ORPHANET BELGIUM DATABASE ACTIVITY REPORT 2022

CONVENTION FOR THE SUPPORT OF STRATEGIC RESEARCH ON RARE DISEASES IN BELGIUM 2020-2024 (CENTRAL REGISTRY OF RARE DISEASES – BELGIAN GENETIC TESTS DATABASE – 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

April 2023 • Brussels • Belgium

CALOMME Annabelle

- The **Orphanet Belgium Management Board** consists of representatives of:

- the Orphanet Belgium team;
- the partners and sponsors of Orphanet Belgium (FPS/SPF/FOD, NIHDI/INAMI/RIZIV);
- ad hoc: experts or representatives of institutes designated for the validation of the data.

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

	SPONSORS & NON-FINANCIAL PARTNERSHIPS	
Members of National Board	sciensano	The **"Health services research"** of Sciensano hosts the Orphanet Belgium team. Within the Rare Diseases Team, Orphanet Belgium collaborates to other rare disease projects that are part of the Belgian plan of rare diseases, 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. Since 2020, a collaboration has been established with the **Belgian Genetic Test Database (BGTD)**, in order to improve the registration and update of diagnostic tests performed by the 8 officially-recognized genetic centres. Internal collaboration with the **Epidemiology of infectious diseases service** has also been set up to validate data on reference laboratories and infectious disease screening tests.
	federal public service HEALTH, FOOD CHAIN SAFETY AND ENVIRONMENT	The **Federal Public Service Health, Food Chain Safety and Environment** is a partner of the Orphanet Belgium team.
	INAMI-RIZIV	The **National Institute of Health and Invalidity Insurance (NIHDI)** finances Sciensano via a convention for the implementation and management of various projects specific to rare diseases including the Orphanet Belgium project. NIHDI provides information on the specialized centres for certain rare conditions including the **reference centres having a convention.**
Ad-hoc experts	RaDiOrg	**Rare Diseases Belgium (RaDiOrg)**, the Belgian umbrella association for people living with a rare disease, plays a role in the validation of data on Belgian patient organizations registered in the Orphanet database.
	COLLEGE GENETICS	The **College of Human Genetics**, which represents the **8 officially-recognized Belgian genetic centres**, collaborates with the Orphanet team to improve and simplify the process of registration and update of data on genetic testing activities in the Orphanet database.

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EXECUTIVE SUMMARY

The **Orphanet portal** plays a key role in research and care spheres for the rare disease community. Over the years, 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 health authorities. **Sciensano has been endorsed by the Ministry of Health to host the Orphanet Belgium team.** A national board consisting of members of Sciensano, the Federal Public Service (FPS) and the National Institute for Health and Disability Insurance (NIHDI) oversees the project.

The management of Belgian data registered in Orphanet is described in the successive agreements "Central Registry of Rare Diseases–Belgian Genetic Tests Database–Orphanet support" concluded between the NIHDI and Sciensano. This convention is monitored by a multistakeholder steering 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 progress made - but also of the challenges encountered - during the year 2022** by the Orphanet Belgium team.

Recording and updating Belgian data on rare diseases in the Orphanet database (expert centres, patient organisations, medical laboratories and diagnostic tests, clinical trials, research projects, registries and biobanks) was the core of our activity in 2022. The successful completion of these tasks required 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. A large part of the first quarter of 2022 was dedicated to **registering all Belgian expert centres that joined a European Reference Network** (ERN) following the second call launched by the European Commission.

Part of our activities also consists of **raising awareness of rare diseases**, in particular by participating in Rare Disease Day which is held annually in February, and **offering assistance** to questions from people living with a rare disease as well as those from experts working in the field. During this year, we have maintained our **close collaboration with many key players in the field of rare diseases in Belgium**, such as RaDiOrg and the College of Human Genetics. We have also strengthened certain contacts, including those with the Terminology Centre of the FPS Public Health, in order to discuss the possible implementation of ORPHAcodes in our national health information systems.

In 2022, the Orphanet Belgium team established **a partnership with a new European project, called "Orphanet Data for Rare Disease" (OD4RD)**. Our participation involves numerous tasks to promote the adoption of ORPHAcodes, which had to be defined in a National Action Plan presented in Paris during the final meeting of the pilot phase of the project. These tasks involve functioning as a helpdesk for end users regarding the content of the Orphanet nomenclature and the correct implementation of ORPHAcodes in local Health Information Systems, providing online or on-site trainings, developing new educational materials on the use of the Orphanet nomenclature and advocating ORPHAcodes towards national decision-makers (e.g. Ministry of Health, hospital managers, etc.).

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[1-3] as well as to the activity reports and procedures[4] published on the Orphanet website.

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ABBREVIATIONS AND ACRONYMS

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 records
EQA	External Quality Assessment
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 Trial 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 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**[5]. For a long time, rare diseases remained a largely underestimated issue. However, in recent years, it has become clear that they actually represent a **huge public health challenge**.

Rare diