exclusion criteria for each type of expert resources.

Two types of RD data (called “expert resources” by Orphanet) are registered:

- **Patient-related activities:** patient organisations, federations and alliances; expert centres, networks of expert centres; medical laboratories and diagnostic tests;

- **Research-related activities:** research projects, clinical trials, networks of experts, patient registries and biobanks.

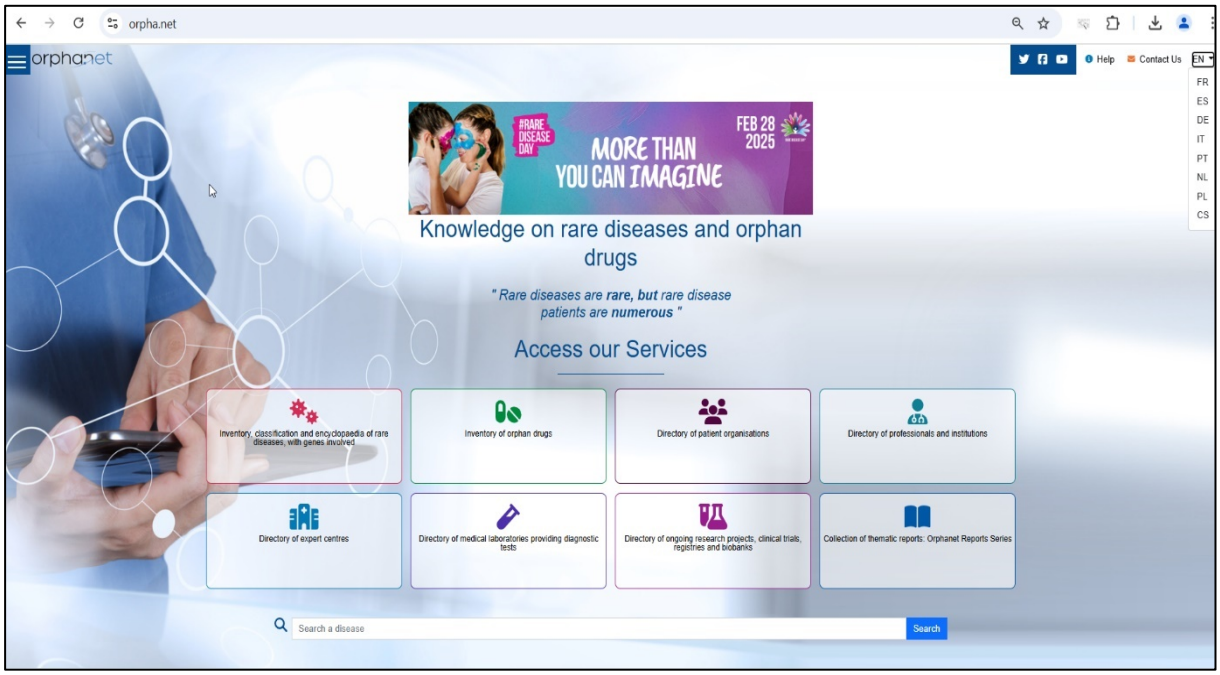


Fig.1. Screenshot of the homepage of the Orphanet website

The current content of the Orphanet database in terms of Belgian data is described in Figure 2.

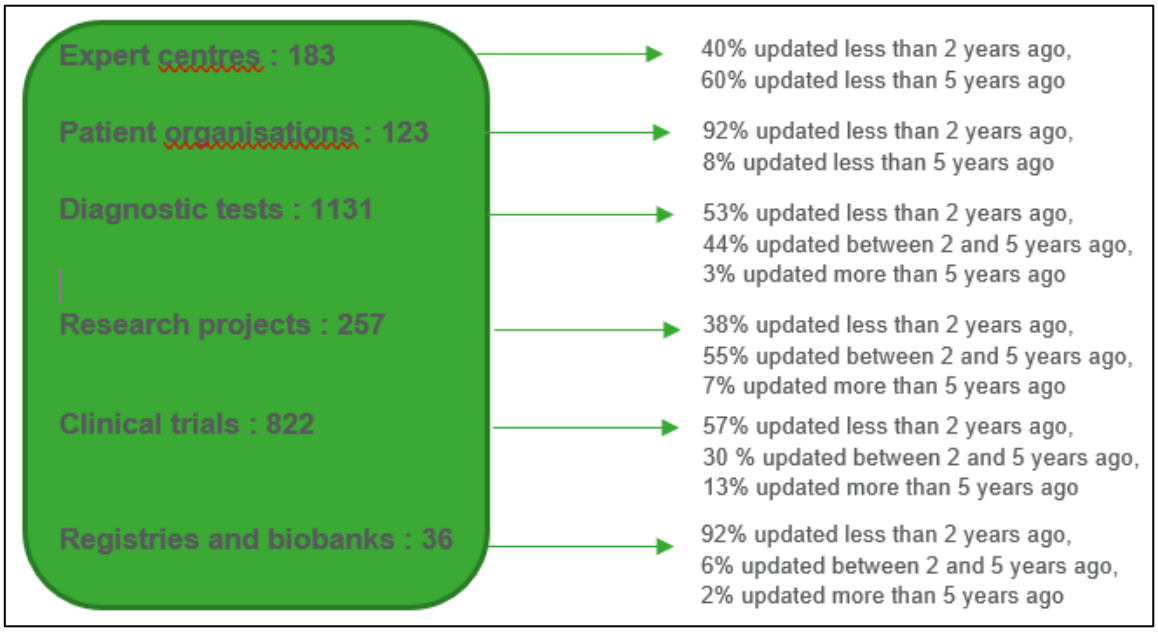


Fig.2. Number of Belgian expert resources registered in the Orphanet database,
with the time since their last update (as of December 2024)

For most types of Belgian expert resources, there has been **an increase in the amount of data collected over the past year** (Figure 3). However, for some resources types, there is no variation or there is a decrease in the total number of registered data, due to update work. Increasing the quantity of collected data improves the value of a database, but at the same time ensuring a high quality of the data listed by deleting data that is no longer up to date or by modifying data already registered, is essential to maintain a relevant database. We therefore apply **regular update cycles** in order to check that the information is still sufficiently accurate, complete and up to date, as well as to identify all kinds of potential errors such as the presence of duplicates.

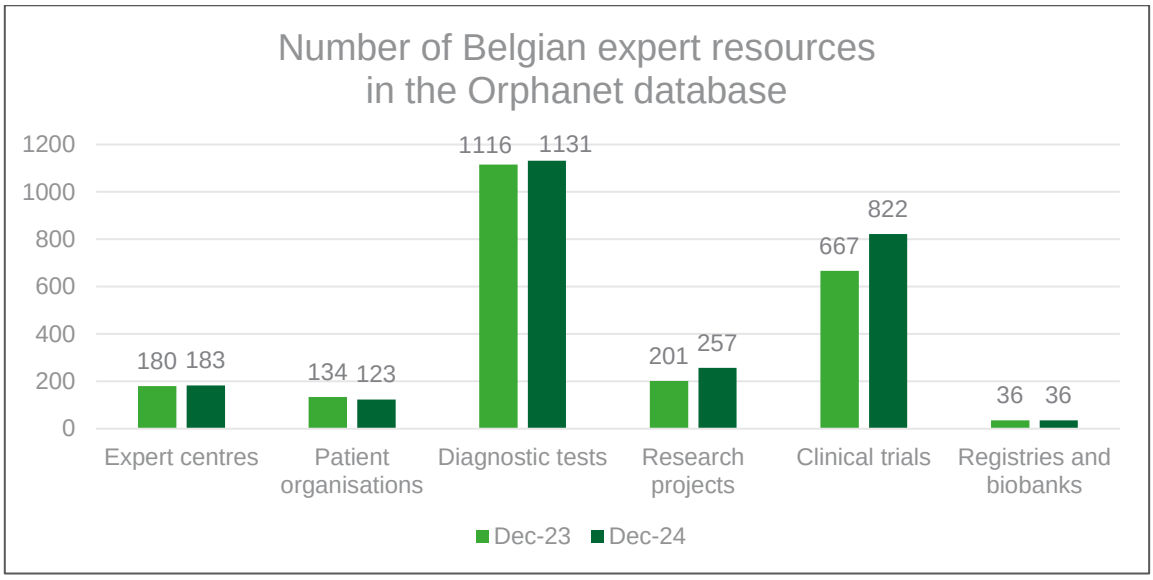
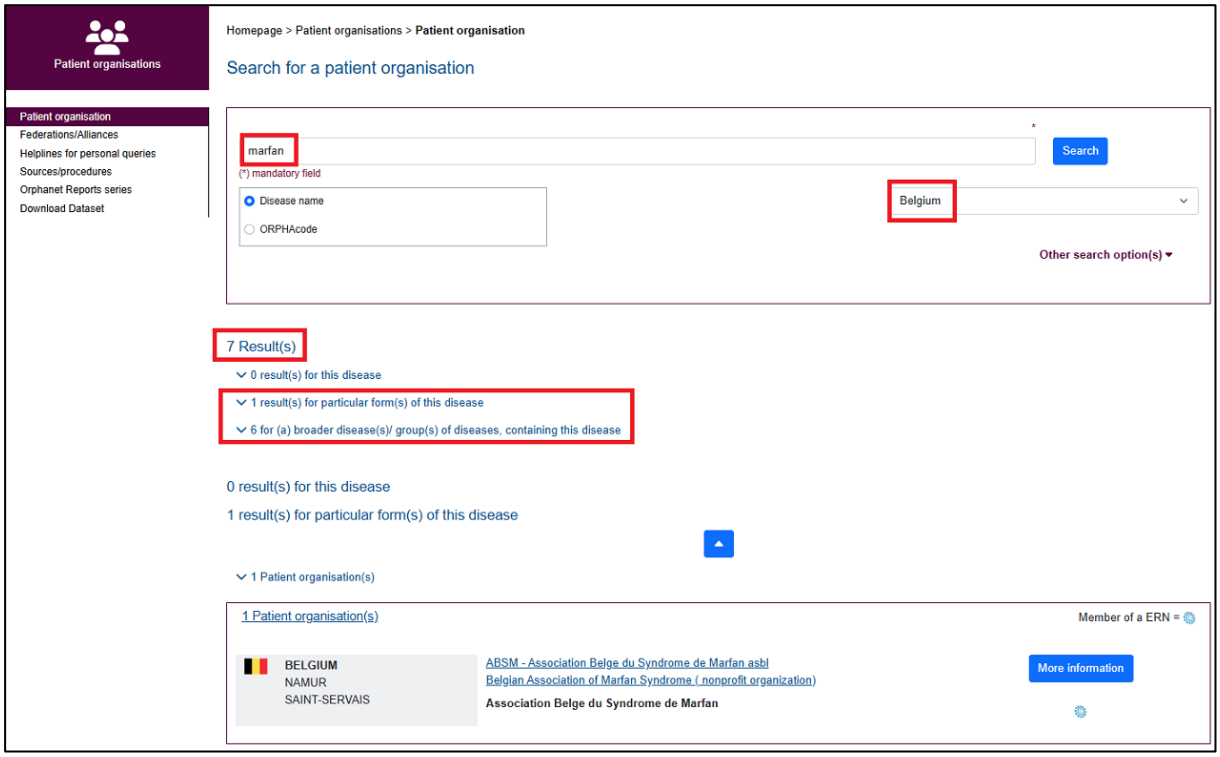


Fig. 3. Evolution of the number of Belgian expert resources registered in the Orphanet database
between December 2023 and December 2024

Each of the registered activities can be identified on the Orphanet website via a search based on the name of the associated (groups of) rare disease(s) or on the name of the activity (Figure 4). Results can be filtered by country and sorted either geographically (by country, region and city, in alphabetical order) or by specificity (from results more focused on a particular disease to those specialised for a group of diseases including the queried disease).



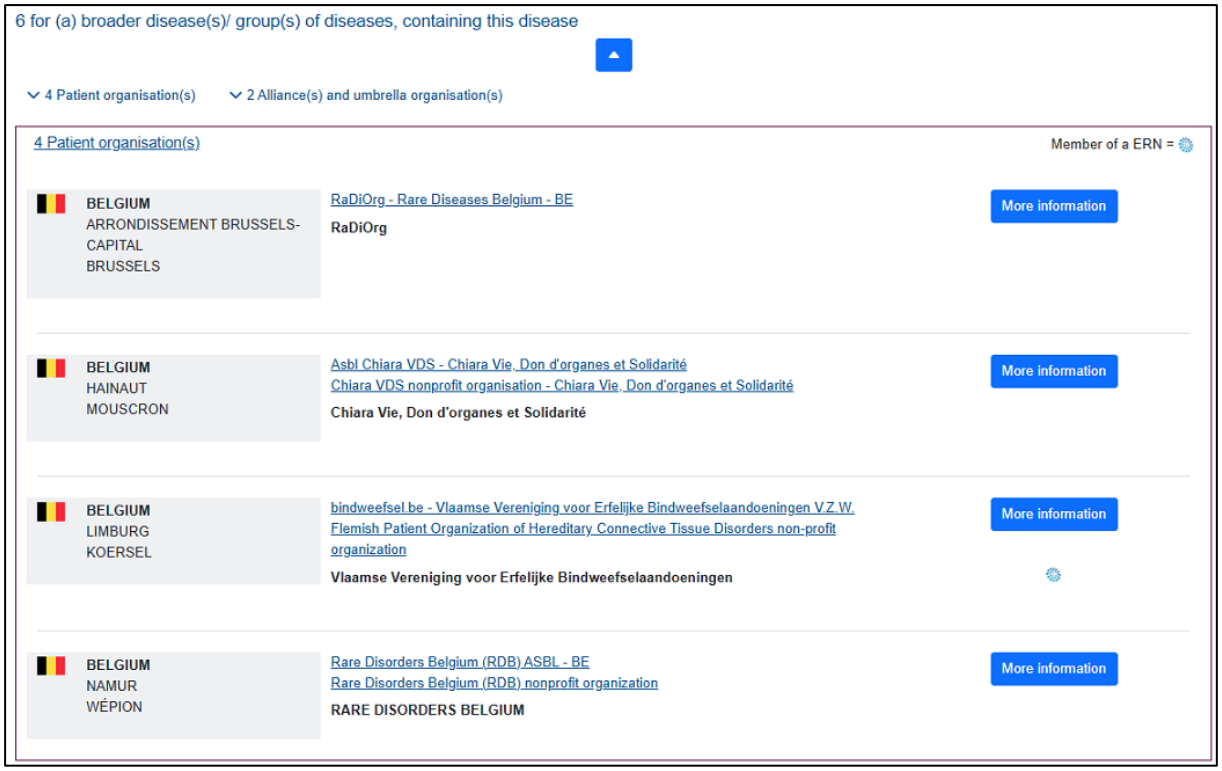


Fig. 4. Example of a search in Orphanet for a Belgian patient organisation dedicated to Marfan syndrome

Any request for creation or modification of Belgian data in Orphanet must be submitted by email to 'orphanetbelgium@sciensano.be'.

The **last update date of data published in Orphanet** (either following a contact with the person in charge of the activity or following the last verification performed by the IS of the reliable official/legitimate source of information) is always visible, as shown in the screenshot below (Figure 5).

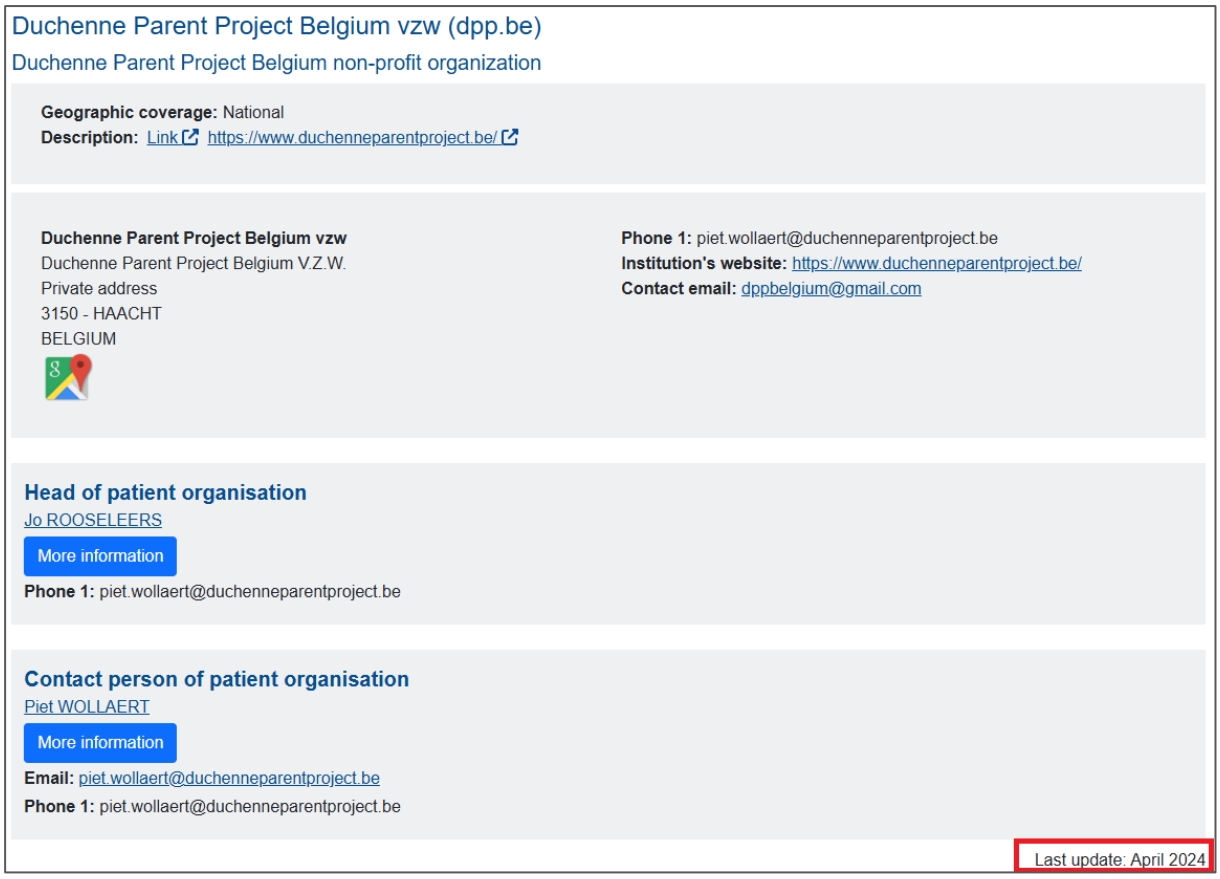


Fig.5. Screenshot of the Orphanet website: the Orphanet Belgium team updated information about a patient organisation following email exchanges. The date of the last update is visible in the lower right corner.

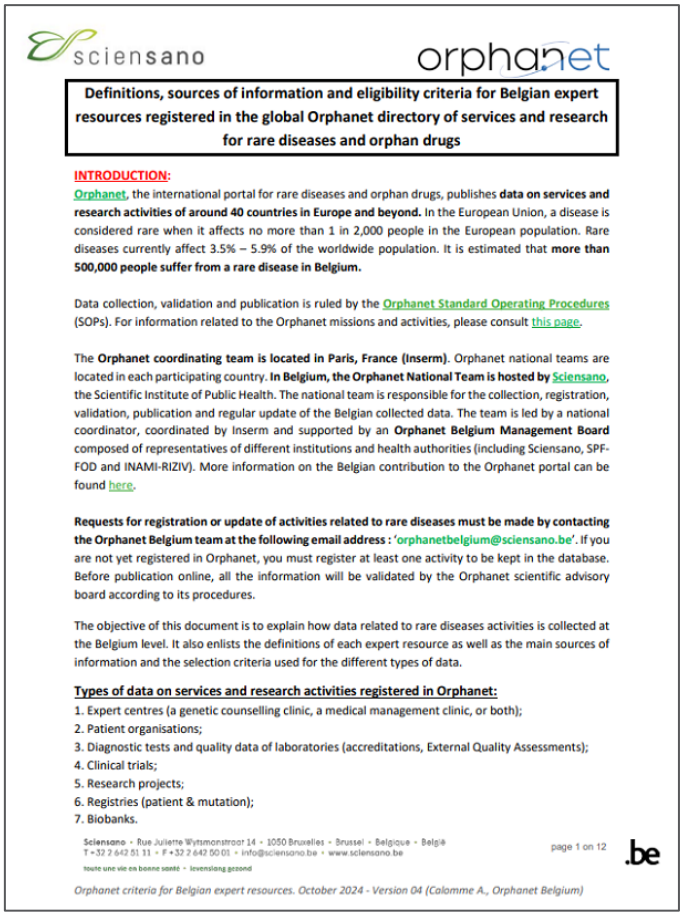
1.2. BELGIAN DATA SOURCES

Data that can be obtained from **international sources recognized as reliable** must be represented in their entirety in Orphanet, and this, for each country that is part of the Orphanet consortium (Table 1).

Expert centers	Patient organisations	Diagnostic tests / laboratories	Research projects	Registries / Biobanks	Clinical trials
- European Reference Networks (ERN) - Officially designated by country	- EURORDIS - National alliances - European Reference Networks (ERN) - Rare Diseases International (RDI)	- Officially designated by country - External quality assessment (EQA) providers	- funded by an IRDiRC member - included in databases specific of rare diseases - European Reference Networks (ERN) (ERICA project)	- belonging to RD-connect - funded by an IRDiRC member - included in databases specific of rare diseases	- funded by an IRDiRC member - included in databases specific of rare diseases (ICTRP) - European Reference Networks (ERN) (ERICA project)

Table 1. International sources for each expert resource to be registered in Orphanet

Documenting the inclusion criteria for expert resources in each country of the Orphanet network is of great importance for Orphanet end users to know how data is collected at the national level, as well as the selection criteria used. To this end, **each country of the Orphanet consortium must provide a list of national sources** which must have maximum coverage in terms of visibility in Orphanet. A document mentioning the definitions, sources of information and inclusion/exclusion criteria for expert resources (Figure 6) is published in the “Documents” section of the Orphanet Belgium website. This document is regularly revised and was updated in October 2024 (version 04) [28].



sciensano orphanet

Definitions, sources of information and eligibility criteria for Belgian expert resources registered in the global Orphanet directory of services and research for rare diseases and orphan drugs

INTRODUCTION:

Orphanet, the international portal for rare diseases and orphan drugs, publishes **data on services and research activities of around 40 countries in Europe and beyond.** In the European Union, a disease is considered rare when it affects no more than 1 in 2,000 people in the European population. Rare diseases currently affect 3.5% – 5.9% of the worldwide population. It is estimated that **more than 500,000 people suffer from a rare disease in Belgium.**

Data collection, validation and publication is ruled by the Orphanet Standard Operating Procedures (SOPs). For information related to the Orphanet missions and activities, please consult this page.

The **Orphanet coordinating team is located in Paris, France (Inserm)**. Orphanet national teams are located in each participating country. **In Belgium, the Orphanet National Team is hosted by Sciensano**, the Scientific Institute of Public Health. The national team is responsible for the collection, registration, validation, publication and regular update of the Belgian collected data. The team is led by a national coordinator, coordinated by Inserm and supported by an **Orphanet Belgium Management Board** composed of representatives of different institutions and health authorities (including Sciensano, SPF-FOD and INAMI-RIZIV). More information on the Belgian contribution to the Orphanet portal can be found here.

Requests for registration or update of activities related to rare diseases must be made by contacting the Orphanet Belgium team at the following email address : 'orphanetbelgium@sciensano.be'. If you are not yet registered in Orphanet, you must register at least one activity to be kept in the database. Before publication online, all the information will be validated by the Orphanet scientific advisory board according to its procedures.

The objective of this document is to explain how data related to rare diseases activities is collected at the Belgium level. It also enlists the definitions of each expert resource as well as the main sources of information and the selection criteria used for the different types of data.

Types of data on services and research activities registered in Orphanet:

1. Expert centres (a genetic counselling clinic, a medical management clinic, or both);
2. Patient organisations;
3. Diagnostic tests and quality data of laboratories (accreditations, External Quality Assessments);
4. Clinical trials;
5. Research projects;
6. Registries (patient & mutation);
7. Biobanks.

Sciensano • Rue Juliette Wytsmanstraat 14 • 1050 Bruxelles • Brussel • Belgique • België
T +32 2 642 51 11 • F +32 2 642 50 01 • info@sciensano.be • www.sciensano.be
toute une vie en bonne santé • levenslang gezond

page 1 on 12

.be

Orphanet criteria for Belgian expert resources. October 2024 - Version 04 (Calomme A., Orphanet Belgium)

Fig. 6. Document listing the eligibility criteria for Belgian resources to be registered in Orphanet

1.3. IMPROVEMENT OF THE COMPLETENESS AND QUALITY OF THE DATABASE

In 2024, all quality tasks assigned by the Orphanet coordinating team (Inserm, France) to the Belgian Information Scientist (IS) were carried out within the given deadlines. To ensure the accuracy of the database, various actions are regularly implemented:

- **Processing of spontaneous requests to create new information or update the information already collected.** This kind of requests can be provided at any time by professionals, by phone or email. The follow-up is ensured by the national teams and the proper implementation by the IS is monitored and validated by the Orphanet coordinating team;

- **Proactive searches for information in order to compare it to that of the database.** To this end, official/legitimate sources of information are regularly consulted (scientific publications, websites of patient organizations or medical laboratories, the BELAC website for accreditations; EQA providers websites, Clinical trials.gov, the European Clinical Trials Database (EudraCT), the database of clinical trials managed by the Federal Agency for Medicines and Health products, the INVENT database, the Belgian official journal, etc.);

- **Carrying out the quality control actions included in the "Quality Assurance Reviews (QAR)".** These documents are provided by the Orphanet coordinating team on a regular basis in order to continually enrich the database and keep it relevant and up-to-date;

- **Carrying out a series of recurrent queries put in place in the frame of the post-release quality control.** Communications about QC tasks can be made by emails or via OrphaNetWork. Information is sent by the coordinating team to the national IS describing the aim of the task, the instructions, the deadline and an Excel file with data concerned;

- **Carrying out a series of recurrent queries according to evolutions in the classification of rare diseases.** The review of the nomenclature and classification of rare diseases is a continuous work. The nomenclature and classification are produced and updated by collaborators of the Orphanet coordinating team with a scientific and/or medical background. They monitor the international scientific literature, consult experts from ERNs and perform internal quality control in order to detect and correct inconsistencies in the nomenclature and classifications (such as missing entities; entities with an incorrect classification level; discrepant representation of a group of disorders between the different classification groups it is included in; inconsistencies of the nomenclature between similar entities, or categories that are empty or no longer in use, among other cases). Decisions proposed by the Orphanet nomenclature managers are discussed and validated during meetings held on a monthly basis with the Orphanet Medical and Scientific Committee, composed of medical doctors and collaborators of the coordinating team. The outcome of these meetings are summarized in “disease meeting reports” and are made available on OrphaNetwork for the national Information Scientists who are in charge of implementing the necessary corrections concerning the data of their country. Consequently, **regular updates are made for data related to diseases that are now classified as obsolete, deprecated or non-rare.**

1.4. ANNUAL UPDATE CAMPAIGN

Professionals registered in the Orphanet database and linked to patient-related activities are contacted yearly by email to invite them to review and, if needed, to submit a request to update of their information. The follow-up of these requests is ensured by the national teams. This action also allows to identify invalid email addresses registered in the Orphanet database that need to be corrected.

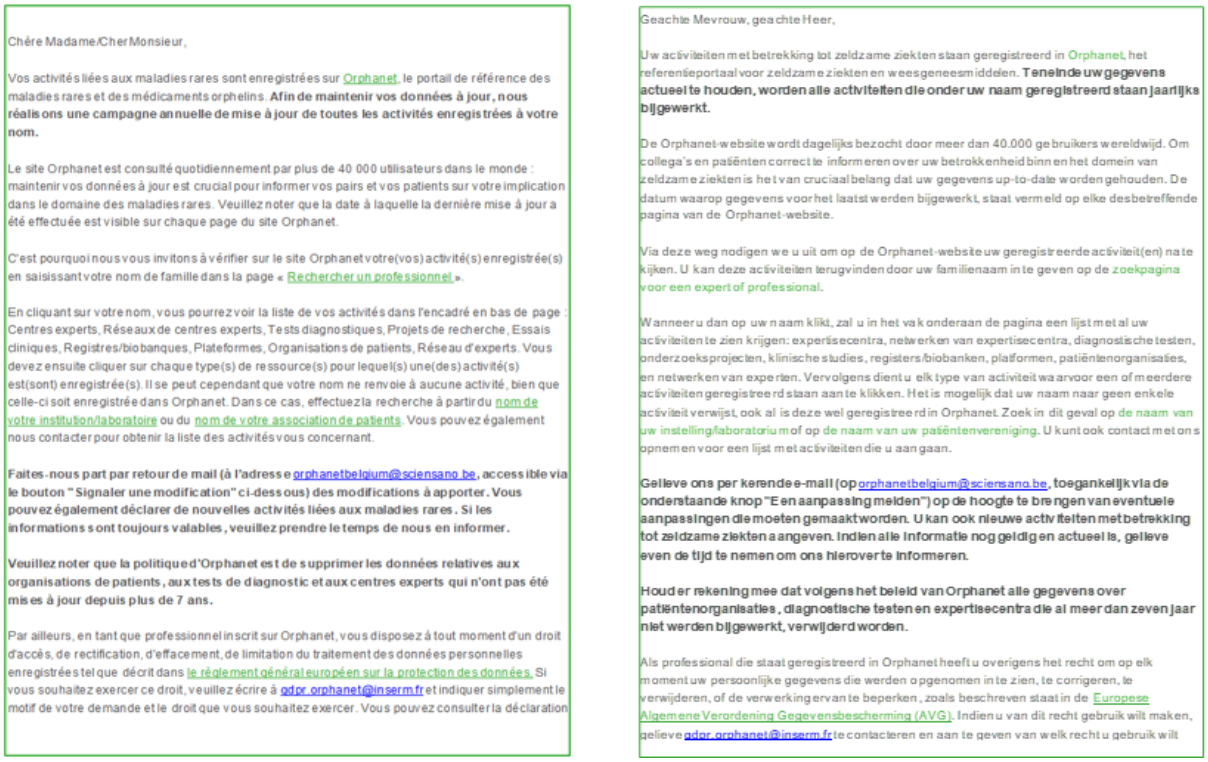
A very low response rate was observed in previous update campaigns in most countries of the Orphanet network. This situation is problematic because the collaboration and feedback of professionals in charge of the activities is essential to maintain a relevant database. The consequence is that in the long term, a part of the registered data is eliminated from the Orphanet database when despite all our efforts, no update is provided by the professionals in charge of these activities.

In 2023, it was decided by a vote of the Orphanet Management Board to launch a test year to assess a new way of inviting professionals to review their data. The email approach has been retained, because sending email communications to a large group of recipients (mass mailing) is an effective way to reach a large audience with limited effort and it also remains the only way to keep contact traceability. Moreover contacting each professional by phone is very difficult to set up (time-consuming, difficulty in directly contacting the right expert who risks being disturbed while working, etc.). **The annual update mailing campaign is conducted by each national team (and no longer centrally, by the coordinating team).** In this way, the email comes from an institution known to the recipient (which prevents the message from being classified as spam) and is written in the local language(s). Additionally, the message emphasizes the risk of erasure of data that has not been updated for a certain period of time (more than seven years for patient associations, diagnostic tests and expert centres) (Figure 7). The expected effect of these measures is to increase the response rate.

In Belgium, the 2024 annual update campaign was launched on December 5 and concerned 892 professionals (513 Dutch speakers, 379 French speakers) registered in the Orphanet database as linked to a non-terminated RD activity.

A specific platform for organizing mass email sendings, Webpower from the Spotler firm, was used by the Orphanet Belgium team. The advantages of this new system are numerous:

- no restrictions on the number of emails that can be sent at once;
- selecting a specific sender's email address to minimize the risk of the message being considered spam;
- presence of many options for adjusting the layout (logos, images, videos);
- automatic generation of reports (who received the email?, who read it?, who clicked on the links contained in the message?, etc.);
- full GDPR compliance (unlike sending emails via Outlook).



Chère Madame/Cher Monsieur,

Vos activités liées aux maladies rares sont enregistrées sur Orphanet, le portail de référence des maladies rares et des médicaments orphelins. **Afin de maintenir vos données à jour, nous réalisons une campagne annuelle de mise à jour de toutes les activités enregistrées à votre nom.**

Le site Orphanet est consulté quotidiennement par plus de 40 000 utilisateurs dans le monde : maintenir vos données à jour est crucial pour informer vos pairs et vos patients sur votre implication dans le domaine des maladies rares. Veuillez noter que la date à laquelle la dernière mise à jour a été effectuée est visible sur chaque page du site Orphanet.

C'est pourquoi nous vous invitons à vérifier sur le site Orphanet votre(vos) activité(s) enregistrée(s) en saisissant votre nom de famille dans la page « Rechercher un professionnel ».

En cliquant sur votre nom, vous pourrez voir la liste de vos activités dans l'encadré en bas de page : Centres experts, Réseaux de centres experts, Tests diagnostiques, Projets de recherche, Essais cliniques, Registres/biobanques, Plateformes, Organisations de patients, Réseau d'experts. Vous devez ensuite cliquer sur chaque type(s) de ressource(s) pour lequel(s) une(des) activité(s) est(sont) enregistrée(s). Il se peut cependant que votre nom ne renvoie à aucune activité, bien que celle-ci soit enregistrée dans Orphanet. Dans ce cas, effectuez la recherche à partir du nom de votre institution/laboratoire ou du nom de votre association de patients. Vous pouvez également nous contacter pour obtenir la liste des activités vous concernant.

Faites-nous part par retour de mail (à l'adresse orphanetbelgium@sciensano.be, accessible via le bouton " Signaler une modification" ci-dessous) des modifications à apporter. Vous pouvez également déclarer de nouvelles activités liées aux maladies rares. Si les informations sont toujours valables, veuillez prendre le temps de nous en informer.

Veuillez noter que la politique d'Orphanet est de supprimer les données relatives aux organisations de patients, aux tests de diagnostic et aux centres experts qui n'ont pas été mises à jour depuis plus de 7 ans.

Par ailleurs, en tant que professionnel inscrit sur Orphanet, vous disposez à tout moment d'un droit d'accès, de rectification, d'effacement, de limitation du traitement des données personnelles enregistrées tel que décrit dans le règlement général européen sur la protection des données. Si vous souhaitez exercer ce droit, veuillez écrire à gdpr.orphanet@inserm.fr et indiquer simplement le motif de votre demande et le droit que vous souhaitez exercer. Vous pouvez consulter la déclaration

Geachte Mevrouw, geachte Heer,

Uw activiteiten met betrekking tot zeldzame ziekten staan geregistreerd in Orphanet, het referentieportaal voor zeldzame ziekten en weesgeneesmiddelen. **Teneinde uw gegevens actueel te houden, worden alle activiteiten die onder uw naam geregistreerd staan jaarlijks bijgewerkt.**

De Orphanet-website wordt dagelijks bezocht door meer dan 40.000 gebruikers wereldwijd. Om collega's en patiënten correct te informeren over uw betrokkenheid binnen het domein van zeldzame ziekten is het van cruciaal belang dat uw gegevens up-to-date worden gehouden. De datum waarop gegevens voor het laatst werden bijgewerkt, staat vermeld op elke desbetreffende pagina van de Orphanet-website.

Via deze weg nodigen we u uit om op de Orphanet-website uw geregistreerde activiteit(en) na te kijken. U kan deze activiteiten terugvinden door uw familienaam in te geven op de zoekpagina voor een expert of professional.

Wanneer u dan op uw naam klikt, zal u in het vak onderaan de pagina een lijst met al uw activiteiten te zien krijgen: expertisecentra, netwerken van expertisecentra, diagnostische testen, onderzoeksprojecten, klinische studies, registers/biobanken, platformen, patiëntenorganisaties, en netwerken van experten. Vervolgens dient u elk type van activiteit waarvoor een of meerdere activiteiten geregistreerd staan aan te klikken. Het is mogelijk dat uw naam naar geen enkele activiteit verwijst, ook al is deze wel geregistreerd in Orphanet. Zoek in dit geval op de naam van uw instelling/laboratorium of op de naam van uw patiëntenvereniging. U kunt ook contact met ons opnemen voor een lijst met activiteiten die u aan gaan.

Gelieve ons per kerende e-mail (op orphanetbelgium@sciensano.be, toegankelijk via de onderstaande knop "Een aanpassing melden") op de hoogte te brengen van eventuele aanpassingen die moeten gemaakt worden. U kan ook nieuwe activiteiten met betrekking tot zeldzame ziekten aangeven. Indien alle informatie nog geldig en actueel is, gelieve even de tijd te nemen om ons hierover te informeren.

Houd er rekening mee dat volgens het beleid van Orphanet alle gegevens over patiëntenorganisaties, diagnostische testen en expertisecentra die al meer dan zeven jaar niet werden bijgewerkt, verwijderd worden.

Als professional die staat geregistreerd in Orphanet heeft u overigens het recht om op elk moment uw persoonlijke gegevens die werden opgenomen in te zien, te corrigeren, te verwijderen, of de verwerking ervan te beperken, zoals beschreven staat in de Europese Algemene Verordening Gegevensbescherming (AVG). Indien u van dit recht gebruik wilt maken, gelieve gdpr.orphanet@inserm.fr te contacteren en aan te geven van welk recht u gebruik wilt

Fig. 7. Emails sent in French and Dutch to Belgian professionals, as part of the 2024 annual update campaign

There are 3 possible types of reactions from the email recipient: not responding, requesting changes or confirming that the data is still valid, which then allows us to adapt the last update date in the Orphanet database. We noticed a **similar response rate compared to last year: 6.73% of professionals (60/892) in 2024** - compared to 7.88% (72/914) in 2023 - contacted the Orphanet Belgium team following this email to validate their data or submit a request to modify it. A strong inequality is observed in the response rate between French and Dutch speakers (Figure 8).

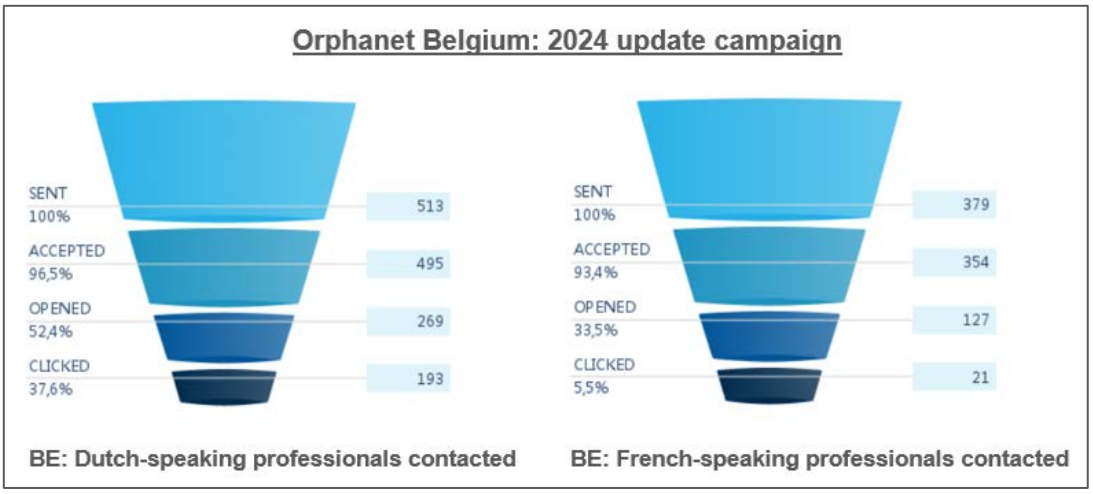


Fig. 8. Results of the 2024 annual campaign in Belgium, in terms of number of emails sent, accepted, opened and browsed (with use of links to respond to them), depending on whether the recipient is Dutch or French speaking

The overall response rate to the annual data update campaign remains low for Belgium, despite all the efforts made to raise awareness among professionals about keeping their Orphanet data up to date, including the upstream involvement of rare disease function coordinators (email sent to each coordinator a few days before the launch of the campaign). The results from the different countries of the Orphanet consortium will be discussed within the network, in order to see how to improve the participation of professionals in updating their data on the Orphanet site.

1.5. REGISTRATION AND UPDATE OF EXPERT CENTRES

The possibility to register an expert centre on Orphanet depends on the specific situation in the different countries of the network. **In Belgium, eligibility criteria are appraised by the Federal Public Service (FPS) Health, Food Chain Safety and Environment.** The country-specific inclusion criteria taken into account during the selection process are indicated in a document [28] published on the Orphanet Belgium website [29] in order to be transparent on how the data selection is determined.

Registration on Orphanet is not compulsory as there is no legislative framework, which means that the professionals in charge of a certain activity can refuse the publication of their data. However, Orphanet falls into the Inserm's Public Interest mission as the legal basis for treatment of personal data. Thus, we do not have to collect consent from professionals to show their data. We must inform them of the registration and give them the possibility to retract if they do not wish their data to be available online or in our databases, in accordance with the General Data Protection Regulation (GDPR). Registration in Orphanet is strongly recommended as it offers visibility at national and international levels to all centres that have acquired recognized expertise in certain rare diseases.

Two categories of Belgian expert centres are registered in Orphanet. A clear visual distinction between these two categories is established thanks to the use of specific flags.

1) THE OFFICIALLY-DESIGNATED CENTRES

These reference centres are considered as validated data and are registered in the Orphanet database with the "Designated centre of expertise" flag .

They include:

- **centres with which NIHDI has established a convention for the multidisciplinary management of specific rare diseases:** neuromuscular diseases, cystic fibrosis, haemophilia, hereditary metabolic diseases, paediatric nephrology, refractory epilepsy and spina bifida [30];
- **genetic centres officially recognized by the health authorities** for their diagnostic and counselling activities [31];
- **hospitals recognized by the health authorities to have a "Rare Disease Function"** [32].

The NIHDI website [30] is consulted regularly to determine whether any new centres under agreement have not yet been listed on Orphanet. Quality controls of all Belgian centres already registered are carried out regularly in order to keep the data up to date.

2) THE CENTRES PARTICIPATING IN A EUROPEAN REFERENCE NETWORK (ERN)

In the RD field, collaboration with international networks of expertise is fundamental, due to the rarity of patients, experts, knowledge, data and resources. To respond to these challenges, **Belgium actively participates in the initiative of the European Reference Networks For Rare Diseases (ERNs)** [33], which are virtual networks of healthcare professionals across Europe working together to support patients with rare and complex diseases. Individuals suffering from a rare disease may struggle to obtain an accurate diagnosis or appropriate treatment in their country because no country alone has the capacity to treat all rare, low-prevalence and complex diseases. ERNs offer patients and clinicians from across Europe access to the best expertise, knowledge and resources, without having to travel to another country. These networks receive support from several EU funding programmes.

The creation of 24 ERNs covering the major rare disease groups was approved in December 2016 and launched in March 2017 (call 1), involving more than 900 highly-specialised healthcare units from over 300 hospitals in 26 member states (MS). A second call for healthcare providers to join existing ERNs was launched in 2019. At the end of 2021, the ERN Board of MS, as given in the Implementing Decision

2014/287/EU Article 10, has approved the application of 620 new members. Since this second call, **Belgium participates in all of the 24 existing ERNs** currently connecting more than 1,600 clinical centres across 27 Member States and Norway, which is particularly remarkable for such a small country.

The Belgian centres participating in an ERN are registered in Orphanet since 2019. **100% of Belgian centres that joined an ERN as full members following the two calls are registered in Orphanet**.

These centres appear on the Orphanet site with the “Member of a ERN” flag .
Centres which are both officially designated and members of an ERN are represented by two flags (Figure 9).

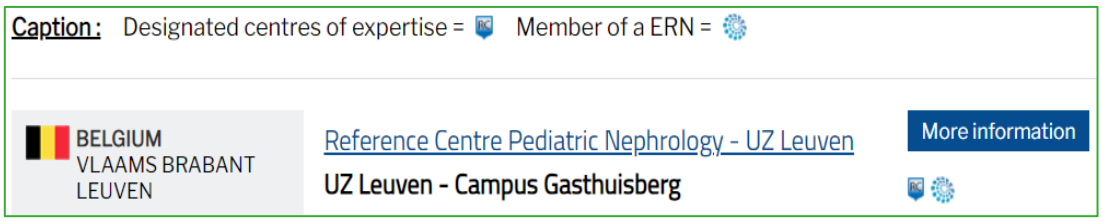


Fig.9. Example of a centre which is both officially-designated at national level and member of an ERN

A **list of the ERNs and the participating Health Care Providers per country** can be consulted on the Orphanet portal [34]. A list of the centres participating in the ERNs in a given country is also available, through a search tool, on the European Commission website [35].

Particular attention is paid to (groups) of rare diseases associated with ERN-centres in Orphanet. A correct choice of ORPHAcodes must be made, in order to best reflect the particular area of expertise of the centre while respecting the following Orphanet rules when we link an activity (i.e. an expert centre, a patient organization, etc.) to a list of rare diseases:

- the fact that "mother diseases" (group head of several diseases) are linked to "daughter diseases" (subtypes) in the hierarchical classification;
- if we associate an activity with a "mother disease", the activity will appear as associated with all its "daughter diseases" on the Orphanet website;
- we cannot at the same time establish a link with a group head and a disease under this group head.

For ERN-centres, this step requires a thorough consultation of the ERN websites or of the application forms for membership (when available). Unfortunately, for some ERNs, the information on the specific disease coverage of each healthcare provider is not sufficiently detailed (or even absent). Moreover, when present, the data rarely provides information on specific ORPHAcodes covered by the centre but rather on large groups of disorders (“Main Thematic Groups”). When available, the information is carefully analysed in order to assign the centres to the ORPHAcodes that most accurately reflect their recognized area of expertise. The detailed Orphanet classification is sent to the experts (in the form of an Excel file) to determine with them, as precisely as possible, the rare diseases (and their related ORPHAcodes) for which their participation in the ERNs has been validated.

It should be noted that in some cases, and in particular for the centres whose ERN membership was validated following the first call launched in 2016, the identification of the specific areas of expertise of the centres was based mainly on a self-declaration by the professionals due to the lack of detailed information available on the ERN websites. With regard to the ERN centres whose membership was validated following the second call launched in 2019, the disease groups (ORPHAcodes) were selected by the Orphanet coordinating team (Inserm, France) based on the declaration the centres made to the EC in order to join the ERNs. If another choice of ORPHAcodes is deemed more relevant by professionals to better reflect the recognized expertise of their centres and to improve patient referral, the Orphanet Belgium team will analyze the request, in consultation with the Orphanet-Inserm coordination team.

It is important to know that **the identification of the specific expertise of the national centres belonging to ERNs is not validated by any designation committee in Belgium.**

*Remark: an Excel file with detailed information on the specific expertise of each ERN-centre is available on the EC website in the following section: "**The scope, criteria and thresholds of the diseases covered by each of the 24 ERNs**"* [36]. *However, this file is under construction (missing or incomplete data). Moreover, some ERNs still use medical terminologies other than ORPHAcodes (such as ICD-10, OMIM, etc.) to provide information on the recognised expertise of the members.*

An **evaluation is conducted every five years by the Board of Member States** after the initial approval (or last evaluation) of the ERN members. In 2023, 24 European Reference Networks, including 836 members, completed their first evaluation (see the report [37] published on the EC website). 1 Belgian healthcare provider, the University Hospital of Liège centre which was a member of eUROGEN, informed the Evaluation Body of its decision to voluntarily withdraw. One Belgian Healthcare Provider, the UZ Leuven centre member of ERN-SKIN, obtained in the evaluation report 'needs improvement' and submitted an improvement plan. This Healthcare Provider will be re-evaluated in one year after the implementation of its improvement plan. Accordingly, **Belgium has currently 94 medical teams which are full members of the ERNs** (Figure 10). These teams belong to 10 different hospitals (Table 2).

Post-release quality controls of all Belgian ERN-centres already registered in Orphanet are conducted regularly to keep the data up-to-date.

	NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	NUMBER OF PARTICIPATING CENTRES IN BELGIUM (calls 1 and 2) Date of last update: March 15, 2024
1	**Endo-ERN:** European Reference Network on Rare Endocrine Conditions	7
2	**EpiCARE:** European Reference Network on Rare and Complex Epilepsies	2
3	**ERKNet:** European Rare Kidney Diseases Reference Network	3
4	**ERN CRANIO:** European Reference Network on Rare craniofacial anomalies and ENT disorders	3
5	**ERN GENTURIS:** European Reference Network on GENetic TUmour RIsk Syndromes	4
6	**ERN LUNG:** European Reference Network on respiratory diseases	6
7	**ERN-BOND:** European Reference Network on Rare Bone Disorders	2
8	**ERN-EYE:** European Reference Network on Rare Eye Diseases	3
9	**ERNICA:** European Reference Network on Rare inherited and congenital anomalies	3
10	**ERN-PaedCan:** European Reference Network for Paediatric Cancer (haemato-oncology)	4
11	**ERN-RND:** European Reference Network on Rare Neurological Diseases	4
12	**ERN-Skin:** European Reference Network on Rare and Undiagnosed Skin Disorders	3
13	**EURACAN:** European Reference Network on Rare Adult Cancers (solid tumors)	6
14	**EuroBloodNet:** European Reference Network on Rare Hematological Diseases	6
15	**eUROGEN:** European Reference Network on urogenital diseases and conditions	3
16	**EURO-NMD:** European Reference Network for Rare Neuromuscular Diseases	5
17	**GUARD-HEART:** Gateway to Uncommon And Rare Diseases of the HEART	3
18	**ITHACA:** European Reference Network on Rare Congenital Malformations and Rare Intellectual Disability	5
19	**MetabERN:** European Reference Network for Rare Hereditary Metabolic Disorders	6
20	**RARE-LIVER:** European Reference Network on Rare Hepatological Diseases	4
21	**ReCONNET:** Rare Connective Tissue and Musculoskeletal Diseases Network	3
22	**RITA:** Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases Network	2
23	**TransplantChild:** European Reference Network on Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	2
24	**VASCERN:** European Reference Network on Rare Multisystemic Vascular Diseases	5
Total		94

CALL 1 (2017):
66 Belgian centres belonging to 23 ERNs

CALL 2 (2019):
28 Belgian centres belonging to 19 ERNs

Belgium (94 centres) participates in the 24 existing ERNs

Fig.10. Number of Belgian centres recognized as full members in the 24 existing ERNs (as of December 2024)

		Endo-ERN	EpiCARE	ERKNet	ERN CRANIO	ERN GENTURIS	ERN-BOND	ERN-EYE	ERNICA	ERN-LUNG	ERN-PaedCan	ERN-RND	ERN-Skin	EURACAN	EuroBloodNet	eUROGEN	EURO-NMD	GUARD-HEART	ITHACA	MetabERN	RARE-LIVER	ReCONNET	RITA	TransplantChild	VASCERN
Leuven University Hospital (UZ Leuven)	22	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
Ghent University Hospital (UZ Gent)	21	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1
Antwerp University Hospital (UZ Antwerpen)	15	1	0	0	1	0	1	1	0	1	0	1	0	1	1	1	1	1	1	1	1	0	0	0	1
University Hospital Brussels (UZ Brussel)	5	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0
AZ Sint-Maarten (Mechelen)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Cliniques universitaires Saint-Luc (UCLouvain)	15	1	1	1	0	0	0	0	1	1	1	0	0	1	1	0	1	0	1	1	1	1	0	1	1
H.U.B - University Hospital Erasme	7	1	0	0	0	0	0	0	0	1	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0
H.U.B - Jules Bordet Institute	2	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
H.U.B - Hôpital Universitaire des Enfants Reine Fabiola (HUDERF)	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	In collaboration with UZ Brussel	0	0	0	0	0
Liège University Hospital (Centre Hospitalier Universitaire de Liège)	5	1	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0
TOTAL	94	7	2	3	3	4	2	3	3	6	4	4	3	6	6	3	5	3	5	6	4	3	2	2	5

Table 2. Number of Belgian centres recognized as full members in the 24 existing ERNs, by hospital (as of December 2024)

The number of Belgian ERN-centres created in Orphanet (i.e. having a unique identifier) is much higher than 94. This is due to the fact that many centres ask to separate the paediatric section from the adult section, or request to create separate centres for each group of diseases for which their expertise is recognized (with different coordinators, team members and contact details). This increases the workload of the Orphanet collaborators, but it makes it easier for patients to identify on the Orphanet portal the expert centres taking care of their specific medical condition.

Table 3 shows the Belgian centres participating in ERNs for rare or complex diseases, listed by hospital (as of December 2024).

NAME OF THE BELGIAN HOSPITAL	NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	DATE OF APPROVAL
Leuven University Hospital (UZ Leuven) (22)	VASCern (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN-LUNG (Respiratory Diseases)	CALL 1 (2017)
	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
	EURO-NMD (Rare Neuromuscular Diseases)	CALL 1 (2017)
	ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	CALL 1 (2017)
	ERN-Skin (Rare and Undiagnosed Skin Disorders)	CALL 1 (2017)
	ERN-RND (Rare Neurological Diseases)	CALL 1 (2017)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 1 (2017)
	ERN-PaedCan (Paediatric Cancer (haemato-oncology))	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
	GUARD-HEART (Gateway to Uncommon And Rare Diseases of the HEART)	CALL 1 (2017)
	ERN-EYE (Rare Eye Diseases)	CALL 2 (2021)
	eUROGEN (Rare urogenital diseases and complex conditions)	CALL 1 (2017)
	ERN GENTURIS (GENetic TUmour RIsk Syndromes)	CALL 1 (2017)
	RARE-LIVER (Rare Hepatological Diseases)	CALL 1 (2017)
	ReCONNET (Rare Connective Tissue and Musculoskeletal Diseases)	CALL 2 (2021)
	ERKNet (Rare Kidney Diseases)	CALL 1 (2017)
	EpiCARE (Rare and Complex Epilepsies)	CALL 1 (2017)
	RITA (Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases)	CALL 1 (2017)
	ERNICA (Rare inherited and congenital anomalies)	CALL 1 (2017)
	CRANIO (Rare craniofacial anomalies and ear, nose and throat disorders)	CALL 2 (2021)
Ghent University Hospital (UZ Gent) (21)	VASCern (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN-LUNG (Respiratory Diseases)	CALL 2 (2021)
	EURO-NMD (Rare Neuromuscular Diseases)	CALL 1 (2017)
	ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	CALL 2 (2021)
	ERN-Skin (Rare and Undiagnosed Skin Disorders)	CALL 1 (2017)
	ERN-RND (Rare Neurological Diseases)	CALL 2 (2021)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 2 (2021)
	ERN-PaedCan (Paediatric Cancer (haemato-oncology))	CALL 1 (2017)
	ERN-BOND (Rare Bone Disorders)	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
	ERN-EYE (Rare Eye Diseases)	CALL 1 (2017)
	eUROGEN (Rare urogenital diseases and complex conditions)	CALL 1 (2017)
	ERN GENTURIS (GENetic TUmour RIsk Syndromes)	CALL 1 (2017)
	RARE-LIVER (Rare Hepatological Diseases)	CALL 1 (2017)
	ReCONNET (Rare Connective Tissue and Musculoskeletal Diseases)	CALL 1 (2017)
	ERKNet (Rare Kidney Diseases)	CALL 2 (2021)
	RITA (Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases)	CALL 2 (2021)
	ERNICA (Rare inherited and congenital anomalies)	CALL 2 (2021)
	CRANIO (Rare craniofacial anomalies and ENT disorders)	CALL 2 (2021)
	TransplantChild (Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	CALL 2 (2021)

NAME OF THE BELGIAN HOSPITAL	NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	DATE OF APPROVAL
Antwerp University Hospital (UZ Antwerpen) (15)	CRANIO (Rare craniofacial anomalies and ear, nose and throat disorders)	CALL 2 (2019)
	Endo-ERN (Rare Endocrine Conditions)	CALL 2 (2019)
	ERN-BOND (Rare Bone Disorders)	CALL 1 (2017)
	ERN-EYE (Rare Eye Diseases)	CALL 2 (2019)
	ERN-LUNG (Respiratory Diseases)	CALL 1 (2017)
	ERN-RND (Rare Neurological Diseases)	CALL 2 (2019)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 2 (2019)
	EuroBloodNet (Rare Hematological Diseases)	CALL 2 (2019)
	eUROGEN (Rare urogenital diseases and complex conditions)	CALL 2 (2019)
	EURO-NMD (Rare Neuromuscular Diseases)	CALL 1 (2017)
	GUARD-HEART (Gateway to Uncommon And Rare Diseases of the HEART)	CALL 2 (2019)
	ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
	RARE-LIVER (Rare Hepatological Diseases)	CALL 2 (2019)
	VASCERN (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
University Hospital Brussels (UZ Brussel) (5)	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN GENTURIS (GENetic TUmour RIsk Syndromes)	CALL 2 (2019)
	ERN-LUNG (Respiratory Diseases)	CALL 2 (2019)
	GUARD-HEART (Gateway to Uncommon And Rare Diseases of the HEART)	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
AZ Sint-Maarten (Mechelen) (1)	VASCERN (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
Cliniques universitaires Saint-Luc (UCLouvain) (15)	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	EpiCARE (Rare and Complex Epilepsies)	CALL 2 (2019)
	ERKNet (Rare Kidney Diseases)	CALL 1 (2017)
	ERNICA (Rare inherited and congenital anomalies)	CALL 2 (2019)
	ERN-LUNG (Respiratory Diseases)	CALL 2 (2019)
	ERN-PaedCan (Paediatric Cancer (haemato-oncology))	CALL 2 (2019)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 2 (2019)
	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
	EURO-NMD (Rare Neuromuscular Diseases)	CALL 1 (2017)
	ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	CALL 2 (2019)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
	RARE-LIVER (Rare Hepatological Diseases)	CALL 1 (2017)
	ReCONNET (Rare Connective Tissue and Musculoskeletal Diseases)	CALL 1 (2017)
	TransplantChild (Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	CALL 1 (2017)
	VASCERN (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)

NAME OF THE BELGIAN HOSPITAL	NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	DATE OF APPROVAL
Liège University Hospital (Centre Hospitalier Universitaire de Liège) (5)	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN GENTURIS (GENetic TUmour RIsk Syndromes)	CALL 1 (2017)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 1 (2017)
	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
HUB - University Hospital Erasme (7)	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN-LUNG (Respiratory Diseases)	CALL 1 (2017)
	ERN-RND (Rare Neurological Diseases)	CALL 1 (2017)
	ERN-Skin (Rare and Undiagnosed Skin Disorders)	CALL 1 (2017)
	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
	EURO-NMD (Rare Neuromuscular Diseases)	CALL 1 (2017)
	ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	CALL 1 (2017)
HUB - Jules Bordet Institute (2)	EURACAN (Rare Adult Cancers (solid tumors)	CALL 1 (2017)
	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
HUB - Hôpital Universitaire des Enfants Reine Fabiola - HUDERF (1)	ERN-PaedCan (Paediatric Cancer (haemato-oncology))	CALL 1 (2017)

Table 3. Belgian hospitals participating in ERNs for rare or complex diseases (as of December 2024)

A **list of all the Belgian centres participating in ERNs for rare or complex diseases** (n = 94, results of calls 1 and 2 launched by the EU) listed by ERN and specifying the recognized areas of expertise identified via the ORPHAcodes can be found in **Annex 1**.

1.6. REGISTRATION AND UPDATE OF PATIENT ORGANISATIONS

The directory of Belgian patient associations registered in Orphanet is regularly revised, usually every two years or more frequently if needed. The Orphanet data is cross-checked with the list of members of RaDiOrg [6] (the Belgian umbrella organization for people living with a rare disease). This work, as well as the consultation of other sources (national and regional alliances; EURORDIS [23], the non-governmental patient-driven alliance of organisations and individuals active in the field of rare diseases in Europe; physicians and researchers working in close collaboration with support groups; congress, symposiums, forums, etc.), made it possible to identify new associations meeting Orphanet's eligibility criteria or to remove associations that have ceased their activities. The results of the regular analyses performed by the Orphanet Belgium team are shared with RaDiOrg, so that they can carry out a similar update on their own website.

An email is systematically sent to each of the organizations newly registered to ask to review the data published and to inform about the possibility of having their data deleted if they do not want it to be published on Orphanet, in accordance with the GDPR.

In 2024, 5 Belgian patient organisations were created in Orphanet :

- Adrenal association NVACP - Flemish section
- AmyBel - Amyloidosis Association Belgium
- NMP Belgique ASBL- Myeloproliferative neoplasms Belgium non-profit association
- NoRa non-profit organisation, Belgian Association for people with achondroplasia
- ORKA Parents of children and adolescents with rheumatic disease nonprofit organization

16 patient organisations were deleted, following their cessation of activity or because they no longer met Orphanet's inclusion criteria:

- ABT- Association Belge de Thalassémie A.S.B.L
- Access and Go_ABP_Association belge des paralysés
- AHOSA_Anders HOren door SpraakAfzien
- Anna Timmerman vzw
- APEDAF - Association des Parents d'Enfants Déficients Auditifs Francophones
- Fondation contre le cancer/Stichting tegen cancer
- Kikov Leuven - Kinderkanker Oudervereniging Leuven vzw
- LCH Belgium
- Les Enfants de Salus Sanguinis
- Ligue Belge du Sjögren asbl
- Multisysteematrofie - Multisysteematrofie V.Z.W./A.S.B.L.
- Patienten Rat & Treff
- STAN Trefpunt VerSTANdelijke Handicap vzw
- Sun child - Prendre un enfant par la main asbl
- Syndrome Moebius
- Uranus - Contact group for people with epilepsy

A **list of the Belgian associations active in the rare disease field published on Orphanet** (n = 123, as of December 2024) specifying the associated (groups of) diseases identified via the ORPHAcodes can be found in **Annex 2**.

1.7. REGISTRATION AND UPDATE OF DIAGNOSTIC TESTS

For people affected by a rare disease, obtaining a timely and accurate diagnosis is key in accessing appropriate medical expertise. The Orphanet database offers, amongst a range of expert resources on rare diseases, a directory of diagnostic tests. Diagnostic test represent approximately 1/4 of the data registered in Orphanet. Registering the portfolio of diagnostic tests makes it easy to identify the laboratories performing a specific test. It has also an added-value for the geneticists since this allows to report on the evolution of techniques. It facilitates cross-border genetic testing, which is particularly interesting in the field of rare diseases. Finally, it contributes to sharing of expertise between professionals and to establishment of collaborations leading to a more efficient use of costly resources.

A total of 1131 tests performed in Belgium laboratories are currently registered in Orphanet. These tests are classified by specialties in table 4.

Specialty	Number of Belgian diagnostic tests registered in Orphanet (Dec 2024)
Bacteriology	37
Biochemical genetics	166
Cytogenetics	22
Hematology	2
Immunology	23
Molecular genetics	832
Mycology	2
Parasitology	11
Pathology	4
Virology	13
Other	19
TOTAL	1131

Table 4: Belgian diagnostic tests registered in the Orphanet database, by specialty (December 2024).

The Orphanet dataset related to diagnostic tests was considered too complex by experts and Orphanet collaborators, in particular the data on techniques. Moreover the content of gene panels changes so often that it is difficult to have the information always up to date, in order to properly reflect the panels that are in use by laboratories at any given time. Therefore **a complete revision of the procedure for diagnostic test registration was recently decided by the Orphanet coordinating team.** The Orphanet Belgium team participates in the working group aiming to discuss different options to develop a **new diagnostic test model.** The main objective is to reduce the dataset and make it more simple, in order to have a better coverage of diagnostic tests in the Orphanet database.

It was decided:

- to stop registering tests for non-rare diseases;
- to stop registering pharmacogenetic tests;
- to simplify the labeling of the tests;
- to remove the persons responsible for each test and link them directly to the lab;
- to remove the techniques from the test and link them directly to the lab;
- to suppress the gene panels and inform users that more information can be found on the lab website (+ link to BGTD for Belgium);
- to review the list of purposes, specialties and techniques and to present the new list (with updated definitions) to the Orphanet Genetic Advisory Board for validation.

As a result, extensive data adjustment work will be required in 2025 to comply with the new rules put in place for recording diagnostic tests in the new Orphanet model.

Genetic tests

The registration and update of the Belgian genetic tests in Orphanet is a task performed in **collaboration with the Belgian Genetic Tests Database** (BGTD) [38]. This database is developed by Sciensano, in collaboration with the geneticists of the 8 officially-recognized genetic centres. It centralizes comprehensive and relevant information about tests offered in Belgium for the diagnosis of diseases with a genetic basis. There is no obligation to register a genetic testing activity in Orphanet. When geneticists register their data in the BGTD, they are asked to specify whether they accept the publication of the data on Orphanet. If they don't give their agreement, the test can be registered but will not be visible on the Orphanet website intended for the general public. It will only be collected and registered in internal databases for analytical purposes.

There is currently no automated system for transferring information from the BGTD to Orphanet, to take into account changes that may be made at any time by geneticists in the BGTD. The conclusion of agreements and the development of application programming interfaces (APIs) between the BGTD and the Orphanet-Inserm platform could enable regular transfers of Belgian diagnostic tests to Orphanet in the future. However, such a system is not yet in place.

The transfer of information from BGTD to Orphanet is neither an automatic injection of data from one database (BGTD) to another (Orphanet) nor a simple copy-paste. The tests are analyzed and validated manually one by one, in order to adapt them to the Orphanet project. The main objective is to provide standardized and harmonized data to Orphanet users (e.g. label of the test in English and in local language, compliance with criteria related to the description of the technical procedure, verification of gene-disease links via specific tool, etc.). This task can also involve the creation of new data in Orphanet (genes, diseases or genes-diseases relationships not yet registered).

The overall objective is for Belgian genetic tests to be created/updated in Orphanet within 3 months of the changes made by geneticists in the BGTD. However, in 2024, the updating of data related to diagnostic tests in Orphanet has been deprioritized, pending the availability of a new registration model that should simplify this task. Only the data of a few genetic centres (IPG, HUB-Erasme and UZ Gent) were partially updated in 2024. The new model for recording test-related data is expected for Q3 or Q4 2025. At that time, the updating of genetic tests will resume on a more regular basis.

Non-genetic tests

The registration and updating of **tests specific to rare diseases performed by the Belgian Reference Centres in Human Microbiology** (virology, bacteriology, parasitology, mycology, etc.) is based on consultation of the Sciensano webpage dedicated to the National Reference Centres (NRC) and the National Reference Laboratories (NRL) for Human Microbiology [39]. This work involves the prior selection of human microbiological tests specific to rare diseases.

The registration and updating of the clinical chemical, coagulation/hemostasis, immunology and hematology tests specific to rare diseases is based on the consultation of the Sciensano webpage dedicated to the Belgian Reference Centres (NRC) for Rare Diseases performed by laboratories of clinical pathology [40]. The data is updated regularly, by comparison with a list provided by the Sciensano Quality of laboratories service [41], responsible for assessing and monitoring the quality of medical and veterinary laboratories in Belgium.

1.8. REGISTRATION AND UPDATE OF CLINICAL TRIALS

A clinical trial for the Orphanet database is an interventional study aiming to evaluate a drug (or a combination of drugs, a biological product, a medical device) to treat or prevent a rare disease or a group of rare diseases. The data collection by the Orphanet consortium concerning clinical trials is of utmost importance as it helps professionals and patients to obtain a centralized, quality controlled access to the current state of the art on these data.

The Orphanet coordinating team is in charge of the centralized collection of clinical trials through a partnership with the International Clinical Trial Registry Platform (ICTRP) [42], supported by the World Health Organization. The ICTRP database centralizes data on clinical trials provided by national and international registries such as:

- the **European Union Drug Regulating Authorities Clinical Trials Database** (EudraCT) [43], a database for all interventional clinical trials on medicinal products that were conducted in the European Union (EU)/European Economic Area (EEA) between 1 May 2004 and 30 January 2025;

- the **European Medicines Agency's (EMA) Clinical Trials Information System (CTIS)** [44]**:** this website provides information on individual clinical trials in the European Union and European Economic Area since its launch on 31 January 2022. All clinical trials in the European Union (EU)/European Economic Area (EEA) that will be ongoing after 30 January 2025 must comply with the Clinical Trial Regulation (EU) 536/2014 and, therefore, should be submitted to the Clinical Trials Information System.

- **Clinical trials.gov** [45] : an online database of clinical research studies and information about their results. It provides information about clinical trials conducted in the United States and around the world.

In 2024, 150 Belgian clinical trials related to rare diseases have been newly registered in the Orphanet database by the Orphanet Belgium team.

National clinical trials

For **national clinical trials** (i.e. clinical trials involving only one country of the Orphanet consortium), a list of clinical trials potentially concerning a rare disease (or a group of rare diseases) is sent monthly by the Orphanet coordinating team to the national teams, in order to be assessed. **For Belgium, this eligibility assessment concerned 44 national clinical trials in 2024.** The dataset of each clinical trial (title, phase, start date, recruitment status, sponsor, intervention, etc.) is checked by the Information Scientist and completed if necessary. The link to be established with the relevant ORPHAcode(s) is analysed. The inclusion/exclusion criteria are verified and only the data meeting the Orphanet inclusion criteria are registered by the IS and revised by the coordinating team in order to be displayed on the Orphanet public website.

Multinational clinical trials

Multinational clinical trials (i.e. involving more than one Orphanet country) collected from ICTRP database and that are missing in Orphanet are also regularly registered. **For Belgium, this task concerned 43 multinational clinical trials in 2024.** For each of these clinical trials, the inclusion/exclusion criteria are checked in order to confirm the disease link suggested by the Orphanet coordinating team. National teams are particularly involved in collecting and registering details on the national investigators and on the location of the investigation centres, in order to create the corresponding national clinical entry.

The ICTRP platform is the major source of information for clinical trials but **registration can also come from self-declarations by professionals and from national monitoring.** National teams are indeed in charge of identifying the other relevant sources of information for clinical trials in their country, in order to complete the centralized collect of clinical trials. However the **online database of Belgian clinical trials** [46], created in 2018 by the Federal Agency for Medicines and Health products (FAMHP), has no longer been populated in 2024 due to the transition of all European tests to the CTIS.

The registration of clinical trials in Orphanet is a priority as part of the collaboration with the European Rare Disease Research Coordination and Support Action (ERICA) consortium [47], in which all 24 European Reference Networks take part. However, the Orphanet database currently has gaps in terms of completeness. A **working group** in which Orphanet Belgium participates has been set up with the aim of improving the representativeness of multinational clinical trials in Orphanet.

Main quality control task performed in 2024 related to clinical trials

In the frame of the post-release quality control, quality control tasks are regularly put in place by the Orphanet coordinating team to ensure the accuracy of the database.

In 2024 a quality control task was set up as part of the state of play IRDiRC [48], a report produced by Orphanet to present an analysis of the rare disease research landscape. This task concerned **dates and status of clinical trials registered in the database.**

The main goal of this quality control task was to :

- update the clinical trials registered in Orphanet, in order to tag them as "terminated" or "ongoing" or to modify their end date according to the reality of the clinical trial ;
- add a start date and/or an end date to clinical trials without date (according to Orphanet business rules, a start date is mandatory and an end date is strongly recommended for analysis purpose and status update).

For Belgium, this QC task involved the **update of 243 clinical trials** (33 national trials, 210 multinational trials). The task was completed within the stipulated deadline.

1.9. REGISTRATION AND UPDATE OF RESEARCH PROJECTS

The Orphanet coordinating team collects the projects funded by the International Rare Diseases Research Consortium (IRDiRC) members at the European level. IRDiRC [48] is a consortium that unites national and international governmental and non-profit funding bodies, companies (including pharmaceutical and biotech enterprises), umbrella patient advocacy organizations and scientific researchers to promote international collaboration and advance rare diseases research worldwide.

In addition, **national teams are in charge of identifying the sources of information for research projects on rare diseases in their country.** In Belgium, national funding institutions are regularly consulted to obtain information on funded projects. The Belgian Federal Science Policy has developed a database, "INVENT" [49] that gathers all the research data collected by:

- the French-speaking Community, via Le Conseil des rectrices et recteurs [50];
- the Flemish Community on the FRIS Research portal [51];
- the Federal Authorities (BELSPO) [52].

In Belgium, there is no database for research projects dedicated specifically to rare diseases. Searches via the databases mentioned above are carried out without the possibility of using a filter specific to rare diseases. It is therefore very time-consuming to identify projects dedicated specifically to rare diseases using these databases. Research projects can also be found in websites of funding bodies, patient organisations, public research organisations, etc. Moreover, like other resources, research projects can be obtained via professionals declaring their activity by email.

In 2024, 63 Belgian research projects related to rare diseases have been newly registered in the Orphanet database by the Orphanet Belgium team.

Polaris, a Web interface for visualization, curation and analysis of rare disease research landscape, is a tool developed in the frame of the IRDiRC roadmap by *MyScienceWork*. This platform was launched in 2023 for the funders members of IRDiRC and for the Orphanet network members.

The main objectives of the Polaris platform are:

- to facilitate the identification and data capture of research projects not yet registered in the Orphanet database (and possibly clinical trials in the future);
- to develop a semi-automatic complete cycle of collection, curation and exploitation of the research project database;
- to allow the exploitation of the Orphanet database at a single web interface (e.g. performing an analysis of research data in terms of disease coverage in a given country);
- to provide a web analysis interface to both Orphanet and IRDiRC members.

Polaris is based on the structure of the Orphanet database and the data contained therein may have several sources. Research projects are either submitted by the funding agencies members of IRDiRC (from an Excel file provided by Orphanet), or submitted via specific partners such as the European Commission (CORDIS) [53] and the German Federal Ministry of Education and Research (BMBF) [54], or collected by the Orphanet Network national teams (Figure 11). It should be noted that for the moment, partners external to Orphanet (including IRDIRC members) do not yet use the tool to inject their data. This under-use of the tool will need to be discussed and improved in the future.

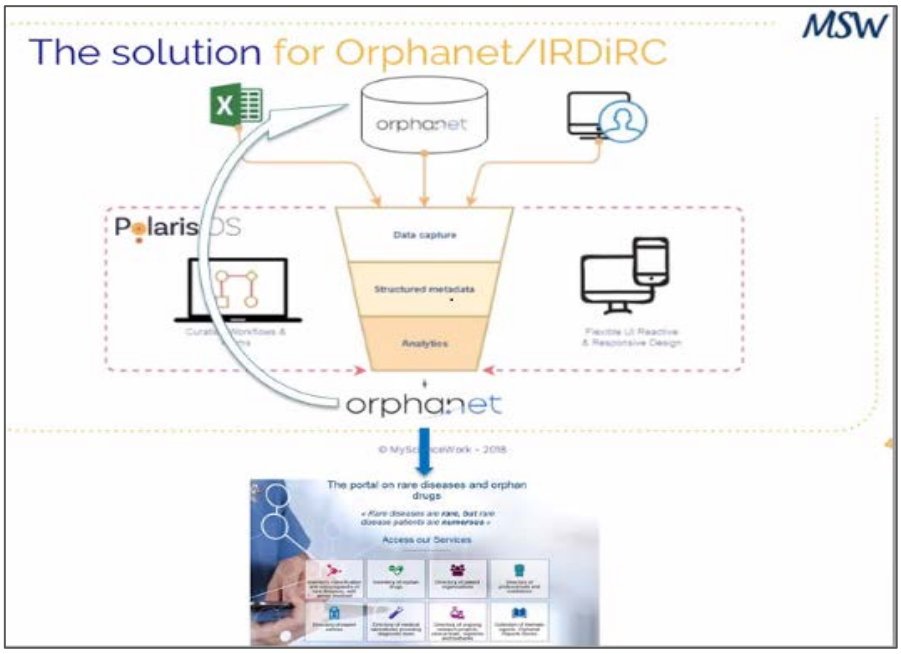


Fig.11. Illustration of the Polaris platform workflow for research projects

Polaris OS analytics dashboards gives access to 3 key performance indicators (KPI):

- Research projects KPI;
- Clinical trials KPI;
- Crossed research projects and clinical trials KPI.

This new tool has many advantages in terms of **data exploitation**: the data can be used in the analysis platform to carry out, for example, statistical analyses between countries or to analyse the medical fields mainly represented in research carried out in a given country (Figure 12).

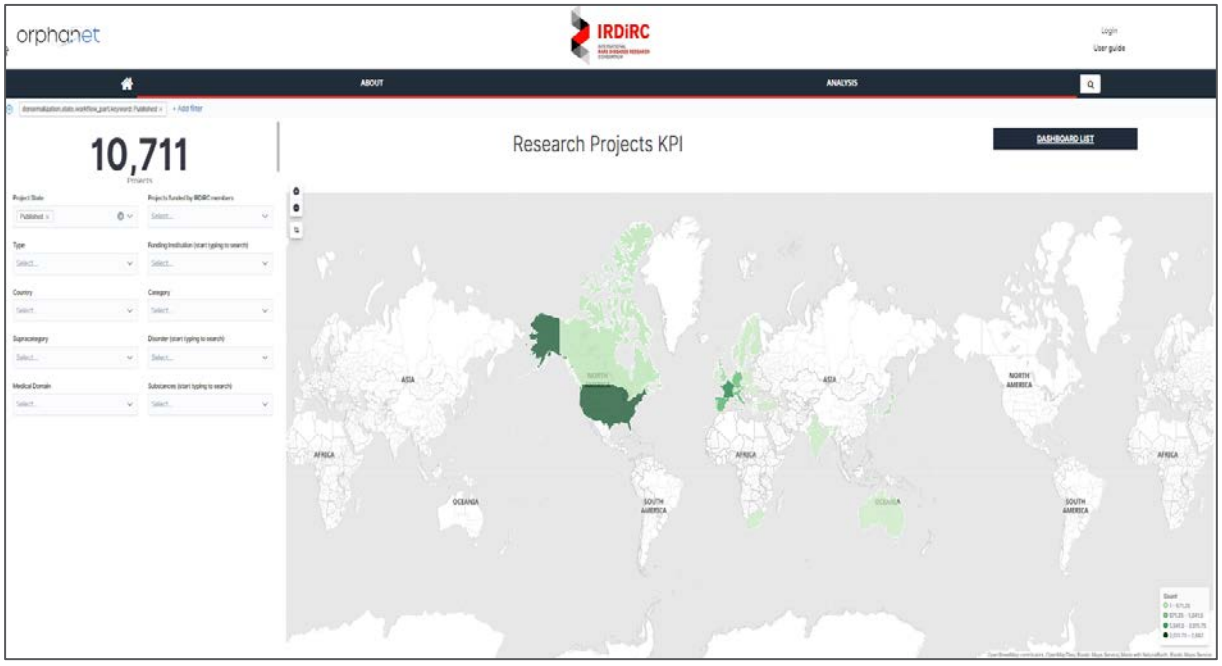


Fig. 12. Overview of the research projects published in the Orphanet database and their distribution by countries

1.10. REGISTRATION AND UPDATE OF REGISTRIES

In Belgium, there is no database for registries dedicated specifically to rare diseases. This type of data is therefore particularly difficult to identify. However patient registries can be identified through research projects, networks, funding bodies, pharmaceutical and biotech companies, patient organisations, peer reviewed publications or following contact with experts in the field.

In 2024, 2 new patient registries related to rare diseases have been registered in the Orphanet database by the Orphanet Belgium team.

2. Monitoring of the Orphanet Belgium team's activity: overview of the activity indicators

A "**National team's Quality Monitoring Dashboard**" is developed each year by the Orphanet coordinating team (Inserm, France) based on a series of indicators and thresholds to define the minimum activity requirements of a national Orphanet team (Table 5).

The objective of this annual exercise is to assess each team's situation and if needed, agree on common action plans that can help improve the work of the teams.

INDICATORS	Threshold for green (calculation based on M(-2)M(-14)
Management Board attendance = Participation in the Governance and Network life	**60% of the Instances in the year**
Article in the internal newsletter/poster AM = Participation Network life	**1/year**
Expert Ressources update = Quality image	**5% of all national Data/year**
Treatment of Collector forms = Quality image NO LONGER RELEVANT	**75%/year**
Quality Contorl Task = Quality image	**50%/year**
Trainings = Teams capacity, Quality image, Network life	**50% of the instances of the year**
Translation Nomenclature = Quality image	**1/year**
Translation abstracts = Quality image	**15**
Translation website = Quality image	**90%**

Table 5. Activity indicators and thresholds to be achieved by Orphanet national teams

Three different status are possible:

- Green: indicating that all Indicators are above the thresholds;
- Almost green: for the teams that only have one red indicator;
- Red: for the teams that have more than one red indicator.

Depending on the results obtained, the following actions are implemented:

- 1 red indicator: a tolerance may be applied, but mitigation measures should be discussed with the national team;
- More than 1 red indicator: urgent meeting needed with the Orphanet coordination team to assess the difficulties and draw up an action plan;
- All indicators in red: the national team is contacted by the Orphanet coordination team to announce the termination process (removal from the network).

The **latest analysis was carried out for the reference period [August 2023 - July 2024]** for all active national teams belonging to the Orphanet consortium (n = 30 in 2024). **For the Orphanet Belgium team, all indicators are green**, as it was already the case in previous years, meaning that the quality of the activities carried out by the Orphanet Belgium team is equal to or above the expected threshold.

MANAGEMENT OF THE ORPHANET BELGIUM WEBSITE

The Orphanet Belgium team ensures the maintenance and update of a national Orphanet website [29] **available in French and Dutch** (Figure 13). The Orphanet national website contains information specific to Belgium. It is complementary to the general Orphanet site, which concerns the entire network.

Fig.13. Screenshot of the homepage of the new version of the Orphanet Belgium website

The following topics are covered:

- **Contact:** the contact details of the Orphanet Belgium team can be found in this section. Links to various interesting websites to consult are also listed. We also specify that we cannot respond to personal requests (whether medical, administrative or legal) and we refer to the appropriate contacts for this type of request (in particular, patient associations).
- **Governance:** description of the accompanying committee and the composition of the Orphanet Belgium team, with mention of the sponsors and partners.
- **Historical background of the Orphanet network:** description of the main stages which marked the course of the Orphanet project, since its creation in 1997.
- **National news and events**: this section includes information about the rare diseases day, calls for patients to participate in clinical research, conferences in Belgium and abroad, patient association initiatives, training opportunities, etc. The calendar of events is regularly updated.
- **Orphanet in short:** this section provide general information about the Orphanet network, rare diseases and orphan drugs (explanations on the activities of the network, organization and financing; latest version of the activity reports; instructional videos on the nomenclature and on the use of the search tool for a disease or a gene, etc.), as well as information on the Orphanet quality commitment.
- **Documents:** this section gives access to several documents such as the Belgian rare diseases plan, the King Baudouin Fund reports, the EC's recommendations on rare diseases, the Orphanet Report Series, the document “Criteria for Belgian Expert Resources” mentioning the definitions, sources of information and inclusion/exclusion criteria for expert resources in use in Belgium, the activity reports relating to the Orphanet Belgium database and newsletters.

PARTICIPATION IN THE OD4RD PROJECT

Rare diseases are still scarcely represented in generic medical terminologies commonly used internationally. The lack of visibility of rare diseases in health information and research systems is one of the main causes of inadequate care for people living with a rare disease. **Orphanet develops and continuously updates the only multilingual standardized terminology dedicated to rare diseases**. Each clinical entity referenced in the Orphanet nomenclature is assigned a unique, time-stable and non-reusable numerical identifier, the ORPHAcode, around which the rest of the data present in the Orphanet database is structured. **ORPHAcodes are recognised as a best practice for clinical coding of rare diseases diagnoses in Europe** [55] [56] [57] **and as a crucial resource contributing to the acceleration of rare diseases research** [58]**.**

One of the main objectives of the **Orphanet Data for Rare Disease project** (OD4RD) [11], co-funded by the EU4Health program of the European Commission, is to **advance the implementation of ORPHAcodes in hospitals hosting the ERN-centres** and to **use the expertise of ERNs to further improve the Orphanet nomenclature.** This should allow to establish a **common language**, with codes specifically created for rare diseases, in order to effectively monitor and report on rare diseases (including undiagnosed cases) at European level.

The OD4RD project was launched in January 2022 for a 15 months period. During this pilot year (OD4RD1), a network of national hubs has been developed in 13 MS countries (Austria, Belgium, Czech Republic, Finland, Germany, Italy, the Netherlands, Norway, Poland, Portugal, Spain, Sweden, Slovenia) and in Switzerland as an observer.

The OD4RD project was renewed until the end of 2025 (OD4RD2). During this second phase (April 2023-December 2025) the network was expanded to 6 new national hubs (Bulgaria, Ireland, Estonia, Latvia, Lithuania and Romania). The OD4RD network is now made up of **operational nomenclature national hubs in twenty countries** (Figure 14).

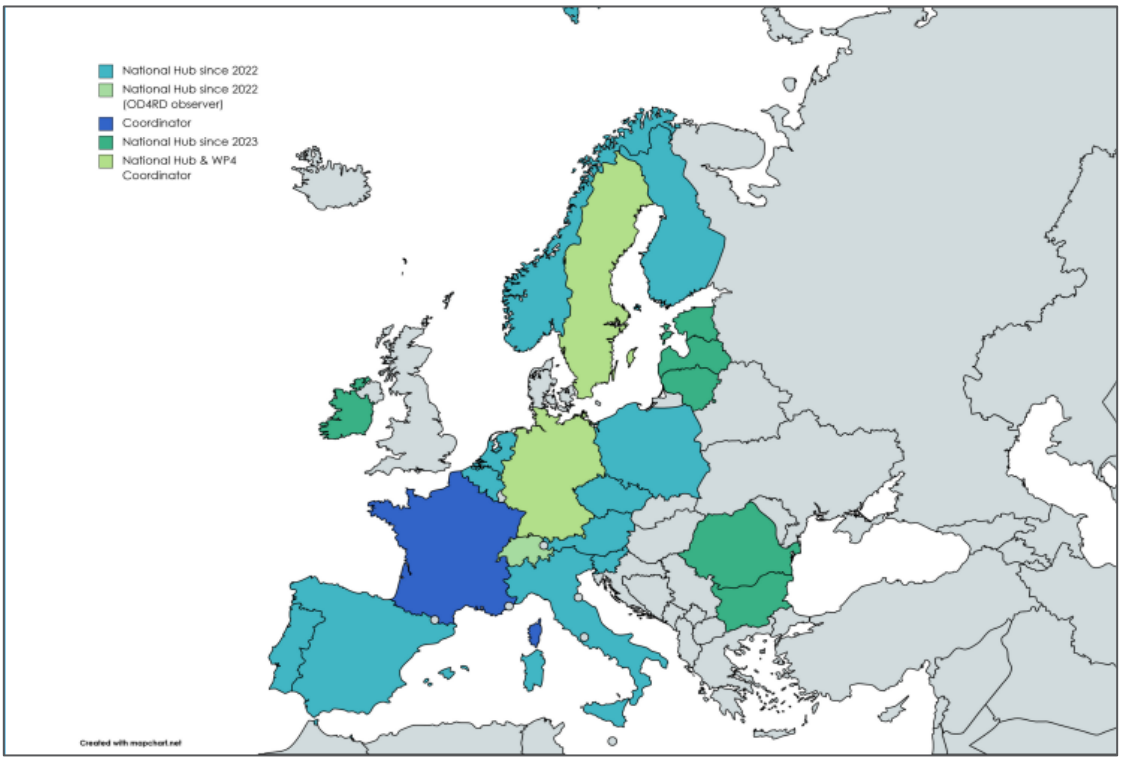


Fig.14 . The coordinated Network of Orphanet Nomenclature National Hubs (OD4RD1/OD4RD2 projects)

General objectives of the OD4RD project

The OD4RD2 project capitalizes on the pilot phase (OD4RD1), with the ambition to increase the number of collaborations with ERNs and to develop new material to explain, using concrete examples, how to deal with issues linked to the coding of rare diseases (e.g. request to create a missing ORPHAcode, difficulty in selecting the correct ORPHAcode for a given diagnosis, question relating to alignment with other terminology such as SNOMED CT, etc.).

The OD4RD1/2 projects build on Orphanet's specific expertise and on its organisation as a long-lasting, well-established network, to fulfil the following general objectives:

1. To contribute to the generation of standardised, interoperable data on RD diagnosis for primary and secondary use, through maintenance of the Orphanet nomenclature of RD in collaboration with ERNs, and active support for its implementation in hospitals hosting ERNs;

2. To contribute to the harmonisation of data collection amongst various settings (health records, registries) and amongst countries, through dissemination of coding good practices at the source (health records, registries, etc.);

3. To support evidence-based decision-making in the frame of the European strategy around ERNs, by providing an exploitable reference corpus of data and information on RDs.

In Belgium, the OD4RD National Hub is hosted by Sciensano and managed by the Orphanet Belgium Project Manager. Sciensano participates in WP4, whose main objective is to provide support for the local implementation of ORPHAcodes into routine coding systems of national HCPs hosting ERNs (or linked to ERNs). The mission of each Orphanet national nomenclature hub is to facilitate real ORPHAcodes implementation (from a technical point of view) and use (from a coding and data exploitation point of view) in health information systems. A page describing the participation of the Sciensano RD team in the OD4RD project has been created on the Sciensano website [59].

A **state of play survey** among participating countries was launched at the beginning of the OD4RD project to assess each national situation in terms of ORPHAcoding implementation. A report compiled from the survey on the situation in each of the national Orphanet nomenclature hubs set up in 2022 is available. It revealed that the **overall picture of RD coding with ORPHAcodes is very different between WP4 participating countries.** The range extends from countries where ORPHAcodes are already implemented with a link to ICD-10 in the national coding systems used in all hospitals (situation in Germany since 2023, where all in-patient cases with a rare disease diagnosis must be coded by an ORPHAcode using the Alpha-ID-SE file) to countries not yet using ORPHAcodes at all.

In Belgium, the situation is complex in terms of ORPHAcoding because a transition to SNOMED CT® as the common national reference terminology in all electronic health records is underway. It is planned that SNOMED CT will be used from 2028 in Belgium not only as the main source for patient record documentation, but also as a reference for all derived classifications, aggregations and reports. Moreover **no legislative framework and no incentive** (i.e. specific financial support deemed necessary by some centres to adopt the ORPHAcodes, which require additional work to record data and adapt and maintain data recording tools) is foreseen to stimulate the use of ORPHAcodes in centres treating patients with rare diseases.

Taking into consideration the different situation and needs of users in regards to ORPHAcodes implementation in the WP4 participating countries, it was necessary to develop individual **national action plans** to achieve the project goals. Each plan is divided into four sections: trainings/workshops, networking, helpdesk implementation and further activities. These topics are discussed during the (bi-)-**monthly WP4 conference calls** and experiences of the different countries are shared in order to benefit from each other and to address common topics in a coordinated manner.

All **OD4RD1/2 projects deliverables** [60] can be accessed on a specific page of the OD4RD website.

An **online survey was launched in December 2023 within all Belgian centres that are members of an ERN** to provide a better overall vision of practices and needs in terms of RD-coding in our country. A total of 76 respondents from 62 Belgian ERN-centres completed the web-based questionnaire. This represents **66.0% of the 94 Belgian ERN centres**, which is a satisfactory participation rate. The results will be the subject of a detailed report but the first analyses show a very heterogeneous situation in terms of coding rare diseases in Belgian ERN-centres, with **practices which differ greatly from one ERN-centre to another**, and even within ERN-centres belonging to the same hospital.

Organisation of trainings on Orphanet nomenclature and classification

One of the main tasks of an OD4RD national hub is to **provide training sessions on Orphanet nomenclature and classification, in local language(s), to clinicians, coders, hospital information managers, statistical services and other stakeholders of ERN-centres (in first intention).**

Table 6 shows the list of Belgian professionals that received training in 2022, 2023 and 2024. **So far, 101 Belgian professionals, including clinicians and coders belonging to 6 of the 8 Rare Diseases Functions, have received the Orphanet nomenclature training.**

Flexibility in the types of training is offered. There are various possibilities in terms of methods (online, on site), duration (from 2 hours to one day, depending on availability and needs) and testing of knowledge autonomously via online quizzes. The training sessions may be recorded, at the request of the centre, so that they can be broadcast to people who were unable to attend live.

	INSTITUTION OF THE TRAINEES	DATE	HOW?	COMMENTS
OD4RD1	UCL Saint-Luc, Brussels	29/04/2022	Online, in French/English	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: clinicians and RD coders (n=15).
	UCL Saint-Luc, Brussels	29/08/2022	Online, in French	Based on the advanced quiz developed by the Orphanet coordinating team (Inserm). Participant: RD coordinator (n=1).
	Ghent University hospital, session 1	19/09/2022	Online, in Dutch	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: clinicians and RD coders (n=15).
	Liège University hospital	21/10/2022	Online, in French/English	One-hour session, Q&A on ORPHAcodes use, advanced level (ORPHAcodes already used in the patient files). Participants: clinicians and RD coders (n=12).
	Sciensano	06/03/2023	On site, in English	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: RD registries managers, data manager (n=7).
OD4RD2	Leuven University hospital, session 1	15/05/2023, 10:00-12:00	Online, in English	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: clinicians and RD coders (n=13).
	Leuven University hospital, session 2	06/06/2023, 09:00-11:00	Online, in Dutch	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: clinicians and RD coders (n=9).
	GP, Dr MA	08/06/2023, 10:00-12:00	Online, in French	This general practitioner contacted us spontaneously to request training in Orphanet nomenclature. She is working on an awareness project concerning rare diseases for general practitioners with the SSMG ("Société Scientifique de Médecine Générale").
	IPG-GHdC, session 1	24/11/2023, 13:00-16:00	On-site, in French/English	Three-hours session, basic training on nomenclature and codification, theoritical part. Participants: clinicians, coordinator nurse RD function and IT specialists (n=8).
	Ghent University hospital, session 2	07/12/2023, 15:00-17:00	Online, in Dutch/English	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: clinicians, study coordinators and data managers (n=7).
	HUB Erasme, Endocrinology service	11/06/2024, 12:30-13:30	On site, in French	One-hour session, introduction to Orphanet and its nomenclature and classification during a lunch seminar of the endocrinology service (adult section). This session should be followed by more in-depth training in September-October 2024. Participants: clinicians and geneticists (n=6).
	HUB (Erasme, HUDERF, Bordet)	18/09/2024, 10:00-12:00	On-site, in French/English	Two-hours session, basic training on nomenclature and codification, theoritical part. Participants: 1 clinician and RDF Medical Director, 1 RDF coordinator, 1 coordinating data manager and 1 grant manager (n=4).
	Sciensano	10/12/24, 10:00-12:30	On-site, in English	Two-hours and a half session, basic training on nomenclature and codification, theoritical part. Participants: 3 registry managers/data managers.
	UZ Antwerpen	Planned for Q1 2025.		
	UZ Brussel	Planned for Q1 2025.		
	Non-university hospitals, ERN-centres and any institutions involved in the RD field	To be planned with the healthcare professionals (2024 - 2025)		

Table 6. Trainings on Orphanet nomenclature and classification delivered to Belgian hospitals in 2022-2024.

Development of educational tools to support training in the Orphanet nomenclature

Each OD4RD national hub must actively participate in **advocating ORPHAcodes towards national decision-makers** (e.g. Ministry of Health, federal and regional institutions, hospital managers, etc.) making use of the **promotional material** (guidelines, flyers, videos, etc.) provided by the Orphanet coordination and adapting or translating it when needed.

Communication material is developed in the context of the OD4RD project:
1. WHY ORPHAcoding vs other generic terminologies - Booklet [61]
2. Making IT easy: ORPHAcode implementation in health information systems - Flyer [62]
3. What is the Orphanet Network of National Hubs – Flyer [63]
4. OD4RD: 2023 Achievements - Leaflet [64]
5. OD4RD: 2024 Achievements - Leaflet [65]

A **flyer (in French and Dutch)** including contact details and describing the achievements of the Belgian team in charge of the OD4RD hub is currently being prepared.

In 2024, an **E-learning on ORPHAcodes** [66] was developed by the Norwegian Orphanet team in collaboration with the Orphanet coordinating team (Inserm, France). The course gives an introduction to the Orphanet nomenclature of rare diseases and the advantages of using ORPHAcodes, compared to generic medical terminologies. It is available in English. The target audience for this course is primarily clinicians. No previous knowledge on ORPHAcoding is required to take this course.

Helpdesk for using the Orphanet nomenclature

The national hubs are in charge of **establishing an ORPHAcodes helpdesk in local languages**. This helpdesk is dedicated to answering questions regarding the content of the Orphanet nomenclature and the implementation of ORPHAcodes in health information systems. It provides advice on implementing the nomenclature and its use for patient coding and analysis of coded data. Questions should be sent by emails at **Orphacodes.Belgium@sciensano.be**.

A **central OD4RD Github** [67] (in English) has also been set up (Figure 15). This is an online ticketing system to store, track, and make available requests from users across all countries participating in the OD4RD project. This system facilitates a simple and interactive workflow of the requests. It is open access to any end users. After creating an account, issues can be posted to interact with the Orphanet-Inserm nomenclature team. External users can use this platform to submit their request related to the coding of rare diseases. They can also contact their national OD4RD hub which will collect the need or request, will contextualize it, translate it in English, and transfer it to the Orphanet coordination team via GitHub if necessary.

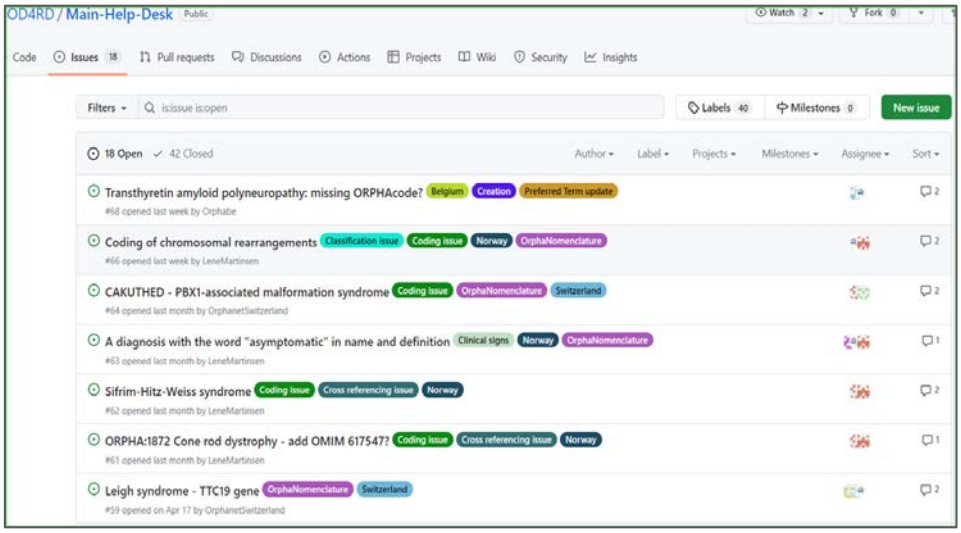


Fig.15. Screenshot of the section “Issues” of the OD4RD GitHub

A **FAQ section within the GitHub** [68] is developed by the Orphanet coordinating team based on users' questions. It provides standardised reference answers among **10 main topics:**

1. ORPHAcodes & Nomenclature
2. Orphanet classification
3. Good practice guidelines on Orphanet Nomenclature
4. Epidemiology in Rare Diseases
5. Alignments with other terminologies
6. Orphanet Tools
7. Education & Communication
8. Orphanet-ERN collaborations
9. ORPHAcodes Technical Implementation
10. Guidance documents for ORPHAcoding implementation and exploitation

Ultimately, thanks to the numerous actions taken and the recommendations drawn up in the form of reports available to all, **the OD4RD project will contribute to better diagnosis and care of patients with rare diseases**, as it will enable comparability of data, and therefore evaluation of current practices and outcomes against standards of care of reference, which is a necessary step to take action and generate real improvements in the rare disease field.

TRAINING ACTIVITIES

1. Trainings for Orphanet Information Scientists

As part of the continuous development of its collaborators, the members of the Orphanet national teams participate in various training courses organised by the Orphanet-Inserm coordinating team. These trainings are mandatory for all new Orphanet national team members, strongly recommended for junior team members and optional for senior team members (but recommended to refresh and strengthen all the concepts).

In 2024, two sessions of online trainings for Information Scientists were organized:

- 1 cycle between March and June: 16 sessions of around 2 hours;
- 1 cycle between October and November: 17 sessions of around 2 hours.

The main focus was on:

- **learning how to use the complex Orphanet rare diseases classification**, in order to fully understand how RDs are organised into classifications and the consequences of linking resources at different levels of classifications on the way resources are displayed on the Orphanet website;
- **using the Orphanet internal tools** (Figure 16) : **Arbor** to explore all the classifications of diseases produced by Orphanet; **Major** and **Major 2** (editorial tool to create, update, delete data in the database), **Plator** (allows pre-defined dataset extraction from the database or inject data if rights allow), **Seqtor** (search the links between different entities in the database), **Uploador** (allows to upload a document into the database), **Redminor** (communication tool between the national teams and the coordinating team).

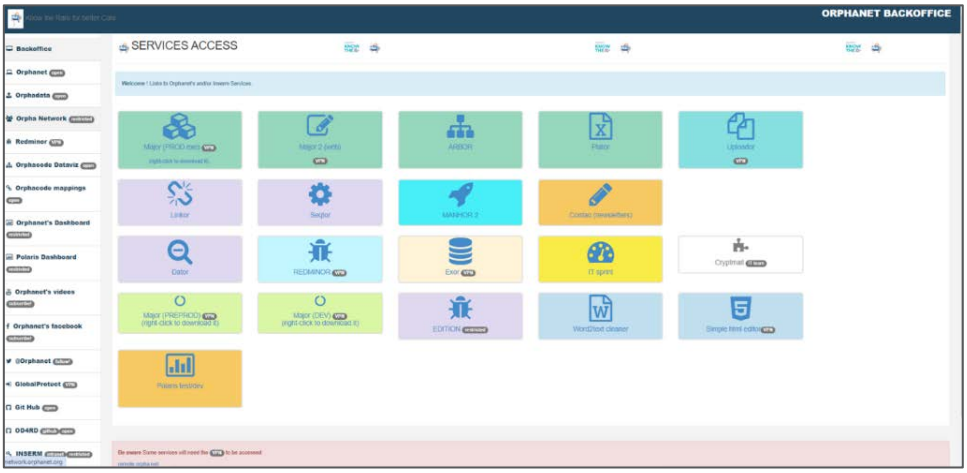


Fig.16. Orphanet Back office: overview of the tools and services

Here are some examples of **topics covered by the 2024 IS Orphanet trainings**:

- Orphanet general presentation: network, funding and portal;
- Orphanet Overview from the Coordinator's perspective;
- Orphanet partnerships and communication strategy;
- Orphanet nomenclature and classification of rare diseases: what is a rare disease ?; characteristics, purpose and organisation; how to access and use them; how they are updated and maintained; how to search for a disease in the database; how to make a request to the nomenclature team;
- How to link an expert resource to a disease in the database: understand how expert resources are displayed on the Orphanet website and get familiar with the functional classifications;

- The Orphanet classification system: Orphanet and Functional classifications;
- Orphanet IT tools, projects and activities;
- Orphanet internal tools for nomenclature and classifications;
- Orphanet gene database: how are genes registered in the database and what is needed to register them;
- Orphanet epidemiology concepts and database;
- Orphanet alignments with international terminologies;
- For each expert resources (expert centres, patient organisations, umbrella organisations/alliances, diagnostic tests, clinical trials, research projects, registries and biobanks): a specific session on data collection, data selection, data validation (pre-release QC), data registration and publication, data post-release quality control;
- Research categories flags ((how to select the most relevant “flag”).

Answering **various quizzes relating to data management linked to expert resources** is mandatory once the Orphanet IS has followed the training courses. This allows the IS to validate the knowledge acquired during the training and at the Orphanet Coordinating Team level, to receive feedback on the content and quality of the training sessions.

2. OD4RD “Train the trainers” program

For the OD4RD project endeavors to be successful, **well-trained National Orphanet Nomenclature hubs are needed to support local implementation of ORPHAcodes.**

In 2024, no specific training was organized by the coordinating team, taking into account that no new countries joined the OD4RD2 project consortium during this year. However the recordings of the basic and advanced sessions organised in September 2023 by the Orphanet nomenclature project manager and the OD4RD national hubs scientific coordinator were available online. These recordings make it possible to train new employees involved in the Orphanet nomenclature and classification training courses organized at the national level.

The main objective of the "Train the Trainers" program is to ensure that all OD4RD national hubs are able to fully explain the advantages of ORPHAcoding over other general medical terminologies. Trainers must present the methodology for alignment with other terminologies, as well as the various services and tools made available by Orphanet. This is to be able to propose, at the level of the hospital/centre where the training is held, the most appropriate solution to implement in order to increase the quality of data generated on rare diseases and lighten the workload of coders as much as possible.

Once trained, each national hub can act as a helpdesk for all questions related to the ORPHAcodes. National teams promote ORPHAcoding to the different stakeholders and organizes trainings in local language(s) for clinicians, geneticists and coders to ensure accurate and standardized RD coding practices (for more details, see the OD4RD project section above).

AWARENESS AND NETWORKING ACTIVITIES

One of the Orphanet network's missions is to **increase the awareness and the dissemination of knowledge on rare disorders.** Several actions concerning the Orphanet database and related tools and services were carried out to this end by the Orphanet Belgium team in 2024.

1. Contribution to the Memorandum on rare diseases

Fig. 17. Memorandum published by RaDiOrg in January 2024

RaDiOrg [6], the Belgian umbrella association for people living with rare diseases, in collaboration with its members and the Rare Diseases Working Group of the Belgian College of Human Genetics and Rare Diseases [8] - of which the Sciensano Rare Disease Team is part - published a **Memorandum** (available in Dutch and French) **containing policy proposals aimed at improving the life of people affected by rare diseases** [69] [70] (Figure 17).

The idea of creating this document comes from the fact that the current Belgian Rare Diseases Plan [25] [26] was published more than 10 years ago (2013). The Belgian Rare Diseases Plan has ensured progress in several key areas, but since its publication, Belgium has undergone a governmental reform which has led to a change of responsibilities in the field of health policy. As a result, some of the actions described in the plan were difficult or impossible to achieve and there remain numerous challenges in the field of rare diseases. With elections due in 2024 and political parties preparing their campaigns, there was a real opportunity to highlight these difficulties and shortcomings to political decision-makers. The memorandum defines **ten concrete proposals to be prioritized**. The Team Rare Diseases of Sciensano, including Orphanet Belgium, contributed to the drafting of the memorandum. The first action defined in this document is the necessity of having prevalence figures for rare disease patients through increased data collection in the Central Registry for Rare Diseases [71] hosted by Sciensano. The key role played by Orphanet is also mentioned, with proposals for new initiatives such as the establishment of a national information centre (helpline) for people with questions on rare diseases to which the Orphanet Belgium team could contribute.

The memorandum was communicated to all Belgian political parties in February 2024. The reception was positive, and led to several meetings with representatives of various Belgian political movements and the office of the Minister of Health. On the occasion of Rare Disease Day 2024, the Minister of Health, Frank Vandenbroucke, officially announced to the House of Representatives that he was instructing the FPS Public Health to develop **a new Belgian Rare Disease Plan**, qualifying the memorandum a beacon for this future project.

2. Oral presentation on rare diseases at the Sciensano EpiTuesdays

EpiTuesdays are **seminars organized every two weeks by the Epidemiology and Public Health department of Sciensano,** the Belgian Scientific Institute of Public Health [2] which has more than 900 employees. These seminars are aimed at all Sciensano collaborators interested in the topics covered and offer a platform to each collaborator to present their work, receive peer feedback and learn from their colleagues about new projects and methodologies. In February 2024, the Orphanet Belgium representative (Annabelle Calomme, Sciensano) made a presentation entitled **"Fight against rare diseases: involvement of Sciensano in several national and European projects"** during which the Orphanet and OD4RD projects were presented.

3. Participation in the 13th edition of the EURORDIS Black Pearl Award ceremony

The annual **EURORDIS Black Pearl Awards** [72] is an event that brings together hundreds of persons living with a rare disease, patient advocates, policy makers including representatives from the European Parliament and Commission, scientists, healthcare professionals, industry representatives, and more from all around the world.

The Orphanet Belgium representative (Annabelle Calomme, Sciensano) attended the 13th EURORDIS Black Pearl Awards which took place in Brussels and online on February 20, 2024 (Figure 18). This annual ceremony is an excellent opportunity to meet Belgian and European partners and to celebrate together the outstanding achievements of people living with a rare disease, as well as those who contribute to improving the care of these people and their visibility in society.


Fig.18. Picture on the left: Annabelle Calomme, Orphanet Belgium Project Manager and member of the Sciensano Rare Disease Team; Loubna Ouriaghli, Head of Government Affairs and Policy at Ipsen; Elisa Balducci, Attaché FPS Public Health, Food Chain Safety and Environment. Picture on the right: Ana Rath, Orphanet Director.

4. Participation in the 2024 Rare Disease Day

To give greater attention to the 300 million people living with a rare disease worldwide and their families, a global awareness campaign is organized every year on the last day of February by EURORDIS [23] and Rare Diseases International [73]. In Belgium, it is RaDiOrg [6], the umbrella association for people living with a rare disease, which is leading the annual awareness campaign.

The key concept of the Belgian campaign is based around the **message conveyed by the hashtag #shareyourcolors**. On February 29, 2024, Belgians were invited to share the colors of rare diseases (pink, blue, green, purple) throughout the country.

As every year, the Orphanet Belgium Team participated in this action. We published a message to raise awareness and draw attention to the projects carried out in the RD field by Sciensano, including our participation in the Orphanet network, on the intranet of our institution. We invited our Sciensano colleagues to participate in this day by sharing the colors of rare diseases, for example by wearing colorful clothes, putting coloured tissue paper on their windows or by sharing on social networks the visuals (Figure 19) and infographics (Figure 20) created by RaDiOrg for this occasion. We also shared information and pictures on our national Orphanet website and on the Sciensano public website section dedicated to rare diseases. A nail painting workshop in the colors of rare diseases and an information stand were organized within Sciensano (Figure 21).

Fig.19. Visuals of the awareness campaign launched by RaDiOrg in 2024 for the International Rare Disease Day

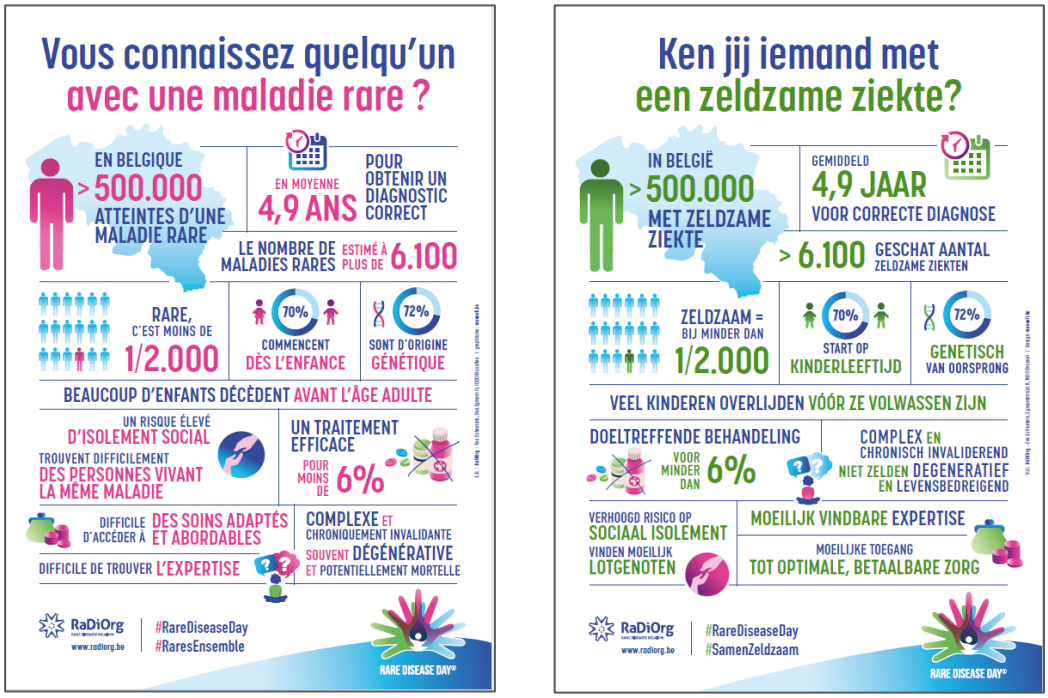


Fig. 20. Infographics developed by RaDiOrg highlighting key facts about rare diseases

Fig. 21. Members of Sciensano showing their support on the occasion of Rare Disease Day 2024

5. Organisation of a webinar on rare diseases for general practitioners

The general practitioners play an essential role in the diagnosis and appropriate referral of people with rare diseases in the health care system. However, a lack of knowledge and appropriate training of Belgian general practitioners regarding rare diseases is described in scientific publications [74].

A webinar was organised on the 1st of March 2024 for the Sentinel General Practitioners (SGP) network [75]**, which includes around 100 general practitioners all over Belgium.** The Orphanet Belgium representative (Annabelle Calomme, Sciensano) and another collaborator of the Sciensano RD team (Laura Debouverie) gave a 1-hour bilingual webinar whose main objective was to familiarize GPs with rare diseases and to answer the following questions: what are the “red flags” to pay attention to? Which specialist/centre should you refer your patient to when you suspect a rare disease? Where can you find reliable, easily accessible and regularly updated sources of information on rare diseases? 27 participants, including general practitioners, colleagues from the Agence wallonne pour une vie de qualité (AVIQ) [76] and from Sciensano [2] took part in this webinar.

A satisfaction survey was sent to the participants. The majority of respondents stated that this webinar met their expectations and will help them in their daily practice. Almost all respondents showed a real interest in exploring the topic of “red flags” further. For some of them we also noted an interest in deepening the information on Orphanet (portal and tools to help with diagnosis). These topics could be targeted during future training sessions.

6. Participation in the JARDIN JA kick-off meeting

The Sciensano RD team takes part in the JARDIN Joint Action [77] **that was launched in 2024 for a period of three years.** This pioneering project involves the 27 EU Member States, Norway and Ukraine and has total funding of 18.75 million euros. It aims to integrate European Reference Networks (ERNs) into national healthcare systems and pave the way for their future sustainability.

Fig. 22. Poster of the conference organized in March 2024 on the occasion of the launch of the JARDIN JA

The workload is divided in several work packages (WPs) and **Sciensano RD Team is involved in WP8 related to data management**. The main objective of this WP is to develop recommendations ensuring the interoperability of data structures at Member States level (local, regional, national) and at ERN level. Among the tasks included in WP8, a national visualization tool for RD expert centres and patient

organisations (“SE-Atlas”) will be developed in interested countries, exploiting the data already present in the Orphanet database.

On March 6 and 7, 2024, JARDIN was officially launched during a kick-off meeting in Brussels. This event was followed by the **Conference “Rare Diseases in the EU: Joint Action shaping the future of ERNs” organized by the European Economic and Social Committee (EESC) and DG SANTE** (Figure 22). Annabelle Calomme attended this event, as representative of the Orphanet Belgium team.

7. Participation in the 12th European Conference on Rare Diseases and Orphan Products (ECRD)

The European Conference on Rare Diseases & Orphan products (ECRD) is recognised globally as the largest, patient-led rare disease policy-shaping event held in Europe. It is organized by EURORDIS [72], the non-profit alliance of over 1000 rare disease patient organisations from 74 countries, and co-organised by Orphanet [1]. **The 12th edition** [78] **took place on May 15-16, 2024 in Brussels and was broadcast online** (Figure 23). It brought together around 700 participants, including patient advocates, policy makers, healthcare industry representatives, clinicians, regulators and Member State representatives.

Fig.23. ECRD Conference organised in May 2024 in Brussels

This conference was a unique opportunity to attend exciting presentations given by various stakeholders of the rare disease ecosystem but also to listen to moving testimonies from patients who motivate us to continue to contribute, each at our own level, to the improvement of diagnosis, care and treatment of the 30 million Europeans living with a rare disease. The major output of this conference was a **co-created, open letter** [79] **addressed to EU Institutions and country leaders to call for the development of an European plan on rare diseases.**

Fig.24. ECRD, May 2024, Brussels. In the left picture: Ana Rath, director of Orphanet.
In the right picture, from left to right: Annabelle Calomme (Sciensano, Orphanet Belgium), Sylvie Maiella and Madeline Cuillerier (Orphanet France) and Houda Ali (EURO-NMD Project Manager)

8. Oral presentation at the scientific symposium "Registry Day"

On May 17, 2024 Sciensano, the Belgian Institute of Public Health [2]**, organized a symposium intended to provide an overview of its contributions in real-world data collection** (Figure 25). The audience numbered around 80 participants, including healthcare professionals, policy makers, representatives of patient organizations, scientists and academic staff. This symposium was a great opportunity to share our work and engage with experts on how to advance patient care and research with real-world data and discuss how this data can be used to improve quality care and health outcomes in Belgium.

Particular attention was paid to the essential instruments of patient registries, with a presentation of the registries of rare diseases, diabetes, cystic fibrosis and neuromuscular diseases. Current challenges in registry data collections were addressed such as disease coding, as well as the use of real-world data in clinical trials, and the role of data providers and patients in this process. The Orphanet Belgium representative (Annabelle Calomme, Sciensano) gave a **presentation on the nomenclature developed by Orphanet** which makes it possible to accurately and unambiguously code the diagnoses of rare diseases in health information systems and to facilitate standardized data sharing.

Program and presentations are available here [80].

Fig.25. Registry Day, May 2024, Sciensano. On the right, presentation entitled “Belgian contribution to Orphanet, the international reference portal on rare diseases and orphan drugs” by Annabelle Calomme

9. Memorandum on rare diseases: meetings with representatives of Belgian political movements

RaDiOrg [6], the Belgian umbrella association for people living with rare diseases, published in February 2024 a Memorandum [69] containing policy proposals aimed at improving the life of people affected by rare diseases in our country. Sciensano also contributed to this memorandum (see point 1 page 49).

On May 21, 2024 the Orphanet Belgium representative (Annabelle Calomme, Sciensano) participated with representatives of patient organisations and Rare Disease Function coordinators, in a meeting at the Mouvement Réformateur (MR) headquarters to present the RD Memorandum (Figure 26). She gave a presentation on the challenges faced by most people with rare diseases in order to initiate a discussion on the main issues related to rare diseases in Belgium. The objective of this meeting was to highlight the need for rare diseases to be taken into account in the priorities of the new Belgian government formed following the June 2024 elections.

Fig. 26. From left to right: Violaine Herbaux, health advisor to the presidency of the MR; Prof. Dr. Karin Dahan, geneticist, medical coordinator of the Rare Disease Function at the Grand Hôpital de Charleroi-Institut de Génétique de Gosselies; Julie Taton, member of the Federal Parliament; Eva Schoeters, Director of RaDiOrg; Annabelle Calomme, member of the Sciensano Rare Disease Team-Orphanet Belgium Project Manager; Ludivine Verboogen, Vice-President of RaDiOrg and Olivia Lacroix, RD Project Coordinator at The Cliniques universitaires Saint-Luc.

10. Oral presentation at the conference organised by the Civil Society Organisations' Group of the European Economic and Social Committee (EESC)

On June 04, 2024 the Orphanet Belgium representative participated as a speaker and member of a panel of experts in a conference entitled "The State of Health in Europe" organised by the Civil Society Organisations' Group of the European Economic and Social Committee (EESC), in partnership with the Centre Hospitalier Universitaire de Liège and the Hôpital de la Citadelle (Figure 27).

The conference was held in the framework of the Belgian presidency of the Council of the EU. A topic was dedicated to **"The global fight against health inadequacies through the prism of European solidarity: the example of rare diseases".** Annabelle Calomme was invited to present the challenges faced by RD patients and health professionals, emphasizing the need for specific coding in health information systems. The **panel of experts dedicated to rare diseases** was composed of Tomasz Grybek, member of the Board of Directors of EURORDIS - Rare Diseases Europe, Ágnes Cser, EESC member of the Group III, Prof. Dr. Vincent Bours, head of the Rare Disease Function at CHU Liège and member of GENTURIS, Anne-Sophie Lapointe, member of the French Ministry of Health and Annabelle Calomme, representative of the Sciensano RD team and Orphanet Belgium.

Program: The State of Health in the EU | EESC [81]

Fig. 27. EESC Conference, June 2024, Liège. On the right, presentation entitled "Les maladies rares, un défi de santé publique" by Annabelle Calomme (Orphanet Belgium, Sciensano)

11. Interview on an ultra-rare disease for the RTL Info television and press

In June 2024, RTL info requested an interview with a representative of the Sciensano Rare Disease team regarding an ultra-rare disease, the Hao-Fountain syndrome (ORPHA:643549), for which a first case was recently diagnosed in Belgium (Figure 28).

A good opportunity for our team to raise awareness among the general public about rare diseases and the many difficulties faced by those who suffer from them, particularly in the absence of treatment and adequate care.

The article devoted to this subject, as well as the television report, are available via the following link: "Une maladie ultra rare": le fils de Yasmina est le premier cas de ce syndrome en Belgique, "on se sent abandonné" | RTL Info [82]

Fig. 28. RTL Info interview, June 2024.
First case diagnosed in Belgium of an ultra-rare disease, the Hao-Fountain syndrome.

12. Participation in a "Rare Disease Brainstorming" at the Belgian Ministry of Public Health

On June 25, 2024 the Federal Minister of Social Affairs and Public Health, Mr. Frank Vandenbroucke, organised a meeting with key players in the field of rare diseases in Belgium. This brainstorming on rare diseases was held in the presence of representatives of the FPS Public Health, INAMI-RIZIV, patients, RD Functions and Sciensano RD Team.

Discussions focused on how to officially recognize RD expertise in Belgium as well as on current and future INAMI-RIZIV conventions dedicated to rare diseases. The intention to put in place a new Belgian RD plan for the next 5 years was confirmed by the Minister. During this meeting, the Orphanet Belgium representative (Annabelle Calomme, Sciensano) had the opportunity to emphasize the need for appropriate coding (ORPHAcodes) for rare disease patients.

13. Meeting with the Terminology Center regarding the implementation of ORPHAcodes

In Belgium, the Terminology Center/ SCT National Release Center [9] within the Federal Public Service (FPS) Health, Food Chain Safety and Environment is the organization responsible for the management and implementation of the Belgian national version of SNOMED CT® in patient files. In 2013, Belgium opted for SNOMED CT® as the common terminology in the medical sector. **A transition to SNOMED CT® as the national reference terminology in all Belgian in electronic health records (EHR) is underway.** By 2028, SNOMED CT® is expected to be used as the primary source for patient record documentation.

The Sciensano rare diseases team actively promotes the use of ORPHAcodes for the diagnoses of RD patients. However **the ORPHAcodes implementation remains a major challenge in our country** knowing that the national health authorities support the use of only one coding system (i.e. SNOMED CT®) in the medical electronic records.

To explore this important topic further, the Sciensano RD team organized a **new meeting with the Terminology Center on July 24, 2024**. We had requested the presence of a clinician experienced in rare disease coding from the Institute of Rare Diseases of the Cliniques Universitaires Saint-Luc, Dr Joëlle Thonnard, so that she could present concrete cases in clinical practice which show how ORPHAcodes are essential for accurately coding RD diagnoses. Our team presented the numerous scientific arguments demonstrating the importance of coding with ORPHAcodes, in addition to SNOMED CT® identifiers, and therefore pleaded in favor of the possibility of double coding in EHRs (Figure 29).

Fig. 29. Meeting with the FPS-Terminology Centre on the use of ORPHAcodes, July 2024.

Although the Terminology Centre recognizes the need to make rare diseases more visible in electronic health records, it considers that making an exception for rare diseases, by allowing a double coding ORPHAcodes-SNOMED CT in the patient electronic files, will create an additional burden on health care professionals. The Terminology Center encourages to use SNOMED CT as primary code system and common terminology with automatic derivations to all other relevant or necessary code systems that are required for specific purposes or use cases. Regarding rare diseases, they consider that the solution should come from the implementation in each hospital of systems allowing the ORPHAcode corresponding to the SNOMED ID to be obtained in an automated manner, based on the mapping file produced by Orphanet France-Inserm.

However, even if all Belgian hospitals would be able to implement such solutions, it is important to note that **a 100% equivalence between the two nomenclatures is not - and will never be - possible to achieve** (due to different objectives and inclusion criteria). Therefore, despite the high level of alignment between both terminologies that consents a good level of interoperability, the entirety of rare disease is not represented in SNOMED CT. Using only SNOMED CT terminology in patient files will therefore not make it possible to reference all diagnostics for rare diseases. Moreover interoperability with other systems that do not use SNOMED CT and with rare diseases registries (using ORPHAcodes like most ERN registries) is not granted by using only SNOMED CT codification.

14. Training of rare disease Patient Experts

The Sciensano RD team was invited by RaDiOrg [6], the umbrella organisation for rare disease patient organisations in Belgium, to contribute to two learning modules dedicated to rare diseases. These modules are part of a very comprehensive training course of 8 modules organized by the Patient Expert Center [83].

Fig.30. The Patient Expert Center (PEC) logo

Patient Experts collaborate with patient associations to guide patients and their families in the difficult journey of medical and administrative procedures. They act as organizational representatives during awareness actions carried out in collaboration with hospitals, companies, ministries, university research groups, etc. Patient Experts also participate in government initiatives at the regional and federal levels that impact patients. The whole training to become a Patient Expert lasts approximately 40 hours, spread over six months. **In 2024, 153 speakers gave 160 training sessions which led to the certification of 253 Patient Experts for various diseases. This was the first time that a training session was specifically dedicated to rare diseases.**

The rare disease training included two part:

- a general part which covers topics relevant to all patients who wish to train as Patient Experts, whatever their pathology. It covers topics such as patient rights, the social map, ethics and informal caregivers;

- a disease-specific part which covers topics specific to rare diseases as a group. The training therefore does not focus on specific rare diseases, but rather on common characteristics and challenges important for rare diseases such as the diagnostic wandering, newborn screening, genetics, conventions, networks, registries and orphan drugs. Our team was responsible for the creation and presentation of 2 modules (i.e. 4 hours of training in total): module 1 dedicated to rare diseases in general (definition, prevalence, common challenges, networks of expertise, etc.) and module 8 dedicated to the rare disease registries managed by Sciensano and to Orphanet (with search exercises on the Orphanet portal).

4 colleagues from Sciensano collaborated on these bilingual training courses, including Annabelle Calomme (Orphanet Belgium) who participated in the development and presentation of the two modules dedicated to rare diseases. These training courses brought together **25 participants.**

Knowledge acquisition was assessed by **questionnaires** prepared by our team and sent to participants at the end of each module. The Orphanet Belgium team greatly appreciated this experience, which made it possible to strengthen its collaboration with patients and introduce them to Orphanet, which some participants knew very little or not at all.

15. Contribution to the NEED project: applicability to rare diseases

In September 2024, the Sciensano RD team started a collaboration with the KCE and our colleagues of the Sciensano Service Health Information regarding the NEED project [84], which aims to **identify and measure unmet health-related needs** for a more needs-driven healthcare policy and innovation in Belgium.

Fig.31. The NEED project logo

The unmet medical needs were one of the central themes of the Belgian presidency of the Council of the European Union, in the first half of 2024. The NEED project, led by the KCE [10] in partnership with Sciensano [2], the Federal Agency for Medicines and Health Products (FAMHP) [85], the NIHDI [5] and the Superior Health Council, FPS Health, Food Chain and Environment [86], aims to identify these needs. The NEED project is financially supported by the Belgian Federal Science Policy (BELSPO) [52] until the end of 2026. It collects evidence on unmet health-related needs via a literature review, a patient survey, individual patient interviews, expert opinion and/or database analysis.

Four use cases have been selected so far as part of this project: Crohn disease, malignant melanoma, long Covid and sickle cell anemia (ORPHA:232), the first case studied for rare diseases. A first report [87] regarding the applicability of the NEED approach to RDs was published in March 2024.

The NEED collaborators work on a **database to store evidence on unmet health-related needs** [88], from both the societal and patients' perspective. The first version of this database is online since October 2024. The database is openly accessible and users can directly download the unmet needs data associated with Crohn's disease, malignant melanoma and long Covid (but not yet with sickle cell anemia). The database will be regularly updated as new data become available. It will include a ranking system which will make it possible to define which (rare) diseases are at a high, medium or low level of unmet needs.

Ultimately the NEED project will help to guide policy decisions on the development, provision and reimbursement of a health intervention, so that resources are allocated preferentially to the areas of greatest need.

Annabelle Calomme (Orphanet Belgium, Sciensano) and Evy Dhondt (CRRD, Sciensano) are members of the NEED steering committee, in order to share their expertise on rare diseases. Special attention must be paid to the fact that as patients with rare diseases are often little or not visible in health information systems, in particular ultra-rare patients (< 1 in 1,000,000), there is a risk that these patients would not be sufficiently taken into account in this study, although they are certainly a population with high unmet medical needs. The NEED project collaborators must therefore be particularly attentive to this point.

16. Participation in a Policy Forum on rare diseases

Members of the Sciensano Rare Diseases Team were invited to participate in the policy forum "Equal opportunities in healthcare, including for rare diseases. Patients, experts and policymakers in dialogue", which took place on November 7th 2024 at the Chamber of Representatives. The forum was organized by University Hospitals Leuven (UZ Leuven), Rare Diseases Belgium (RaDiOrg) and the Rare Disease Diagnosis Alliance (RADDIAL) [89], with the support of the seven other Rare Disease Functions (Figures 32 and 33).

This event brought together **nearly a hundred participants**, including Members of Parliament, patient representatives, civil servants of multiple relevant administrations (Sciensano, the Belgian Health Data Agency, the National Institute for Health and Disability Insurance, the Belgian Healthcare Knowledge Centre, and the Federal Public Service Health), healthcare providers and pharmaceutical industry representatives. The event made it possible to inform, raise awareness and further involve the political world in the issue of rare diseases. It was held at a particularly opportune time, in the weeks preceding the formation of the new Belgian government.

Fig. 32. Participants in the Policy Forum on Rare Diseases, November 2024, Chamber of Representatives

Presentations and debates revolved around the following main themes:

- European Reference Networks (ERNs) and their integration into national networks (JARDIN: Joint Action on Integration of ERNs into National Healthcare Systems);
- Transparent identification of expertise about rare diseases and facilitation of access to this expertise for each patient;
- Implementation of multidisciplinary and integrated care with case management for each person suffering from a rare and complex disease, regardless of the diagnosis.

During the debate related to the first theme, the Orphanet Belgium representative (Annabelle Calomme, Sciensano) had the opportunity to point out the critical importance of uniform and systematic registration of rare disease data by all relevant stakeholders. She highlighted the current absence in Belgium of a legal framework guaranteeing effective collaboration between various healthcare stakeholders on data relating to rare diseases patients. This framework should include an obligation for expert centres to use the terminology specific to rare diseases (ORPHAcodes) and incentives (financial support) to encourage healthcare providers to implement the actions necessary for the use of these codes and the registration of patients in the Central Registry of Rare Diseases [71].

A **report** [90] summarizing the discussions and recommendations of the policy forum is available.

Fig. 33. Picture on the left, from left to right: Béatrice Gulbis (Hôpital Universitaire de Bruxelles), Marion Delcroix (UZ Leuven), Eva Schoeters (Rare Diseases Belgium – RaDiOrg), Christophe Deborsu (moderator). Picture on the right, from left to right: Evy Dhondt (CRRD, Sciensano), Annabelle Calomme (Orphanet Belgium, Sciensano).

17. Participation in the 2024 RaDiOrg Members Day

The Sciensano RD team (Annabelle Calomme, representative of Orphanet Belgium and Evy Dhondt, manager of the Central Registry Rare Diseases) were invited to the RaDiOrg 2024 members day organised on November 09 at the Pullman Brussels hotel. The day began with a photo and video session for the Rare Disease Day 2025 campaign. This event was an excellent opportunity to interact with patients and to better understand their needs and expectations (Figure 34).

The following topics were addressed during the event:

- presentation of the NEED project [84] by Irina Cleemput, from the Federal Center of Expertise for Health Care Belgian health;
- presentation of the CATT-CAIT “unmet medical needs” project, by Valentin Mutemberezi from the NIHDI;
- presentation of federal policy regarding “unmet needs” by Anouk Waeytens, advisor to the Minister of Public Health
- round table: How to identify “unmet” needs in the field of rare diseases?
- sneak peek at the Rare Disease Day 2025 campaign.

Fig. 34. Patients, healthcare professionals, representatives of Sciensano, NIDHI, KCE and Minister of Public Health present at the RaDiOrg Members' Day 2024

18. Participation in the Orphanet annual meeting

The Orphanet Annual meeting, organised by the Orphanet Network Coordinating team (INSERM), was held online on November 14-15, 2024. This meeting gathered 61 participants from 27 countries the first day and 57 participants from 25 countries the second day (including representatives of ERNs). The report produced following this meeting is accessible only to members of the Orphanet network.

The objectives of the annual meeting are multiple:

- assess what has been done over the past year by the coordination team, by each national team and by the network as a whole;
- agree on the strategic annual action plan and priorities for the following year;
- discuss on potential improvements, additional tasks and challenges to be addressed in 2025, in particular regarding the incorporation of an AISBL.

A **poster summarizing the main activities and achievements of the Orphanet Belgium team in 2024** was presented on this occasion (Figure 35).

Fig.35. Poster of the main activities and achievements of the Orphanet Belgium team in 2024

19. Participation in the Technical Workshop on the implementation of the Orphanet nomenclature

A workshop dedicated to the technical aspects of ORPHAcoding was organised online on December 18th, 2024 by the Orphanet coordinating team.

The main objective was to give an overview of the existing solutions to ease the adoption of the Orphanet nomenclature and the implementation of ORPHAcodes in Health Information Systems by delivering the "Orphanet Nomenclature Pack" and the ORPHAcodes API. This workshop aimed also to collect feedback from stakeholders already using ORPHAcodes (or in the process of implementing them), in order to list and prioritize possible technical improvements for the future releases of the tools developed by Orphanet.

109 people from 24 countries participated in this Workshop. Thanks to the intense communication campaign led by Orphanet Belgium, our country was particularly well represented: more than 20 participants, with each of the 8 Belgian Rare Disease Functions represented by 1 or even several members.

A **report** [91] summarizing the information provided and that collected from participants during this workshop is available is available.

20. Contribution to the OrphaNetWork News

OrphaNetWork News is an **internal newsletter** published by Orphanet approximately every 3 months (Figure 36)**.** It aims to inform all partners on the conclusions of the Orphanet Management Board monitoring meetings. It also ensures circulation of information related to each national team's activities and outputs in order to facilitate the acquisition of comprehensive knowledge by the network.

This newsletter is sent within the Orphanet Network to Orphanet national teams. National Advisory Board members and scientific board members can also subscribe.

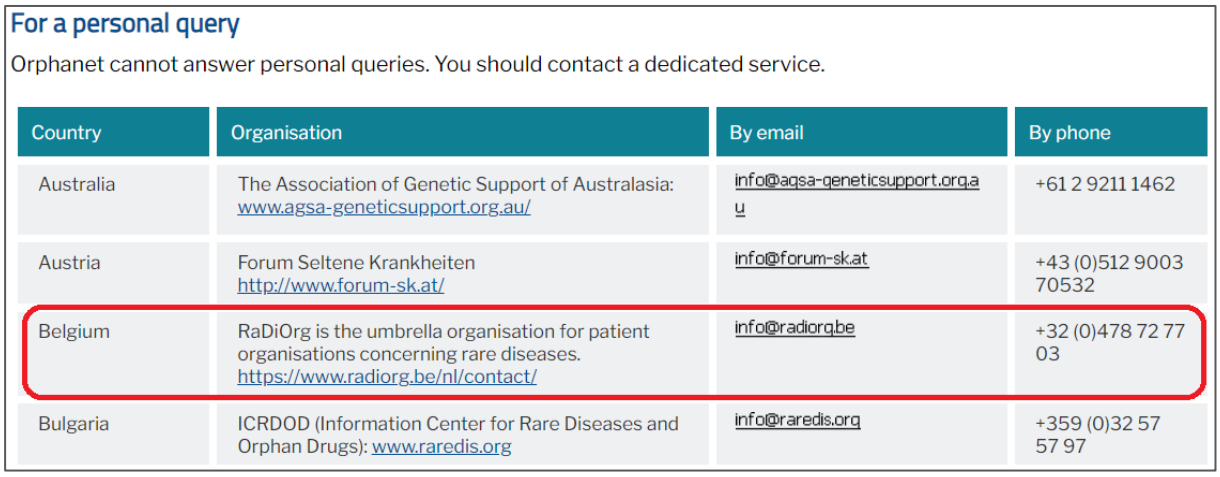
National teams are invited to submit relevant information to the OrphaNetWork newsletter, to systematically read every issue and to carry out the action points posted in this document. **The Orphanet Belgium team has published information on its activities in all 3 issues published during the year 2024** (communication about participation in meetings, conferences, congresses, trainings, etc.).

Fig.36. Cover page of the January-March 2024 issue of the OrphaNetWork internal newsletter

SERVICE ACTIVITIES: ASSISTANCE TO PATIENTS AND PROFESSIONALS

The Orphanet Belgium team regularly receives questions about rare diseases via e-mail (orphanetbelgium@sciensano.be) **or by phone calls from patients, researchers and healthcare professionals.** The team provides answers to these questions whenever possible, for example by helping to find correct information on a pathology, by referring to an association of patients specific to the pathology (if it exists), by helping in the search for an optimal expertise, or by explaining why a disease cannot be found on the Orphanet portal (based on the definition of the inclusion criteria to be considered a rare disease). When necessary, we refer patients to the authorized persons as we as Orphanet team may not answer personal queries, whether medical or administrative.

Since RaDiOrg [6], the umbrella organisation for people living with a rare disease in Belgium, acts as "helpline for personal queries", its contact details are available on the Orphanet Belgium website, as well as on the Orphanet international portal (Figure 37). In this context, RaDiOrg can connect people suffering from the same rare condition, give advice to create a patient association and offer visibility to a rare condition by posting a patient testimonial on their website.



For a personal query

Orphanet cannot answer personal queries. You should contact a dedicated service.

Country	Organisation	By email	By phone
Australia	The Association of Genetic Support of Australasia: www.agsa-geneticsupport.org.au/	info@agsa-geneticsupport.org.au	+61 2 9211 1462
Austria	Forum Seltene Krankheiten http://www.forum-sk.at/	info@forum-sk.at	+43 (0)512 9003 70532
Belgium	RaDiOrg is the umbrella organisation for patient organisations concerning rare diseases. https://www.radiorg.be/nl/contact/	info@radiorg.be	+32 (0)478 72 77 03
Bulgaria	ICRDOD (Information Center for Rare Diseases and Orphan Drugs): www.raredis.org	info@raredis.org	+359 (0)32 57 57 97

Fig.37. Screenshot of the Orphanet website: RaDiOrg is listed as the Belgian Helpline for personal queries

When questions related to **possible changes in the nomenclature and classification of rare diseases** (for example, a request to create a new entity not yet listed in Orphanet) are received, these are transferred to the members of the Orphanet-Inserm coordinating team in charge of these aspects. Prior scientific research work is provided by the national team to support the request (identification and transmission of recent and relevant scientific publications concerning the disease). It should be noted that the time necessary to get a complete answer from Orphanet-Inserm is generally quite long (up to several months). This is explained by the fact that this task requires a thorough review of the recent literature and the consultation of external experts such as those who collaborate with the ERNs.

The frequency of questions coming from external users and the workload it entails are difficult to estimate because the frequency is quite random and while some requests require a short time to be resolved, others involve long-term follow-up and multiple stakeholders. A listing of the requests received from patients and professionals is kept in our internal files.

Overview of what the Orphanet Belgium team can or cannot do to help you:

WHAT WE CAN DO

- Provide expert-reviewed general information on a rare condition (based on the texts produced by Orphanet).
- Identify the national and international centres recognized as experts for a given rare condition (centres registered in Orphanet, based on the current inclusion criteria).
- Identify a patient association specific to a rare condition (if it exists) and referral to RaDiOrg, our collaborator as a helpline.
- Identify a clinical trial, a research project, a registry, a medical laboratory offering a diagnostic test specific to a given rare condition (if any).
- Create, remove or update data in Orphanet (subjected to final validation by the Orphanet-Inserm coordinating team).
- Submit requests to add, remove or modify a rare clinical entity in the Orphanet nomenclature to the Orphanet-Inserm coordinating team.
- For clinicians/coders: provide support and guidance to identify the most relevant ORPHAcode for a RD diagnosis (in connection with the OD4RD project).
- For clinicians/coders: provide Orphanet nomenclature and classification trainings (in connection with the OD4RD project).

WHAT WE CANNOT DO

- We can't answer personal queries (whether medical, legislative or administrative). In this case, a dedicated service should be contacted.
- We cannot comment on the relevance of the medical advice you have received from your medical team.
- We cannot give assistance for administrative procedures relating to a treatment trajectory or a request for reimbursement from a health insurance fund.
- We cannot offer financial support, nor help to find medicines, medical equipment or any other material support.

SUSTAINIBILITY OF THE ORPHANET NETWORK: NEW AISBL STRUCTURE

Orphanet was created in 1997 in France (Inserm). From 2000, the European Commission (EC) supported the initiative by allocating dedicated funds, thanks to which Orphanet became an international network, today encompassing around 40 countries.

It is important to distinguish **2 main activities carried out by Orphanet**:

1. **Improve the visibility of RDs in the fields of healthcare and research by maintaining the Orphanet nomenclature and classification (ORPHAcodes)**. Since 2021, the activities aiming to contribute to standardized RD data generation by the implementation of ORPHAcodes in hospitals hosting ERNs benefit from a direct grant from the European Commission (EU4Health programme). The Orphanet data for rare diseases project [11], involving 20 national teams including Orphanet Belgium, will end in December 2025. Orphanet should receive other European funding to continue this part of its activities, via new projects for which they have already applied.

2. **Provide high-quality information on RDs, by giving access to a directory of expert services by disease** - such as expert centres, laboratories and diagnostic tests, patient organisations, research projects, clinical trials, registries - in each country of the network. In addition, Orphanet produces an **encyclopaedia of RDs**, progressively translated into the 9 languages of the database. These activities are no longer financed by European fundings and are threatened by lack of budget (at least, for countries of the Orphanet consortium that do not have the resources to finance these activities).

In order to plan a sustainable future for Orphanet, the EC set up a working group, which suggested changing its legal and organisational structure and enhancing its service sales activity (valorisation), which has been almost non-existent up to now. With the support of a consulting company, **the Orphanet Management Board agreed to create a new legal form for the network, i.e. an AISBL** (international non-profit association under Belgian law). This structure will allow Orphanet to continue to access European grants and national subsidies, while at the same time having ample scope to develop fee-based services from a non-profit perspective.

Participation in the AISBL requires the payment of an annual fee, the amount of which will depend on the number of Orphanet national teams joining the initiative.

In 2024, the Orphanet Belgium team led the discussions with Sciensano and with its sponsor (NIHDI) in order to assess the interest and willingness to continue to be part of the Orphanet network under the conditions of the new AISBL. The final phase of the Orphanet AISBL incorporation process of the different national institutions was launched in December 2024 and it was decided that **Belgium - via Sciensano - will be one of the founding members of the Orphanet AISBL.**

The benefits of Sciensano joining the Orphanet AISBL will be:

- continued representation of Belgium in the Orphanet network and consequently participation in international projects to which the network is admitted;
- possibility, as a founding member, to draw up the deed and agree on the amount of annual dues;
- contribute to developing specific services during the resource enhancement process, with the consequent reduction, in perspective, of the annual fee and a return on investment.

Several meetings of the Orphanet AISBL General Assembly will be scheduled in 2025 to agree on the internal regulations, the annual action plan and the membership fees calculation.

CONCLUSION AND PERSPECTIVES

Most people living with a rare disease face numerous barriers in their daily live. Among the initiatives aimed at improving the lives of these people and their loved ones, one of the most recognized is the Orphanet portal and associated tools. **Orphanet is the international reference source for the nomenclature and classification of rare diseases, both for healthcare and for research**. Since its creation in 1997, Orphanet has grown on the European scene and is now designated by the Global Bio Data Coalition as an essential and indispensable resource for research in the field of rare diseases**.** Its freely-accessible website and associated tools contribute to help all audiences access high quality expert-reviewed information on rare diseases. Orphanet provides the means to identify and make rare disease patients visible in health and research information systems thanks to a time-stable and unique identifier (ORPHAcode), to guide patients and physicians towards relevant services for an efficient patient care pathway and to generate knowledge by producing massive, computable and reusable scientific data.

The Orphanet multi-stakeholder network, developed thanks to sustained European and national efforts, is a good example of successful cross-European cooperation. The consortium, which expanded gradually to around 40 countries within Europe and beyond, is coordinated by the Inserm in Paris. National teams are located in each participating country of the network. **Belgium is part of this collective effort for almost 25 years (since 2001).**

In 2024, the Orphanet Belgium team carried out the fundamental database management tasks, which consist of **recording new data and regularly updating existing data** for all types of expert resources related to rare diseases listed in Orphanet (expert centres, patient organisations, medical laboratories and diagnostic tests, clinical trials, research projects and registries). The day-to-day management of the Orphanet database content is a continuous task based on regularly revised standard operating procedures, in order to provide all users with a reliable and up-to-date database on rare diseases.

A particular effort was made in 2024 to develop a **more effective annual update campaign**, in order to increase the participation of professionals in updating their Orphanet data, an essential step to guarantee a relevant database for our end-users. However, the hoped-for improvement in the number of responses was not observed, with the response rate of Belgian professionals having their activities recorded in Orphanet still remaining low (around 7%).

Accurate estimation of the impact of rare diseases on the population in terms of the number of affected patients is hampered by their underrepresentation in health information systems. The use of a coding system specific to rare diseases developed by Orphanet, the ORPHAcodes, is recognized as best practice to address this issue. Time has therefore also been invested in 2024 to provide **training to health professionals on the coding of rare diseases, as part of the European OD4RD project (2022-2025).** The main objective of this project is to achieve a real implementation of ORPHAcodes in hospitals hosting ERNs. These efforts are starting to bear fruit in our country but much work remains to be done to generalize the use of the Orphanet nomenclature in Belgium and internationally.

In addition, we continued to carry out our **service activities**, such as providing assistance and information to people living with a rare disease and to healthcare professionals who contact us regularly via email or phone. We also actively participated in **many national and international awareness-raising activities, forums, conferences and congresses concerning rare diseases** (as a participant, speaker or member of expert panels).

Our networking activities allowed us to **strengthen our collaborations with many key players in the field** (patient organisations, RD Functions, College of Genetics and Rare Diseases, etc.). Moreover we started a collaboration with the experts in charge of the NEED project, in order to evaluate its applicability in the field of rare diseases.

In 2024, we also devoted time to **raising awareness among general practitioners regarding rare diseases**. Indeed, various studies have shown that these first-line professionals feel insufficiently trained in the care of patients (potentially) suffering from rare diseases. However, general practitioners have a crucial role to play in reducing the time - that is still far too long (typically almost five years) - required for the diagnosis of rare diseases. In particular general practitioners should all be aware of the warning signs (“red flags”) that may suggest a diagnosis of a rare disease. They must also be informed of the expert centres to which to refer their patients, so that they can benefit from the most optimal care for their rare disease.

With over 6,400 rare diseases affecting an estimated 36 million people in Europe, the need for effective networking and cooperation in diagnosis and treatment is paramount. **The Sciensano RD team takes part in the Joint Action JARDIN** [77] that was launched in 2024 for a period of three years. This pioneering project involves the 27 EU Member States, Norway and Ukraine and has total funding of 18.75 million euros. It aims to integrate European Reference Networks (ERNs) into national health systems and pave the way for their future sustainability, by developing patient pathways linked to ERNs, by developing reference networks reflecting and complementing ERNs and by developing structures for undiagnosed patients. JARDIN should ultimately stimulate the development of improved national plans and strategies for rare diseases in each Member State, including Belgium. The workload is divided in several work packages and Sciensano is involved in WP8 related to data management. The main objective of this WP is to develop recommendations ensuring the interoperability of data structures at MS level (local, regional, national) and at ERN level. Among the tasks included in WP8, a national visualization tool for RD expert centres and patient organisations (SE-Atlas) is under development in each participating country, exploiting the data present in the Orphanet database.

The Sciensano RD team also participates in the **European Rare Disease Research Alliance (ERDERA)** [92] launched in September 2024, whose ultimate goal is to make Europe a world leader in rare diseases research and innovation. This new partnership integrates over 170 organisations from the public and private sectors to advance prevention, diagnosis and treatment research in rare diseases.

The sustainability of Orphanet and its national teams is essential to meet the challenges arising from a rapidly evolving political, scientific and informatics landscape. Several approaches have been explored to ensure the long-term sustainability of the Orphanet database activities, which no longer benefit from European funding. Among these avenues, the creation of a new legal structure in the form of an AISBL was chosen to ensure the network's continuity. **Belgium, thanks to the involvement of Sciensano, will be one of the five founding members of the Orphanet AISBL during its first year of operation (2025)**. This new structure will have its own legal entity with shared governance and should increase the Orphanet network's capacity to leverage its resources through the establishment of a service development unit.

REFERENCES

[1] “Orphanet Portal,” [Online]. Available: https://www.orphanet.org.

[2] “Sciensano homepage,” [Online]. Available: https://www/sciensano.be.

[3] “Orphanet Belgium - The Belgian contribution to the international Orphanet database for rare diseases and orphan drugs,” [Online]. Available: https://www.sciensano.be/en/projects/belgian-contribution-international-orphanet-database-rare-diseases-and-orphan-drugs.

[4] “Federal Public Service (FPS) Public Health, Food Chain Safety and Environment website,” [Online]. Available: https://www.health.belgium.be/en .

[5] “National Institute for Health and Disability Insurance (NIHDI, INAMI, RIZIV) website,” [Online]. Available: https://www.inami.fgov.be/fr.

[6] “RaDiOrg, Rare Diseases Belgium website,” [Online]. Available: https://www.radiorg.be/ .

[7] “Royal decree setting the standards corresponding to a “rare diseases function”,” [Online]. Available: https://etaamb.openjustice.be/fr/arrete-royal-du-25-avril-2014_n2014024248 .

[8] “College for Genetics and Rare Diseases website,” [Online]. Available: https://www.college-genetics.be/fr/about.html.

[9] “FPS Public Health Terminology Centre website,” [Online]. Available: https://www.health.belgium.be/en/node/24909.

[10] “KCE - Belgian Health Care Knowledge Centre,” [Online]. Available: https://kce.fgov.be/en/home-en.

[11] “Orphanet Data For Rare Diseases (OD4RD) website,” [Online]. Available: https://od4rd.eu/ .

[12] A. Calomme, “Orphanet Belgium activity report 2017-2019, DOI : https://doi.org/10.25608/4d5z-2q16,” Sciensano, Brussels, 2020.

[13] A. Calomme, “Orphanet Belgium activity report 2020, DOI : https://doi.org/10.25608/72vb-ay88,” Sciensano, Brussels, 2021.

[14] A. Calomme, “Orphanet Belgium activity report 2021, DOI : https://doi.org/10.25608/5bev-y998,” Sciensano, Brussels, 2022.

[15] A. Calomme, “Orphanet Belgium activity report 2022, DOI: https://doi.org/10.25608/1rw7-7t76,” Sciensano, Brussels, 2023.

[16] A. Calomme, “Orphanet Belgium activity report 2023, DOI: https://doi.org/10.25608/y7eb-js39,” Sciensano, Brussels, 2024.

[17] Orphanet-Inserm, “Orphanet Reports Series,” [Online]. Available: https://www.orpha.net/en/other-information/reports.

[18] Orphanet-Inserm, “Orphanet Procedures,” [Online]. Available: https://www.orpha.net/en/other-information/procedures.

[19] “Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products,” [Online]. Available: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32000R0141&from=FR.

[20] Wakap, S., Lambert, D.M., Olry, A. et al, “Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database,” *European Journal of Human Genetics,* no. 28, p. 165–173, 2020.

[21] “Orphanet Report Series - Prevalence of rare diseases: Bibliographic data – October 2024, https://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf,” Orphanet-Inserm, 2024.

[22] Faye, F., Crocione, C., Anido de Peña, R. et al. , “Time to diagnosis and determinants of diagnostic delays of people living with a rare disease: results of a Rare Barometer retrospective patient survey,” *European Journal of Human Genetics,* no. 32, p. 1116–1126, 2024.

[23] “EURORDIS website,” [Online]. Available: https://www.eurordis.org/.

[24] Orphanet-Inserm, “Orphanet – 2023 Activity report, Orphanet Report Series, Reports Collection, July 2024 (V1.2), http://www.orpha.net/orphacom/cahiers/docs/GB/ActivityReport2023.pdf,” 2024.

[25] “Belgian Plan for Rare Diseases, Brussels (French version),” December 2013. [Online]. Available: https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/plan_belge_maladies_rares.pdf.

[26] “Belgian Plan for Rare Diseases, Brussels (Dutch version),” December 2013. [Online]. Available: https://www.health.belgium.be/sites/default/files/uploads/fields/fpshealth_theme_file/belgisch_plan_voor_zeldzame_ziekten.pdf.

[27] “European Commission webpage on rare diseases,” [Online]. Available: https://health.ec.europa.eu/european-reference-networks/rare-diseases_en.

[28] A. Calomme, “Orphanet evaluation criteria for Belgian expert resources, version 4,” October 2024. [Online]. Available: https://orphanet.site/user/env/belgique/themes/orphanet/files/Orphanet_Belgian%20criteria%20document_version%2009OCT2024.pdf.

[29] “Orphanet Belgium website,” [Online]. Available: https://orphanet.site/belgium.

[30] “NIHDI website, list of centres with a NIHDI convention,” [Online]. Available: https://www.inami.fgov.be/fr/professionnels/etablissements-et-services-de-soins/centres-specialises-et-centres-de-reeducation.

[31] “Collège belge de génétique - Les centres de génétique en Belgique,” [Online]. Available: https://www.college-genetics.be/fr/pour-les-professionnels/liens-utiles-prof/les-centres-de-genetique-en-belgique.html.

[32] “RaDiOrg website - Webpage dedicated to the eight Rare Diseases Functions,” [Online]. Available: https://www.radiorg.be/fr/guide-en-cas-de-maladie-rare/fonctions-maladies-rares/.

[33] “European Commission - Rare diseases and European Reference Networks,” [Online]. Available: https://health.ec.europa.eu/rare-diseases-and-european-reference-networks_en.

[34] “Orphanet website - European reference networks,” [Online]. Available: https://www.orpha.net/en/expert_centres/european-reference-network.

[35] “European Commission website - List of the 24 European Reference Networks,” [Online]. Available: https://health.ec.europa.eu/rare-diseases-and-european-reference-networks/european-reference-networks_en.

[36] “European Commission - 2019 call for membership to the existing European Reference Networks (ERNs),” [Online]. Available: https://health.ec.europa.eu/consultations/2019-call-membership-existing-european-reference-networks-erns_en.

[37] “European Commission website - Evaluation of European Reference Networks,” 2024. [Online]. Available: https://health.ec.europa.eu/publications/evaluation-european-reference-networks-0_en.

[38] “Belgian Genetic Tests Database (BGTD),” Sciensano, [Online]. Available: https://gentest.healthdata.be/ .

[39] “Sciensano website - National Reference Centres in Human Microbiology,” [Online]. Available: https://www.sciensano.be/en/national-reference-centers-human-microbiology.

[40] “Sciensano website - National Reference Centres in Clinical pathology, Rare diseases,” [Online]. Available: https://www.sciensano.be/en/quality-laboratories/nrc-i-clinical-pathology-i-rare-diseases.

[41] “Sciensano website - Quality of laboratories,” [Online]. Available: https://www.sciensano.be/en/about-sciensano/sciensanos-organogram/quality-laboratories.

[42] “International Clinical Trials Registry Platform,” [Online]. Available: https://trialsearch.who.int/.

[43] “EudraCT website,” [Online]. Available: https://eudract.ema.europa.eu/.

[44] “CTIS - Clinical Trials Information System website,” [Online]. Available: https://euclinicaltrials.eu/.

[45] “ClinicalTrials.gov website,” [Online]. Available: https://clinicaltrials.gov/.

[46] “Database for clinical trials in Belgium,” [Online]. Available: https://www.famhp.be/en/news/new_database_for_clinical_trials_in_belgium.

[47] “European Rare Disease Research Coordination and Support Action consortium (ERICA) website,” [Online]. Available: https://erica-rd.eu/ .

[48] “IRDiRC – International Rare Diseases Research Consortium website,” [Online]. Available: https://irdirc.org/.

[49] “INVENT - Database of research projects,” [Online]. Available: https://www.belspo.be/belspo/invent/intro_en.stm.

[50] “CREF - Conseil des rectrices et recteurs,” [Online]. Available: http://www.cref.be/.

[51] “FRIS research portal,” [Online]. Available: https://www.researchportal.be/en.

[52] “BELSPO - Federal Public Planning Service Science Policy website,” [Online]. Available: https://www.belspo.be/.

[53] “CORDIS website (EU Research & Development projects),” [Online]. Available: https://cordis.europa.eu/ .

[54] “BMBF - German Federal Ministry of Education and Research,” [Online]. Available: https://fundit.fr/en/institutions/german-federal-ministry-education-and-research-bmbf.

[55] “eHealtNetwork - Guideline on the electronic exchange of health data under Cross-Border Directive 2011/24/EU, Release 3.4, https://health.ec.europa.eu/document/download/e020f311-c35b-45ae-ba3d-03212b57fa65_en?filename=ehn_guidelines_patientsummary_en.pdf,” Nov 2024.

[56] European Commission Expert Group on Rare Diseases, “Recommendation on ways to improve codification for rare diseases in health information systems,” 2014. [Online]. Available: https://health.ec.europa.eu/system/files/2016-11/recommendation_coding_cegrd_en_0.pdf .

[57] EU Monitor - DG Health and Food Safety, “SGPP- Steering Group on Health Promotion, Disease Prevention and Management of Non-Communicable Diseases,” 2018. [Online]. Available: https://www.eumonitor.eu/9353000/1/j9vvik7m1c3gyxp/vkql59etwmzw.

[58] “IRDiRC website - Orphadata Science granted Global Core Biodata Resource status,” [Online]. Available: https://irdirc.org/orphadata-science-granted-global-core-biodata-resource-status/.

[59] “Sciensano website - OD4RD - Codification of rare diseases,” [Online]. Available: https://www.sciensano.be/en/projects/codification-rare-diseases.

[60] “OD4RD1/OD4RD2 Deliverables,” [Online]. Available: https://od4rd.eu/03-deliverables .

[61] “OD4RD project - Why ORPHAcoding,” [Online]. Available: https://od4rd.eu/communication-material/WHY%20ORPHAcoding%20vs%20Other%20Terminologies_VF.pdf.

[62] “OD4RD project - Making IT easy: ORPHAcode implementation in health information systems,” [Online]. Available: https://od4rd.eu/user/pages/10.communication-material/ORPHAcodes-IT_Flyer-VF.pdf.

[63] “OD4RD project - What is the Orphanet Network of National Hubs,” [Online]. Available: https://od4rd.eu/communication-material/What%20is%20the%20ORPHANET%20Network%20of%20National%20hubs%20Flyer_final-3.pdf.

[64] “OD4RD project: 2023 achievements,” [Online]. Available: https://od4rd.eu/communication-material/OD4RD-achievements%20booklet.pdf.

[65] “OD4RD project: 2024 achievements,” [Online]. Available: https://od4rd.eu/communication-material/Copie%20de%20Achievements_ORPHANET%20Network%20of%20National%20hubs%20Flyer_final%20(1080%20x%201350%20px).pdf.

[66] “E-learning on ORPHAcodes,” [Online]. Available: https://sjelden.no/nettkurs/orphacodes-for-rare-diseases/ .

[67] “ORPHAcoding Helpdesk by Orphanet (GitHub),” [Online]. Available: https://github.com/OD4RD/Main-Help-Desk.

[68] “OD4RD GitHub - Wikipage,” [Online]. Available: https://github.com/OD4RD/Main-Help-Desk/wiki.

[69] RaDiOrg, “Mémorandum aux partis politiques,” 2024. [Online]. Available: https://www.radiorg.be/wp-content/uploads/2024/03/Memorandum-Maladies-Rares_RaDiOrg-College-de-genetique_.pdf.

[70] RaDiOrg, “Memorandum aan politieke partijen,” [Online]. Available: https://www.radiorg.be/wp-content/uploads/2024/03/Memorandum_Zeldzame-Ziekten_RaDiOrg-College-Genetica_NDL.pdf.

[71] “Sciensano website, CRRD - Central Registry Rare Diseases,” [Online]. Available: https://www.sciensano.be/en/projects/central-registry-rare-diseases.

[72] “EURORDIS Black Pearl Awards,” [Online]. Available: https://www.eurordis.org/black-pearl-awards/.

[73] “Rare Diseases International website,” [Online]. Available: https://www.rarediseasesinternational.org/.

[74] Vandeborne, L., van Overbeeke, E., Dooms, M. et al., “Information needs of physicians regarding the diagnosis of rare diseases: a questionnaire-based study in Belgium, https://doi.org/10.1186/s13023-019-1075-8,” *Orphanet Journal of Rare Diseases,* no. 14, 2019.

[75] “Sciensano website, SGPs - Network of General Practitioners,” [Online]. Available: https://www.sciensano.be/en/projects/network-general-practitioners.

[76] “AVICQ website,” [Online]. Available: https://www.aviq.be/fr.

[77] “JARDIN Joint Action website,” [Online]. Available: https://jardin-ern.eu/.

[78] “ECRD 2024,” [Online]. Available: https://www.rare-diseases.eu/.

[79] “ECRD 2024 - Open Letter from the Rare Disease Community,” [Online]. Available: https://download2.eurordis.org/ecrd/2024/ECRD_2024_Open_Letter.pdf.

[80] “Sciensano website, Registry Day,” 17 May 2024. [Online]. Available: https://www.sciensano.be/en/events/registry-day-advancing-patient-care-and-research-through-real-world-data.

[81] European Economic and Social Committee, “The State of Health in the EU, Conference in the framework of the Belgian presidency of the Council of the European Union,” 04 June 2024. [Online]. Available: https://www.eesc.europa.eu/en/agenda/our-events/events/state-health-eu.

[82] RTL Info, “"Une maladie ultra rare": le fils de Yasmina est le premier cas de ce syndrome en Belgique, "on se sent abandonné"," pp. https://www.rtl.be/actu/vos-temoignages/une-maladie-ultra-rare-le-fils-de-yasmina-est-le-premier-cas-de-ce-syndrome-en/2024-06-11/article/671869, 11 June 2024.

[83] “Patient Expert Centre website,” [Online]. Available: https://patientexpertcenter.be/.

[84] “NEED project,” [Online]. Available: https://health-needs.eu/index.php/en/.

[85] “FAMHP - Federal agency for medicines and health products website,” [Online]. Available: https://www.famhp.be/en.

[86] “Superior Halth Counsil website,” [Online]. Available: https://www.hgr-css.be/en.

[87] Claessens Z, Vanneste A, Broekmans J, Verbeke C, Wens I, Van Isterdael C, Janssens R, Barbier L, Claerman, “KCE REPORT 377C4, Needs Examination, Evaluation and Dissemination (NEED): applicability to rare diseases, DOI: https://doi.org/10.57598/R377C4,” Health Services Research (HSR) : Belgian Health Care Knowledge Centre (KCE), Brussels, 2024.

[88] “NEED database,” [Online]. Available: https://healthinformation.sciensano.be/shiny/NEED/.

[89] “Rare Disease Diagnosis Alliance (RADDIAL) website,” [Online]. Available: https://raddial.be/.

[90] “Policy Forum, “Equal opportunities in healthcare, including for rare diseases”, Patients, experts and policymakers in dialogue, summary report,” UZ Leuven, https://www.uzleuven.be/nl/media/bdbdf01e-2b8f-4f5c-af05-bdefb2109d14/Event%20Report_Policy%20Forum_FINAL_EN.pdf, 2024.

[91] M. Hanauer, “OD4RD2 Technical Workshop Report, Implementation of ORPHAcodes,” Orphanet, 2024.

[92] “ERDERA website,” [Online]. Available: https://erdera.org/.

ANNEXES

1. Belgian centres participating in ERNs for rare diseases (as recorded in Orphanet in 12/2024)

NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	NAME OF THE BELGIAN HOSPITAL	DATE OF APPROVAL	PARTICULAR AREA OF EXPERTISE OF THE CENTRE WITHIN THE ERN
VASCern (Rare Multisystemic Vascular Diseases)	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:68419 Vascular anomaly or angioma
	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:285014 Rare disease with thoracic aortic aneurysm and aortic dissection ORPHA:881 Turner syndrome
	AZ Sint-Maarten (Mechelen)	CALL 1 (2017)	ORPHA:77240 Primary lymphedema
	Antwerp University Hospital (UZ Antwerpen)	CALL 1 (2017)	ORPHA:285014 Rare disease with thoracic aortic aneurysm and aortic dissection
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:77240 Primary lymphedema
Endo-ERN (Rare Endocrine Conditions)	University Hospital Erasme (ULB) / Hôpital Universitaire des Enfants Reine Fabiola (HUDERF)	CALL 1 (2017)	ORPHA:90771 Disorder of sex development ORPHA:101954 Rare adrenal disease ORPHA:181384 Rare hypothalamic or pituitary disease ORPHA:68415 Rare parathyroid disease and phosphocalcic metabolism anomaly ORPHA:101955 Rare thyroid disease ORPHA:77828 Genetic obesity ORPHA:90692 Rare endocrine growth disease
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:90771 Disorder of sex development ORPHA:77828 Genetic obesity ORPHA:443095 Hyperinsulinemic hypoglycaemia ORPHA:877 Neuroendocrine neoplasm ORPHA:101956 Polyendocrinopathy ORPHA:101954 Rare adrenal disease ORPHA:101952 Rare diabetes mellitus ORPHA:181441 Rare disorder with hypergonadotropic hypogonadism ORPHA:90692 Rare endocrine growth disease ORPHA:181384 Rare hypothalamic or pituitary disease ORPHA:68415 Rare parathyroid disease and phosphocalcic metabolism anomaly ORPHA:101955 Rare thyroid disease
	University Hospital Brussels (UZ Brussel)	CALL 1 (2017)	ORPHA:97978 Rare endocrine disease
	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:90771 Disorder of sex development ORPHA:325690 Genetic disorder of sex development ORPHA:68415 Rare parathyroid disease and phosphocalcic metabolism anomaly
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:528 Congenital generalized lipodystrophy ORPHA:98305 Genetic lipodystrophy ORPHA:552 MODY ORPHA:225 Maternally-inherited diabetes and deafness ORPHA:90159 Panniculitis-induced localized lipodystrophy ORPHA:300382 Progeroid and marfanoid aspect-lipodystrophy syndrome ORPHA:1667 Wolcott-Rallison syndrome
	Liège University Hospital (Centre Hospitalier Universitaire de Liège)	CALL 1 (2017)	ORPHA:174590 Congenital hypogonadotropic hypogonadism ORPHA:755 Leydig cell hypoplasia ORPHA:276161 Multiple endocrine neoplasia ORPHA:99408 Pituitary adenoma ORPHA:300373 X-linked acrogigantism
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:95502 Acquired pituitary hormone deficiency ORPHA:100091 Adrenal/paraganglial tumor ORPHA:100094 Multiple polyglandular tumor ORPHA:101958 Primary adrenal insufficiency ORPHA:68415 Rare parathyroid disease and phosphocalcic metabolism anomaly
ERN-LUNG (Rare respiratory Diseases)	Antwerp University Hospital (UZ Antwerpen)	CALL 1 (2017)	ORPHA:50251 Pleural mesothelioma ORPHA:3398 Thymic epithelial neoplasm (overlap with expertise recognised by EURACAN)
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:586 Cystic fibrosis ORPHA:1303 Bronchiolitis obliterans with obstructive pulmonary disease ORPHA:182095 Interstitial lung disease ORPHA:1164 Allergic bronchopulmonary aspergillosis ORPHA:60033 Idiopathic bronchiectasis ORPHA:244 Primary ciliary dyskinesia ORPHA:71198 Rare pulmonary hypertension ORPHA:306644 Complication after organ transplantation ORPHA:658602 Transplant-related bronchiolitis obliterans ORPHA:797 Sarcoidosis (overlap with expertise recognised by ERN RITA)
	University Hospital Erasme (ULB)	CALL 1 (2017)	ORPHA:182095 Interstitial lung disease ORPHA:1164 Allergic bronchopulmonary aspergillosis ORPHA:60033 Idiopathic bronchiectasis ORPHA:71198 Rare pulmonary hypertension
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 2 (2021)	ORPHA:586 Cystic fibrosis ORPHA:182095 Interstitial lung disease ORPHA:60033 Idiopathic bronchiectasis ORPHA:244 Primary ciliary dyskinesia
	University Hospital Brussels (UZ Brussel)	CALL 2 (2021)	ORPHA:586 Cystic fibrosis
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:586 Cystic fibrosis ORPHA:50251 Pleural mesothelioma ORPHA:60033 Idiopathic bronchiectasis ORPHA:244 Primary ciliary dyskinesia Other Rare Lung Diseases (ORLD): no specific ORPHAcodes defined
EuroBloodNet (Rare Hematological Diseases)	University Hospital Erasme (ULB)	CALL 1 (2017)	ORPHA:846 Alpha-thalassemia ORPHA:848 Beta-thalassemia ORPHA:466026 Class I glucose-6-phosphate dehydrogenase deficiency ORPHA:3202 Dehydrated hereditary stomatocytosis ORPHA:99138 Hemolytic anemia due to erythrocyte adenosine deaminase overproduction ORPHA:712 Hemolytic anemia due to glucophosphate isomerase deficiency ORPHA:766 Hemolytic anemia due to red cell pyruvate kinase deficiency ORPHA:288 Hereditary elliptocytosis ORPHA:822 Hereditary spherocytosis ORPHA:3203 Overhydrated hereditary stomatocytosis ORPHA:275752 Sickle cell disease and related diseases
	Jules Bordet Institute	CALL 1 (2017)	ORPHA:171898 Lymphoid hemopathy
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:248315 Rare hemorrhagic disorder due to a coagulation factors defect ORPHA:248326 Rare hemorrhagic disorder due to a platelet anomaly
	Liège University Hospital (Centre Hospitalier Universitaire de Liège)	CALL 1 (2017)	ORPHA:68364 Hemoglobinopathy ORPHA:171895 Myeloid hemopathy ORPHA:220489 Rare hereditary hemochromatosis
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:248315 Rare hemorrhagic disorder due to a coagulation factors defect
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:68364 Hemoglobinopathy ORPHA:68334 Rare hemorrhagic disorder due to a constitutional coagulation factors defect ORPHA:71202 Rare hemorrhagic disorder due to a constitutional platelet anomaly
EURO-NMD (Rare Neuromuscular Diseases)	University Hospital Erasme (ULB)	CALL 1 (2017)	ORPHA:68381 Neuromuscular disease
	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:68381 Neuromuscular disease
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:68381 Neuromuscular disease
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:68381 Neuromuscular disease
	Antwerp University Hospital (UZ Antwerpen)	CALL 1 (2017)	ORPHA:68381 Neuromuscular disease

NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	NAME OF THE BELGIAN HOSPITAL	DATE OF APPROVAL	PARTICULAR AREA OF EXPERTISE OF THE CENTRE WITHIN THE ERN
ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	Antwerp University Hospital (UZ Antwerpen)	CALL 1 (2017)	ORPHA:404448 ADNP syndrome ORPHA:477765 COL4A1 or COL4A2-related cerebral small vessel disease with hemorrhagic tendancy ORPHA:1465 Coffin-Siris syndrome ORPHA:908 Fragile X syndrome ORPHA:68385 Neurometabolic disease
	University Hospital Erasme (ULB)	CALL 1 (2017)	ORPHA:93890 Rare developmental defect during embryogenesis
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:98044 Central nervous system malformation ORPHA:90771 Disorder of sex development ORPHA:183576 Genetic branchial arch or oral-acral syndrome ORPHA:183536 Genetic congenital limb malformation ORPHA:183557 Genetic developmental defect of the eye ORPHA:471383 Genetic lethal multiple congenital anomalies/dysmorphic syndrome ORPHA:183570 Genetic malformation syndrome with short stature ORPHA:330206 Genetic multiple congenital anomalies/dysmorphic syndrome without intellectual disability ORPHA:98196 Malformation syndrome with hamartosis ORPHA:102283 Multiple congenital anomalies/dysmorphic syndrome-intellectual disability ORPHA:93460 Overgrowth syndrome ORPHA:139033 Progeroid syndrome ORPHA:139012 Rare bone development disorder ORPHA:68335 Rare chromosomal anomaly ORPHA:139393 Syndromic craniosynostosis ORPHA:90642 Syndromic genetic deafness ORPHA:165707 Syndromic urogenital tract malformation
	Cliniques universitaires Saint-Luc (UCLouvain) and Institut de Pathologie et Génétique (IPG), Gosselies	CALL 2 (2021)	ORPHA:567 22q11.2 deletion syndrome ORPHA:870 Down syndrome ORPHA:68341 Multiple congenital anomalies/dysmorphic syndrome ORPHA:102283 Multiple congenital anomalies/dysmorphic syndrome-intellectual disability ORPHA:528084 Non-specific syndromic intellectual disability ORPHA:102369 Rare syndromic intellectual disability ORPHA:1991 Cleft lip with or without cleft palate ORPHA:823 Isolated spina bifida
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:68341 Multiple congenital anomalies/dysmorphic syndrome ORPHA:102283 Multiple congenital anomalies/dysmorphic syndrome-intellectual disability ORPHA:528084 Non-specific syndromic intellectual disability ORPHA:108989 Non-syndromic central nervous system malformation ORPHA:109011 Non-syndromic limb malformation ORPHA:68335 Rare chromosomal anomaly ORPHA:101685 Rare non-syndromic intellectual disability ORPHA:102369 Rare syndromic intellectual disability ORPHA:823 Isolated spina bifida
ERN-Skin (Rare and Undiagnosed Skin Disorders)	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:209 Cutis laxa ORPHA:98249 Ehlers-Danlos syndrome ORPHA:758 Pseudoxanthoma elasticum
	University Hospital Erasme (ULB)	CALL 1 (2017)	ORPHA:69126 PAPA syndrome ORPHA:289478 PASH syndrome ORPHA:793 SAPHO syndrome ORPHA:641385 PASS syndrome ORPHA:641380 PAPASH syndrome ORPHA:641390 PsAPASH syndrome
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:626 Large congenital melanocytic nevus ORPHA:1556 Cutis marmorata telangiectatica congenita ORPHA:744 Proteus syndrome ORPHA:3205 Sturge-Weber syndrome ORPHA:2451 Mucocutaneous venous malformations ORPHA:2874 Phakomatosis pigmentokeratotica ORPHA:2330 Kasabach-Merritt syndrome ORPHA:35125 Epidermal nevus syndrome ORPHA:42775 PHACE syndrome ORPHA:60040 Megalencephaly-capillary malformation-polymicrogyria syndrome ORPHA:79357 Hereditary palmoplantar keratoderma ORPHA:79361 Inherited epidermolysis bullosa ORPHA:79376 Hypopigmentation of the skin ORPHA:140944 CLOVES syndrome ORPHA:183435 Inherited ichthyosis
ERN-RND (Rare Neurological Diseases)	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:98535 Frontotemporal degeneration with dementia ORPHA:95432 Primary progressive aphasia ORPHA:399 Huntington disease ORPHA:685 Hereditary spastic paraplegia ORPHA:102002 Rare ataxia ORPHA:454887 Corticobasal syndrome ORPHA:102 Multiple system atrophy ORPHA:683 Progressive supranuclear palsy ORPHA:2828 Young-onset Parkinson disease
	University Hospital Erasme (ULB)	CALL 1 (2017)	ORPHA:183518 Hereditary ataxia ORPHA:685 Hereditary spastic paraplegia
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:98535 Frontotemporal degeneration with dementia
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:98535 Frontotemporal degeneration with dementia ORPHA:102 Multiple system atrophy ORPHA:68402 Rare parkinsonian disorder
EURACAN (Rare Adult Cancers (solid tumors)	Jules Bordet Institute	CALL 1 (2017)	ORPHA:100091 Adrenal/paraganglial tumor ORPHA:223727 Bone sarcoma ORPHA:50251 Pleural mesothelioma ORPHA:100087 Rare thyroid tumor ORPHA:3394 Soft tissue sarcoma ORPHA:99868 Thymic carcinoma ORPHA:99867 Thymoma
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:223727 Bone sarcoma ORPHA:3394 Soft tissue sarcoma ORPHA:304055 Pituitary tumor ORPHA:98062 Rare nervous system tumor ORPHA:424010 Epithelial tumor of anal canal ORPHA:168807 Primary malignant peritoneal tumor ORPHA:101943 Rare hepatic and biliary tract tumor ORPHA:100091 Adrenal/paraganglial tumor ORPHA:100088 Rare thyroid carcinoma ORPHA:182130 Tumor of endocrine glands ORPHA:254685 Gestational trophoblastic disease ORPHA:213500 Ovarian cancer ORPHA:398043 Malignant tumor of penis ORPHA:363472 Tumor of testis and paratestis ORPHA:877 Neuroendocrine neoplasm ORPHA:50251 Pleural mesothelioma ORPHA:99868 Thymic carcinoma ORPHA:99867 Thymoma ORPHA:617910 Conjunctival malignant melanoma ORPHA:79140 Cutaneous neuroendocrine carcinoma ORPHA:31112 Dermatofibrosarcoma protuberans ORPHA:33276 Kaposi sarcoma ORPHA:39044 Uveal melanoma
	Liège University Hospital (Centre Hospitalier Universitaire de Liège)	CALL 1 (2017)	ORPHA:254685 Gestational trophoblastic disease ORPHA:144 Lynch syndrome ORPHA:180220 Rare uterine adnexal tumor ORPHA:213564 Rare uterine cancer ORPHA:180312 Rare vulvovaginal tumor
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 2 (2021)	ORPHA:223727 Bone sarcoma ORPHA:873 Desmoid tumor ORPHA:178342 Inflammatory myofibroblastic tumor ORPHA:247762 Lipoblastoma ORPHA:97338 Melanoma of soft tissue ORPHA:3394 Soft tissue sarcoma ORPHA:617910 Conjunctival malignant melanoma ORPHA:39044 Uveal melanoma ORPHA:213500 Ovarian cancer ORPHA:424933 Rare malignant epithelial tumor of liver and intrahepatic biliary tract ORPHA:182067 Glial tumor ORPHA:616 Medulloblastoma ORPHA:2495 Meningioma ORPHA:251934 Mixed neuronal-glial tumor ORPHA:251905 Pineal tumor of neuroepithelial tissue ORPHA:304055 Pituitary tumor ORPHA:46135 Primary central nervous system lymphoma
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:113 Bazex-Dupré-Christol syndrome ORPHA:223727 Bone sarcoma ORPHA:79140 Cutaneous neuroendocrine carcinoma ORPHA:377 Gorlin syndrome ORPHA:423798 Mesenchymal tumor of small intestine ORPHA:213500 Ovarian cancer ORPHA:542 Primary cutaneous lymphoma ORPHA:100088 Rare thyroid carcinoma ORPHA:3394 Soft tissue sarcoma
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:877 Neuroendocrine neoplasm ORPHA:50251 Pleural mesothelioma ORPHA:3398 Thymic epithelial neoplasm

NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	NAME OF THE BELGIAN HOSPITAL	DATE OF APPROVAL	PARTICULAR AREA OF EXPERTISE OF THE CENTRE WITHIN THE ERN
ERN-PaedCan (Paediatric Cancer (haemato-oncology))	Ghent University Hospital (UZ Gent) *Centre linked to 97 ORPHAcodes (disorder(s)/groups of disorders). For a full overview, please consult the Orphanet website.*	CALL 1 (2017)	ORPHA:55881 Adamantinoma ORPHA:1501 Adrenocortical carcinoma ORPHA:569164 Angiomatoid fibrous histiocytoma ORPHA:3261 Autoimmune lymphoproliferative syndrome ORPHA:252164 Benign schwannoma ORPHA:125 Bloom syndrome ORPHA:223727 Bone sarcoma ORPHA:424936 Carcinoma of liver and intrahepatic biliary tract ORPHA:404507 Chondromyxoid fibroma ORPHA:178 Chordoma ORPHA:457246 Clear cell sarcoma of kidney ORPHA:211277 Complex vascular malformation with associated anomalies ORPHA:458758 Composite hemangioendothelioma ORPHA:458775 Congenital hemangioma ORPHA:2665 Congenital mesoblastic nephroma ORPHA:54595 Craniopharyngioma ORPHA:79140 Cutaneous neuroendocrine carcinoma ORPHA:206470 Cystadenoma of childhood ORPHA:3226 Deafness-lymphedema-leukemia syndrome ORPHA:873 Desmoid tumor ORPHA:2123 Diffuse neonatal hemangiomatosis ORPHA:213711 Endometrial stromal sarcoma ORPHA:423982 Epithelial tumor of the appendix ORPHA:157791 Epithelioid hemangioendothelioma ORPHA:289638 Epstein-Barr Virus-related tumor ORPHA:618 Familial melanoma ORPHA:44890 Gastrointestinal stromal tumor ORPHA:3399 Germ cell tumor ORPHA:363504 Germ cell tumor of testis ORPHA:391651 Glomus tumor
	Hôpital Universitaire des Enfants Reine Fabiola - HUDERF *Centre linked to 32 ORPHAcodes (disorder(s)/groups of disorders). For a full overview, please consult the Orphanet website.*	CALL 1 (2017)	ORPHA:519 Acute myeloid leukemia ORPHA:1501 Adrenocortical carcinoma ORPHA:457246 Clear cell sarcoma of kidney ORPHA:211277 Complex vascular malformation with associated anomalies ORPHA:458758 Composite hemangioendothelioma ORPHA:2665 Congenital mesoblastic nephroma ORPHA:251852 Embryonal tumor of neuroepithelial tissue ORPHA:157791 Epithelioid hemangioendothelioma ORPHA:3399 Germ cell tumor ORPHA:182067 Glial tumor ORPHA:449 Hepatoblastoma ORPHA:210589 Infantile hemangioma of rare localization ORPHA:464329 Kaposiform lymphangiomatosis ORPHA:389 Langerhans cell histiocytosis ORPHA:223735 Lymphoma ORPHA:52688 Myelodysplastic syndrome ORPHA:98275 Myelodysplastic/myeloproliferative disease ORPHA:98274 Myeloproliferative neoplasm ORPHA:150 Nasopharyngeal carcinoma ORPHA:654 Nephroblastoma ORPHA:668 Osteosarcoma ORPHA:33402 Pediatric hepatocellular carcinoma ORPHA:64742 Pleuropulmonary blastoma ORPHA:64741 Pulmonary blastoma ORPHA:71209 Rare soft tissue tumor ORPHA:100088 Rare thyroid carcinoma ORPHA:276142 Rare tumor of salivary glands ORPHA:217071 Renal cell carcinoma ORPHA:458763 Retiform hemangioendothelioma ORPHA:319 Skeletal Ewing sarcoma
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:519 Acute myeloid leukemia ORPHA:1501 Adrenocortical carcinoma ORPHA:55880 Chondrosarcoma ORPHA:251896 Choroid plexus tumor ORPHA:457246 Clear cell sarcoma of kidney ORPHA:54595 Craniopharyngioma ORPHA:618 Familial melanoma ORPHA:3399 Germ cell tumor ORPHA:182067 Glial tumor ORPHA:449 Hepatoblastoma ORPHA:389 Langerhans cell histiocytosis ORPHA:223735 Lymphoma ORPHA:251934 Mixed neuronal-glial tumor ORPHA:52688 Myelodysplastic syndrome ORPHA:98275 Myelodysplastic/myeloproliferative disease ORPHA:98274 Myeloproliferative neoplasm ORPHA:150 Nasopharyngeal carcinoma ORPHA:654 Nephroblastoma ORPHA:251924 Neuronal tumor ORPHA:668 Osteosarcoma ORPHA:33402 Pediatric hepatocellular carcinoma ORPHA:251905 Pineal tumor of neuroepithelial tissue ORPHA:100088 Rare thyroid carcinoma ORPHA:217071 Renal cell carcinoma ORPHA:790 Retinoblastoma ORPHA:3394 Soft tissue sarcoma
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 2 (2021)	ORPHA:223727 Bone sarcoma ORPHA:54595 Craniopharyngioma ORPHA:618 Familial melanoma ORPHA:3399 Germ cell tumor ORPHA:59305 Gestational trophoblastic neoplasm ORPHA:449 Hepatoblastoma ORPHA:389 Langerhans cell histiocytosis ORPHA:223735 Lymphoma ORPHA:168999 Malignant melanoma of the mucosa ORPHA:97338 Melanoma of soft tissue ORPHA:171895 Myeloid hemopathy ORPHA:33402 Pediatric hepatocellular carcinoma ORPHA:46135 Primary central nervous system lymphoma ORPHA:251995 Primary germ cell tumor of central nervous system ORPHA:279897 Primary oculocerebral lymphoma ORPHA:93619 Rare renal tumor ORPHA:251558 Rare tumor of neuroepithelial tissue ORPHA:790 Retinoblastoma ORPHA:3394 Soft tissue sarcoma ORPHA:252025 Tumor of meninges ORPHA:178315 Undifferentiated embryonal sarcoma of the liver
ERN-BOND (Rare Bone Disorders)	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:93447 Primary bone dysplasia with defective bone mineralization
	Antwerp University Hospital (UZ Antwerpen)	CALL 1 (2017)	ORPHA:15 Achondroplasia ORPHA:1328 Camurati-Engelmann disease ORPHA:429 Hypochondroplasia ORPHA:436 Hypophosphatasia ORPHA:240 Léri-Weill dyschondrosteosis ORPHA:93429 Multiple epiphyseal dysplasia and pseudoachondroplasia ORPHA:93430 Multiple metaphyseal dysplasia ORPHA:666 Osteogenesis imperfecta ORPHA:2779 Osteopathia striata-pigmentary dermopathy-white forelock syndrome ORPHA:2781 Osteopetrosis and related disorders ORPHA:3152 Sclerosteosis ORPHA:94068 Spondyloepiphyseal dysplasia congenita ORPHA:254 Spondylometaphyseal dysplasia ORPHA:828 Stickler syndrome
MetabERN (Rare Hereditary Metabolic Disorders)	Liège University Hospital (Centre Hospitalier Universitaire de Liège)	CALL 1 (2017)	ORPHA:68367 Rare inborn errors of metabolism
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:68367 Rare inborn errors of metabolism
	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:324 Fabry disease ORPHA:355 Gaucher disease ORPHA:676 Hereditary chronic pancreatitis ORPHA:79213 Mucopolysaccharidosis ORPHA:220489 Rare hereditary hemochromatosis ORPHA:905 Wilson disease
	Antwerp University Hospital (UZ Antwerpen)	CALL 1 (2017)	ORPHA:68367 Rare inborn errors of metabolism
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:68367 Rare inborn errors of metabolism
	University Hospital Erasme (ULB)/HUDERF - University Hospital Brussels (UZ Brussel)	CALL 1 (2017)	ORPHA:68367 Rare inborn errors of metabolism
GUARD-HEART (Gateway to Uncommon And Rare Diseases of the HEART)	University Hospital Brussels (UZ Brussel)	CALL 1 (2017)	ORPHA:247 Arrhythmogenic right ventricular cardiomyopathy ORPHA:130 Brugada syndrome ORPHA:3286 Catecholaminergic polymorphic ventricular tachycardia ORPHA:217604 Dilated cardiomyopathy ORPHA:768 Familial long QT syndrome ORPHA:217569 Rare hypertrophic cardiomyopathy ORPHA:217632 Restrictive cardiomyopathy ORPHA:217678 Unclassified cardiomyopathy
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:363618 LMNA-related cardiocutaneous progeria syndrome ORPHA:218436 Rare cardiac rhythm disease ORPHA:167848 Rare cardiomyopathy
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:218436 Rare cardiac rhythm disease ORPHA:167848 Rare cardiomyopathy

NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	NAME OF THE BELGIAN HOSPITAL	DATE OF APPROVAL	PARTICULAR AREA OF EXPERTISE OF THE CENTRE WITHIN THE ERN
ERN-EYE (Rare Eye Diseases)	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:519315 Rare retinal disorder
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:98634 Anterior segment developmental anomaly without extraocular manifestations ORPHA:98639 Rare lens disease
	Leuven University Hospital (UZ Leuven)	CALL 2 (2021)	ORPHA:140653 Neuro-ophthalmological disease ORPHA:519282 Rare corneal disorder ORPHA:520814 Rare disorder of the visual organs ORPHA:98639 Rare lens disease ORPHA:98618 Rare refraction anomaly ORPHA:519315 Rare retinal disorder
eUROGEN (Rare urogenital diseases and complex conditions)	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:2795 Fowler urethral sphincter dysfunction syndrome ORPHA:398043 Malignant tumor of penis ORPHA:654 Nephroblastoma ORPHA:506213 Rare disorder potentially indicated for kidney transplant ORPHA:93545 Renal or urinary tract malformation ORPHA:83001 Urogenital tract malformation
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:101433 Rare urogenital disease ORPHA:182114 Rare urogenital tumor
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:37202 Interstitial cystitis ORPHA:557 Non-syndromic anorectal malformation ORPHA:165704 Non-syndromic urogenital tract malformation ORPHA:363472 Tumor of testis and paratestis
ERN GENTURIS (GENetic TUmour RIsk Syndromes)	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:100 Ataxia-telangiectasia ORPHA:220460 Attenuated familial adenomatous polyposis ORPHA:289539 BAP1-related tumor predisposition syndrome ORPHA:109 Bannayan-Riley-Ruvalcaba syndrome ORPHA:122 Birt-Hogg-Dubé syndrome ORPHA:125 Bloom syndrome ORPHA:1359 Carney complex ORPHA:252202 Constitutional mismatch repair deficiency syndrome ORPHA:201 Cowden syndrome ORPHA:733 Familial adenomatous polyposis ORPHA:404560 Familial atypical multiple mole melanoma syndrome ORPHA:84 Fanconi anemia ORPHA:377 Gorlin syndrome ORPHA:145 Hereditary breast and/or ovarian cancer syndrome ORPHA:26106 Hereditary diffuse gastric cancer ORPHA:523 Hereditary leiomyomatosis and renal cell cancer ORPHA:157794 Hereditary mixed polyposis syndrome ORPHA:443909 Hereditary nonpolyposis colon cancer ORPHA:47044 Hereditary papillary renal cell carcinoma ORPHA:29072 Hereditary pheochromocytoma-paraganglioma ORPHA:319462 Inherited cancer-predisposing syndrome due to biallelic BRCA2 mutations ORPHA:2929 Juvenile polyposis syndrome ORPHA:524 Li-Fraumeni syndrome ORPHA:293822 MITF-related melanoma and renal cell carcinoma predisposition syndrome ORPHA:306498 PTEN hamartoma tumor syndrome ORPHA:2869 Peutz-Jeghers syndrome ORPHA:157798 Serrated polyposis syndrome ORPHA:892 Von Hippel-Lindau disease
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:140162 Inherited cancer-predisposing syndrome
	Liège University Hospital (Centre Hospitalier Universitaire de Liège)	CALL 1 (2017)	ORPHA:2678 Familial isolated café-au-lait macules ORPHA:637 Full NF2-related schwannomatosis ORPHA:93921 Full schwannomatosis ORPHA:145 Hereditary breast and/or ovarian cancer syndrome ORPHA:137605 Legius syndrome ORPHA:636 Neurofibromatosis type 1 ORPHA:638 Neurofibromatosis-Noonan syndrome
	University Hospital Brussels (UZ Brussel)	CALL 2 (2021)	ORPHA:145 Hereditary breast and/or ovarian cancer syndrome
RARE-LIVER (Rare Hepatological Diseases)	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:280071 ALG11-CDG ORPHA:52 Alagille syndrome ORPHA:60 Alpha-1-antitrypsin deficiency ORPHA:498345 Biliary atresia and associated disorders ORPHA:79506 Cholesterol ester transfer protein deficiency ORPHA:79239 Classic galactosemia ORPHA:205 Crigler-Najjar syndrome ORPHA:79167 Disorder of urea cycle metabolism and ammonia detoxification ORPHA:234 Dubin-Johnson syndrome ORPHA:355 Gaucher disease ORPHA:79201 Glycogen storage disease ORPHA:469 Hereditary fructose intolerance ORPHA:391665 Homozygous familial hypercholesterolemia ORPHA:77292 Infantile neurovisceral acid sphingomyelinase deficiency ORPHA:565 Menkes disease ORPHA:309136 Mitochondrial disorder due to a defect in assembly or maturation of the respiratory chain complexes ORPHA:446 Neonatal hemochromatosis ORPHA:59303 Neonatal ichthyosis-sclerosing cholangitis syndrome ORPHA:416 Primary hyperoxaluria ORPHA:79306 Progressive familial intrahepatic cholestasis type 1 ORPHA:79304 Progressive familial intrahepatic cholestasis type 2 ORPHA:79305 Progressive familial intrahepatic cholestasis type 3 ORPHA:773 Refsum disease ORPHA:3111 Rotor syndrome ORPHA:3402 Transient tyrosinemia of the newborn ORPHA:905 Wilson disease ORPHA:75233 Wolman disease ORPHA:912 Zellweger syndrome
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:60 Alpha-1-antitrypsin deficiency ORPHA:2137 Autoimmune hepatitis ORPHA:70567 Cholangiocarcinoma ORPHA:480501 Choledochal cyst ORPHA:284385 Familial intrahepatic cholestasis ORPHA:284264 IgG4-related disease ORPHA:30391 Isolated biliary atresia ORPHA:2924 Isolated polycystic liver disease ORPHA:186 Primary biliary cholangitis ORPHA:171 Primary sclerosing cholangitis ORPHA:101938 Rare vascular liver disease ORPHA:905 Wilson disease
	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:60 Alpha-1-antitrypsin deficiency ORPHA:2137 Autoimmune hepatitis ORPHA:498345 Biliary atresia and associated disorders ORPHA:70567 Cholangiocarcinoma ORPHA:284385 Familial intrahepatic cholestasis ORPHA:284264 IgG4-related disease ORPHA:2924 Isolated polycystic liver disease ORPHA:186 Primary biliary cholangitis ORPHA:171 Primary sclerosing cholangitis ORPHA:101938 Rare vascular liver disease ORPHA:905 Wilson disease
	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:60 Alpha-1-antitrypsin deficiency ORPHA:243367 Acute fatty liver of pregnancy ORPHA:2137 Autoimmune hepatitis ORPHA:498345 Biliary atresia and associated disorders ORPHA:284385 Familial intrahepatic cholestasis ORPHA:244242 HELLP syndrome ORPHA:447764 IgG4-related sclerosing cholangitis ORPHA:69665 Intrahepatic cholestasis of pregnancy ORPHA:2924 Isolated polycystic liver disease ORPHA:186 Primary biliary cholangitis ORPHA:562639 Primary biliary cholangitis/primary sclerosing cholangitis and autoimmune hepatitis overlap syndrome ORPHA:100085 Primary hepatic neuroendocrine carcinoma ORPHA:171 Primary sclerosing cholangitis ORPHA:101941 Rare biliary tract disease ORPHA:424933 Rare malignant epithelial tumor of liver and intrahepatic biliary tract ORPHA:101940 Rare metabolic liver disease ORPHA:101938 Rare vascular liver disease

NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	NAME OF THE BELGIAN HOSPITAL	DATE OF APPROVAL	PARTICULAR AREA OF EXPERTISE OF THE CENTRE WITHIN THE ERN
ReCONNET (Rare Connective Tissue and Musculoskeletal Diseases)	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:98482 Idiopathic inflammatory myopathy ORPHA:90291 Systemic sclerosis ORPHA:536 Systemic lupus erythematosus
	Ghent University Hospital (UZ Gent)	CALL 1 (2017)	ORPHA:98249 Ehlers-Danlos syndrome ORPHA:98482 Idiopathic inflammatory myopathy ORPHA:90291 Systemic sclerosis
	Leuven University Hospital (UZ Leuven)	CALL 2 (2021)	ORPHA:98482 Idiopathic inflammatory myopathy ORPHA:90291 Systemic sclerosis ORPHA:536 Systemic lupus erythematosus
ERKNet (Rare Kidney Diseases)	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 1 (2017)	ORPHA:93626 Rare renal disease
	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	Adults section: ORPHA:730 Autosomal dominant polycystic kidney disease ORPHA:93548 Glomerular disease ORPHA:93603 Rare renal tubular disease ORPHA:156162 Renal ciliopathy ORPHA:93545 Renal or urinary tract malformation ORPHA:93573 Thrombotic microangiopathy Pediatric section: ORPHA:93626 Rare renal disease
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	Adults section: ORPHA:730 Autosomal dominant polycystic kidney disease ORPHA:88924 Autosomal dominant polycystic kidney disease type 1 with tuberous sclerosis ORPHA:93587 Genetic cystic renal disease ORPHA:93548 Glomerular disease ORPHA:544458 Hemolytic uremic syndrome ORPHA:93593 Nephropathy secondary to a storage or other metabolic disease ORPHA:93603 Rare renal tubular disease ORPHA:93545 Renal or urinary tract malformation ORPHA:805 Tuberous sclerosis complex Pediatric section: ORPHA:93626 Rare renal disease
EpiCARE (Rare and Complex Epilepsies)	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:101998 Rare epilepsy
	Brussels Rare and Complex Epilepsies Consortium BRACE (Cliniques Universitaires Saint-Luc and Centre William Lennox, UCLouvain; Hôpital Universitaire Erasme and Hôpital Universitaire des Enfants Reine Fabiola, ULB; Institut de Pathologie et Génétique (IPG), Gosselies)	CALL 2 (2021)	ORPHA:166478 Cerebral malformation with epilepsy ORPHA:166469 Chromosomal anomaly with epilepsy as a major feature ORPHA:166463 Epilepsy syndrome ORPHA:166490 Infectious disease with epilepsy ORPHA:166484 Inflammatory and autoimmune disease with epilepsy ORPHA:166481 Metabolic diseases with epilepsy ORPHA:166472 Monogenic disease with epilepsy ORPHA:98257 Neonatal epilepsy syndrome ORPHA:137577 Neonatal hypoxic and ischemic brain injury ORPHA:439175 Pediatric arterial ischemic stroke ORPHA:101998 Rare epilepsy
RITA (Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases)	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:93665 Autoinflammatory syndrome ORPHA:101997 Primary immunodeficiency ORPHA:182064 Rare neuroinflammatory or neuroimmunological disease ORPHA:280342 Rare systemic or rheumatological disease of childhood ORPHA:98715 Uveitis ORPHA:52759 Vasculitis
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:93665 Autoinflammatory syndrome ORPHA:101997 Primary immunodeficiency ORPHA:486955 Rare pediatric rheumatologic disease ORPHA:280373 Rare pediatric systemic disease
ERNICA (Rare inherited and congenital anomalies)	Leuven University Hospital (UZ Leuven)	CALL 1 (2017)	ORPHA:98043 Diaphragmatic or abdominal wall malformation
	Cliniques universitaires Saint-Luc (UCLouvain)	CALL 2 (2021)	ORPHA:103919 Autoimmune pancreatitis ORPHA:586 Cystic fibrosis ORPHA:101050 Familial hypocalciuric hypercalcemia type 3 ORPHA:676 Hereditary chronic pancreatitis ORPHA:2315 Johanson-Blizzard syndrome ORPHA:199337 Pancreatic insufficiency-anemia-hyperostosis syndrome ORPHA:699 Pearson syndrome ORPHA:180824 Rare tumor of pancreas ORPHA:811 Shwachman-Diamond syndrome
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:88993 Esophageal malformation ORPHA:97944 Gastroduodenal malformation ORPHA:97945 Intestinal malformation ORPHA:104009 Rare disease involving intestinal motility ORPHA:104012 Rare inflammatory bowel disease
TransplantChild (Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	Cliniques universitaires Saint-Luc (UCLouvain) *Centre linked to 51 ORPHAcodes (disorder(s)/groups of disorders). For a full overview, please consult the Orphanet website.*	CALL 1 (2017)	ORPHA:52 Alagille syndrome ORPHA:60 Alpha-1-antitrypsin deficiency ORPHA:2137 Autoimmune hepatitis ORPHA:300345 Autosomal systemic lupus erythematosus ORPHA:116 Beckwith-Wiedemann syndrome ORPHA:244283 Biliary atresia with splenic malformation syndrome ORPHA:131 Budd-Chiari syndrome ORPHA:53035 Caroli disease ORPHA:480520 Caroli syndrome ORPHA:480501 Choledochal cyst ORPHA:77293 Chronic visceral acid sphingomyelinase deficiency ORPHA:79239 Classic galactosemia ORPHA:95507 Congenital anomaly of hepatic vein ORPHA:480531 Congenital portosystemic shunt ORPHA:205 Crigler-Najjar syndrome ORPHA:586 Cystic fibrosis ORPHA:309810 Disorder of peroxisomal alpha-, beta- and omega-oxidation ORPHA:540 Familial hemophagocytic lymphohistiocytosis ORPHA:284385 Familial intrahepatic cholestasis ORPHA:35063 Fulminant viral hepatitis ORPHA:355 Gaucher disease ORPHA:364 Glycogen storage disease due to glucose-6-phosphatase deficiency ORPHA:367 Glycogen storage disease due to glycogen branching enzyme deficiency ORPHA:366 Glycogen storage disease due to glycogen debranching enzyme deficiency ORPHA:890 Hepatic veno-occlusive disease ORPHA:469 Hereditary fructose intolerance ORPHA:480512 Idiopathic ductopenia ORPHA:77292 Infantile neurovisceral acid sphingomyelinase deficiency ORPHA:30391 Isolated biliary atresia ORPHA:485426 Isolated congenital hepatic fibrosis
	Ghent University Hospital (UZ Gent, Princess Elisabeth Children's Hospital)	CALL 2 (2021)	ORPHA:244275 De novo thrombotic microangiopathy after kidney transplantation ORPHA:39812 Graft versus host disease ORPHA:506225 Rare disorder potentially indicated for heart transplant ORPHA:506219 Rare disorder potentially indicated for hematopoietic stem cell transplant ORPHA:506213 Rare disorder potentially indicated for kidney transplant ORPHA:506210 Rare disorder potentially indicated for liver transplant
CRANIO (Rare craniofacial anomalies and ear, nose and throat disorders)	Antwerp University Hospital (UZ Antwerpen)	CALL 2 (2021)	ORPHA:87884 Non-syndromic genetic deafness
	Ghent University Hospital (UZ Gent)	CALL 2 (2021)	ORPHA:87884 Non-syndromic genetic deafness ORPHA:164001 Rare odontal or periodontal disorder
	Leuven University Hospital (UZ Leuven)	CALL 2 (2021)	ORPHA:155832 Rare head and neck malformation ORPHA:98026 Rare odontologic disease

2. Belgian patient organisations for rare diseases (as recorded in Orphanet in 12/2024)

NAME OF THE BELGIAN PATIENT ORGANISATION REGISTERED IN ORPHANET	(GROUPS OF) RARE DISEASE(S) - ORPHAcode(s)
A.B. Drepa - Association Belge des Drépanocytaires a.s.b.l.	ORPHA:232 (Disorder) Sickle cell anemia
ABeFAO-Association Belge des Familles Touchées par l'Atrésie de l'Oesophage / Belgische Vereniging voor Families Getroffen door Slokdarmatresie	ORPHA:1199 (Disorder) Esophageal atresia
ABFFP- Association Belge Francophone contre la Fibrose Pulmonaire ASBL	ORPHA:2032 (Disorder) Idiopathic pulmonary fibrosis
ABMM - Association Belge contre les Maladies neuro-Musculaires A.S.B.L.	ORPHA:166 (Group of disorders) Charcot-Marie-Tooth disease/Hereditary motor and sensory neuropathy ORPHA:2103 (Group of disorders) Guillain-Barré syndrome ORPHA:685 (Group of disorders) Hereditary spastic paraplegia ORPHA:68381 (Group of disorders) Neuromuscular disease
ABN-BVN A.S.B.L. - Association Belge de Narcolepsie - Cataplexie / Belgische Vereniging voor Narcolepsie	ORPHA:33208 (Disorder) Idiopathic hypersomnia ORPHA:2073 (Disorder) Narcolepsy type 1 ORPHA:83465 (Disorder) Narcolepsy type 2
ABSM - Association Belge du Syndrome de Marfan asbl	ORPHA:284963 (Subtype of disorder) Marfan syndrome type 1 ORPHA:284973 (Subtype of disorder) Marfan syndrome type 2 ORPHA:284979 (Disorder) Neonatal Marfan syndrome
Action Parkinson Asbl	ORPHA:2828 (Disorder) Young-onset Parkinson disease
AFBOI - Association Francophone Belge de l'Ostéogenèse Imparfaite A.S.B.L.	ORPHA:666 (Disorder) Osteogenesis imperfecta
AHVH - Association de l'hémophilie, von Willebrand et autres pathologies de la coagulation / Vereniging van hemofilie-, von Willebrand en andere stollingsstoornissen	ORPHA:68334 (Group of disorders) Rare hemorrhagic disorder due to a constitutional coagulation factors defect
AIRG-Belgique - Association pour l'Information et la Recherche sur les maladies Rénales Génétiques A.S.B.L.	ORPHA:98056 (Group of disorders) Rare genetic renal disease
AKABE - Association syndrome Kabuki Belgium asbl	ORPHA:2322 (Disorder) Kabuki syndrome
ALICE ASBL - Association Libre d'Informations sur la Croissance des Enfants « Silver Russell »	ORPHA:813 (Disorder) Silver-Russell syndrome
Alpha-1 Plus Belgium asbl/vzw	ORPHA:60 (Disorder) Alpha-1-antitrypsin deficiency
ALS Liga België V.Z.W./ Ligue SLA Belgique A.S.B.L.	ORPHA:803 (Disorder) Amyotrophic lateral sclerosis ORPHA:275872 (Disorder) Frontotemporal dementia with motor neuron disease
ALWB - Action Lymphome Wallonie Bruxelles ASBL	ORPHA:223735 (Group of disorders) Lymphoma
Alzheimer Liga Vlaanderen vzw	ORPHA:89043 (Group of disorders) Rare dementia
AmyBel - Amyloidosis Association Belgium vzw / Association Amylose Belgique asbl	ORPHA:69 (Group of disorders) Amyloidosis
ANB-Association Neurofibromatose Belgique ASBL	ORPHA:636 (Disorder) Neurofibromatosis type 1
Angelman Syndroom België V.Z.W.	ORPHA:228402 (Disorder) 2q23.1 microdeletion syndrome ORPHA:72 (Disorder) Angelman syndrome ORPHA:85278 (Disorder) Christianson syndrome
Angioedema a.s.b.l. - v.z.w. (HAE Belgium)	ORPHA:658 (Group of disorders) Non-histaminic angioedema
APK - Association Parkinson A.S.B.L.	ORPHA:2828 (Disorder) Young-onset Parkinson disease
APSB - Association des Patients Sclérodermiques de Belgique A.S.B.L.	ORPHA:801 (Group of disorders) Scleroderma
ASBBF - Association Spina Bifida Belge Francophone ASBL	ORPHA:3388 (Group of disorders) Neural tube defect
Asbl Chiara VDS - Chiara Vie, Don d'organes et Solidarité	All rare diseases (see the Orphanet website for the 33 linked ORPHAcodes (Groups of disorders)
Association Belge de Lutte contre la Mucoviscidose A.S.B.L. - Belgische Vereniging voor Strijd tegen Mucoviscidose V.Z.W.	ORPHA:586 (Disorder) Cystic fibrosis
Association belge du Syndrome de Williams [Section de l'A.S.B.L. INCLUSION]	ORPHA:904 (Disorder) Williams syndrome
Association Lupus Erythémateux ASBL	ORPHA:300345 (Disorder) Autosomal systemic lupus erythematosus ORPHA:464343 (Disorder) Catastrophic antiphospholipid syndrome ORPHA:93552 (Disorder) Pediatric systemic lupus erythematosus ORPHA:535 (Group of disorders) Rare cutaneous lupus erythematosus
Association Syndrome de Cornelia de Lange - BE (point de contact pour la Belgique francophone)	ORPHA:199 (Disorder) Cornelia de Lange syndrome
AXFB -Association X fragile Belgique ASBL	ORPHA:908 (Disorder) Fragile X syndrome ORPHA:93256 (Disorder) Fragile X-associated tremor/ataxia syndrome
B.R.S.V. - Belgische Rett Syndroom Vereniging vzw	ORPHA:778 (Disorder) Rett syndrome
Belgische Vereniging voor Dystoniepatiënten V.Z.W. - Association Belge des Patients Dystoniques A.S.B.L.	ORPHA:68363 (Group of disorders) Rare dystonia
Belgische Vereniging voor Longfibrose vzw	ORPHA:2032 (Disorder) Idiopathic pulmonary fibrosis
Belgische Vereniging Ziekte van Hirschsprung vzw/Association belge de la maladie de Hirschsprung asbl	ORPHA:388 (Disorder) Hirschsprung disease
BePOPI - Belgische organisatie van en voor PID-patiënten/Organisation belge de et pour des patients DIP	ORPHA:101997 (Group of disorders) Primary immunodeficiency
be-TSC vzw/ be-STB asbl	ORPHA:805 (Disorder) Tuberous sclerosis complex
Bijniervereniging NVACP - Vlaamse afdeling	ORPHA:101954 (Group of disorders) Rare adrenal disease
bindweefsel.be - Vlaamse Vereniging voor Erfelijke Bindweefselaandoeningen V.Z.W.	ORPHA:166100 (Disorder) Autosomal dominant otospondylomegaepiphyseal dysplasia ORPHA:284993 (Group of disorders) Marfan syndrome and Marfan-related disorders ORPHA:3164 (Disorder) Omphalocele syndrome, Shprintzen-Goldberg type ORPHA:251312 (Group of disorders) Overlapping connective tissue disease ORPHA:275798 (Group of disorders) Pulmonary arterial hypertension associated with connective tissue disease ORPHA:139030 (Group of disorders) Rare developmental defect with connective tissue involvement ORPHA:285014 (Group of disorders) Rare disease with thoracic aortic aneurysm and aortic dissection ORPHA:828 (Disorder) Stickler syndrome ORPHA:3377 (Disorder) Trismus-pseudocamptodactyly syndrome ORPHA:90002 (Disorder) Undifferentiated connective tissue syndrome ORPHA:166277 (Disorder) Wormian bone-multiple fractures-dentinogenesis imperfecta-skeletal dysplasia
BOKS - Belgische Organisatie voor Kinderen en Volwassenen met een Stofwisselingsziekte V.Z.W. - Association belge pour les enfants et adultes atteints d'une maladie métabolique A.S.B.L.	ORPHA:59 (Disorder) Allan-Herndon-Dudley syndrome ORPHA:68367 (Group of disorders) Rare inborn errors of metabolism
BorstkankerMAN vzw	ORPHA:227535 (Disorder) Hereditary breast cancer
CIB-Liga - Liga voor Chronische Inflammatoire Bindweefselziekten vzw	ORPHA:221 (Disorder) Dermatomyositis ORPHA:809 (Disorder) Mixed connective tissue disease ORPHA:732 (Disorder) Polymyositis ORPHA:289390 (Disorder) Primary Sjögren syndrome ORPHA:801 (Group of disorders) Scleroderma ORPHA:536 (Disorder) Systemic lupus erythematosus ORPHA:52759 (Group of disorders) Vasculitis
CLAIR ASBL - Contre Les Affections Inflammatoires Rhumatismales	ORPHA:300345 (Disorder) Autosomal systemic lupus erythematosus ORPHA:92 (Group of disorders) Juvenile idiopathic arthritis ORPHA:93552 (Disorder) Pediatric systemic lupus erythematosus ORPHA:535 (Group of disorders) Rare cutaneous lupus erythematosus ORPHA:801 (Group of disorders) Scleroderma ORPHA:536 (Disorder) Systemic lupus erythematosus
CMP Vlaanderen vzw [Contactgroep Myeloom en Waldenström Patiënten Vlaanderen]	ORPHA:29073 (Disorder) Multiple myeloma ORPHA:33226 (Disorder) Waldenström macroglobulinemia
Collectif Auguste et les autres ASBL	ORPHA:1020 (Disorder) Early-onset autosomal dominant Alzheimer disease ORPHA:98535 (Group of disorders) Frontotemporal degeneration with dementia
Collectif Drépanocytose ASBL	ORPHA:232 (Disorder) Sickle cell anemia
Cri-du-Chat vzw	ORPHA:281 (Disorder) Monosomy 5p syndrome
Debra Belgium vzw / Debra Belgium asbl	ORPHA:79361 (Group of disorders) Inherited epidermolysis bullosa
Donner des ailes ASBL - Association belge du syndrome d'Angelman	ORPHA:72 (Disorder) Angelman syndrome
Duchenne Parent Project Belgium vzw (dpp.be)	ORPHA:98896 (Disorder) Duchenne muscular dystrophy
Dyskinesia A.S.B.L.	ORPHA:244 (Disorder) Primary ciliary dyskinesia
Dysmelia asbl-vzw	ORPHA:93457 (Group of disorders) Non-syndromic limb reduction defect
ELA Belgique A.S.B.L. - Association européenne contre les leucodystrophies [Antenne Belge]	ORPHA:68356 (Group of disorders) Leukodystrophy
Ensemble pour Lola et les Enfants de la Lune ASBL	ORPHA:910 (Disorder) Xeroderma pigmentosum
Epilepsie Liga VZW	ORPHA:101998 (Group of disorders) Rare epilepsy
Eye Hope Foundation	ORPHA:3463 (Disorder) Wolfram syndrome
FAPA - Familial Adenomatous Polyposis Association A.S.B.L./V.Z.W.	ORPHA:220460 (Disorder) Attenuated familial adenomatous polyposis ORPHA:733 (Disorder) Familial adenomatous polyposis ORPHA:443909 (Group of disorders) Hereditary nonpolyposis colon cancer

NAME OF THE BELGIAN PATIENT ORGANISATION REGISTERED IN ORPHANET	(GROUPS OF) RARE DISEASE(S) - ORPHAcode(s)
Fondation Lou - fondation privée	ORPHA:3157 (Disorder) Septo-optic dysplasia spectrum
Fragiele X Vlaanderen - contactgroep	ORPHA:908 (Disorder) Fragile X syndrome ORPHA:642691 (Disorder) Fragile X-associated primary ovarian insufficiency ORPHA:93256 (Disorder) Fragile X-associated tremor/ataxia syndrome
GESED - Groupe d'Entraide des Syndromes d'Ehlers-Danlos A.S.B.L.	ORPHA:98249 (Group of disorders) Ehlers-Danlos syndrome
Groupe de soutien aux personnes atteintes du syndrome de Guillain-Barré et leur famille [Groupe de l'ABMM]	ORPHA:2103 (Group of disorders) Guillain-Barré syndrome
HME-MO Lotgenoten Contactgroep - België	ORPHA:321 (Disorder) Multiple osteochondromas
Hodgkin en non-Hodgkin vzw	ORPHA:98293 (Group of disorders) Hodgkin lymphoma ORPHA:547 (Group of disorders) Non-Hodgkin lymphoma
Hope4AT asbl/vzw	ORPHA:100 (Disorder) Ataxia-telangiectasia
HTAP Belgique - Association des patients souffrant d'HyperTension Artérielle Pulmonaire en Belgique A.S.B.L.	ORPHA:422 (Disorder) Idiopathic/heritable pulmonary arterial hypertension
Huntington Liga vzw	ORPHA:399 (Disorder) Huntington disease
Ichthyosis België V.Z.W. - Ichthyosis Belgique A.S.B.L.	ORPHA:79354 (Group of disorders) Ichthyosis
IKAROS Epilepsie-contactgroep vzw [Contactgroep Oost-Vlaanderen]	ORPHA:101998 (Group of disorders) Rare epilepsy
Imagene CAPS Association in Belgium asbl/vzw	ORPHA:575 (Disorder) Muckle-Wells syndrome
INCLUSION asbl	ORPHA:87277 (Group of disorders) Rare intellectual disability
Intersekse Vlaanderen - Vereniging voor Intersekse Personen VZW	ORPHA:90771 (Group of disorders) Difference of sex development
Les Services de l'APEM-T21 A.S.B.L.	ORPHA:870 (Disorder) Down syndrome
Leven met Acromegalie vzw	ORPHA:963 (Disorder) Acromegaly
LFBE - La Ligue francophone belge contre l'Epilepsie ASBL	ORPHA:101998 (Group of disorders) Rare epilepsy
LGD Alliance Belgium vzw	ORPHA:141209 (Disorder) Diffuse lymphatic malformation ORPHA:73 (Disorder) Gorham-Stout disease ORPHA:464329 (Disorder) Kaposiform lymphangiomatosis
LHFB - Ligue Huntington Francophone Belge A.S.B.L. [Région Wallonne et Communauté Française]	ORPHA:399 (Disorder) Huntington disease
Liga Myasthenia Gravis vzw	ORPHA:589 (Disorder) Myasthenia gravis
Ligue Alzheimer ASBL	ORPHA:1020 (Disorder) Early-onset autosomal dominant Alzheimer disease
Lucas' Droom vzw	ORPHA:85279 (Disorder) KDM5C-related syndromic X-linked intellectual disability
LVV - Lymfklierkanker Vereniging Vlaanderen vzw	ORPHA:391 (Disorder) Classic Hodgkin lymphoma ORPHA:168966 (Disorder) Composite lymphoma ORPHA:547 (Group of disorders) Non-Hodgkin lymphoma
Mijnlever Patiëntenvereniging Zeldzame Leverziekten vzw (Mijnlever vzw)	ORPHA:2137 (Disorder) Autoimmune hepatitis ORPHA:186 (Disorder) Primary biliary cholangitis ORPHA:562639 (Disorder) Primary biliary cholangitis/primary sclerosing cholangitis and autoimmune hepatitis overlap syndrome ORPHA:171 (Disorder) Primary sclerosing cholangitis
MRKH.be (België - Belgique - Belgium)	ORPHA:180068 (Group of disorders) Partial bilateral aplasia of the Müllerian ducts
Myeloproliferatieve Neoplasmen België (MPN België vzw)	ORPHA:98274 (Group of disorders) Myeloproliferative neoplasm
Mymu Wallonie-Bruxelles ASBL - Groupement de patients atteints de myélome multiple	ORPHA:29073 (Disorder) Multiple myeloma
NET & MEN Kanker VZW België/Belgique	ORPHA:276161 (Group of disorders) Multiple endocrine neoplasia ORPHA:877 (Group of disorders) Neuroendocrine neoplasm
NF Kontakt - Vereniging voor patiënten met neurofibromatose vzw	ORPHA:637 (Disorder) Full NF2-related schwannomatosis ORPHA:137605 (Disorder) Legius syndrome ORPHA:636 (Disorder) Neurofibromatosis type 1
NMP Belgique ASBL	ORPHA:98274 (Group of disorders) Myeloproliferative neoplasm
NoRa ASBL, Association belge pour personnes achondroplases	ORPHA:15 (Disorder) Achondroplasia
ORKA Ouders van ReumaKinderen en -Adolescenten vzw	ORPHA:486955 (Group of disorders) Rare pediatric rheumatologic disease
OSTC - Overdruksyndroom en Tarlov cysten vzw	ORPHA:238624 (Disorder) Idiopathic intracranial hypertension
P.H. België - Belgische Patiëntenvereniging voor Pulmonale Hypertensie vzw	ORPHA:422 (Disorder) Idiopathic/heritable pulmonary arterial hypertension
Postpolio België vzw	ORPHA:2942 (Disorder) Postpoliomyelitis syndrome
Prader-Willi Vlaanderen vzw	ORPHA:739 (Disorder) Prader-Willi syndrome
RaDiOrg - Rare Diseases Belgium - BE	All rare diseases (see the Orphanet website for the 33 linked ORPHAcodes (Groups of disorders)
Rare Disorders Belgium (RDB) ASBL - BE	All rare diseases (see the Orphanet website for the 33 linked ORPHAcodes (Groups of disorders)
Relais 22 asbl	ORPHA:567 (Disorder) 22q11.2 deletion syndrome
RetinaPigmentosa asbl, association belge francophone de la rétinopathie d'origine génétique	ORPHA:71862 (Group of disorders) Inherited retinal disorder
Ring14 Belgium vzw	ORPHA:1440 (Disorder) Ring chromosome 14 syndrome
ROHHAD Association Belgium A.S.B.L.	ORPHA:293987 (Disorder) Rapid-onset childhood obesity-hypothalamic dysfunction-hypoventilation-autonomic dysregulation syndrome
Sang pour Sang asbl	ORPHA:232 (Disorder) Sickle cell anemia
Sclero'ken vzw	ORPHA:90291 (Disorder) Systemic sclerosis
Smith Magenis syndroom België vzw	ORPHA:819 (Disorder) Smith-Magenis syndrome
Spierziekten Vlaanderen vzw	ORPHA:99 (Group of disorders) Autosomal dominant cerebellar ataxia ORPHA:1172 (Group of disorders) Autosomal recessive cerebellar ataxia ORPHA:166 (Group of disorders) Charcot-Marie-Tooth disease/Hereditary motor and sensory neuropathy ORPHA:337 (Disorder) Fibrodysplasia ossificans progressiva ORPHA:306577 (Disorder) Hereditary sodium channelopathy-related small fibers neuropathy ORPHA:685 (Group of disorders) Hereditary spastic paraplegia ORPHA:68381 (Group of disorders) Neuromuscular disease ORPHA:98496 (Group of disorders) Rare peripheral neuropathy
Stichting PTEN België/Nederland - Belgisch aanspreekpunt voor Nederlandstaligen	ORPHA:306498 (Disorder) PTEN hamartoma tumor syndrome
Tous ensemble, main dans la main A.S.B.L.	ORPHA:68366 (Group of disorders) Lysosomal disease
Turnerkontakt vzw	ORPHA:881 (Disorder) Turner syndrome
VAGA vzw - Vereniging voor Aangeboren GelaatsAfwijkingen	ORPHA:141229 (Group of disorders) Facial cleft ORPHA:68329 (Group of disorders) Rare maxillo-facial surgical disease
VASCAPA (Vascular Anomaly Patient Association) A.S.B.L./V.Z.W.	ORPHA:68419 (Group of disorders) Rare vascular anomaly
Vecarfa 22q11ds Vlaanderen	ORPHA:567 (Disorder) 22q11.2 deletion syndrome
Vereniging Cornelia de Lange syndroom - BE (aanspreekpunt voor Nederlandstalig België)	ORPHA:199 (Disorder) Cornelia de Lange syndrome
Vereniging MED-SED, Belgisch contactpunt voor Nederlandstaligen	ORPHA:251 (Group of disorders) Multiple epiphyseal dysplasia ORPHA:253 (Group of disorders) Spondyloepiphyseal dysplasia and spondyloepimetaphyseal dysplasia
Vereniging voor sarcoïdosepatiënten vzw	ORPHA:90340 (Disorder) Blau syndrome ORPHA:797 (Disorder) Sarcoidosis
von Hippel-Lindau België	ORPHA:892 (Disorder) Von Hippel-Lindau disease
VPL -Vlaamse Parkinson Liga vzw	ORPHA:2828 (Disorder) Young-onset Parkinson disease
VSH - Vereniging voor Spina Bifida en Hydrocephalus vzw	ORPHA:275543 (Disorder) L1 syndrome ORPHA:3388 (Group of disorders) Neural tube defect ORPHA:3176 (Disorder) Spina bifida-hypospadias syndrome
VVA - Vlaamse Vereniging Autisme vzw	ORPHA:168778 (Group of disorders) Rare pervasive developmental disorder
vzw 22q13	ORPHA:48652 (Disorder) Phelan-McDermid syndrome
Vzw Cum Cura	ORPHA:223727 (Group of disorders) Bone sarcoma ORPHA:873 (Disorder) Desmoid tumor ORPHA:363976 (Disorder) Giant cell tumor of bone ORPHA:3394 (Group of disorders) Soft tissue sarcoma ORPHA:66627 (Disorder) Tenosynovial giant cell tumor
Vzw-Gen.be - Gentherapie - SLC6A1	ORPHA:1942 (Disorder) Epilepsy with myoclonic-atonic seizures
WBS - Williams-Beuren Syndroom vzw	ORPHA:904 (Disorder) Williams syndrome
Werkgroep Hersentumoren vzw (WG-HT)	ORPHA:98062 (Group of disorders) Rare nervous system tumor
Wij Ook Belgium vzw	ORPHA:1331 (Disorder) Familial prostate cancer
XLH Belgium A.S.B.L.	ORPHA:89936 (Disorder) X-linked hypophosphatemia
Zebrapad VZW	ORPHA:98249 (Group of disorders) Ehlers-Danlos syndrome
ZOI - Zelfhulp Osteogenesis Imperfecta VZW	ORPHA:666 (Disorder) Osteogenesis imperfecta
Last update: December 17, 2024 (n total=123)	
Many people living with a rare disease do not have a formal patient organisation focused on their disease. Contact **RaDiOrg** (Rare Diseases Belgium asbl/vzw), the umbrella patient organisation, if you have a non-medical question related to a rare disease: https://www.radiorg.be/, 'info@radiorg.be', +32 (0)478 72 77 03. French speakers can also contact **Rare Disorders Belgium**: https://maladies-rares.be/, 'secretariat@rd-b.be', 0800-9 28 02 (helpline).	

CONTACT
Annabelle Calomme • T+32 2 642 54 47 • orphanetbelgium@sciensano.be

MORE INFORMATION

–

Visit our website
>www.sciensano.be or
contact us at
>info@sciensano.be

Sciensano • Rue Juliette Wytsmanstraat 14 • Brussels • Belgium • T + 32 2 642 51 11 • info@sciensano.be •
www.sciensano.be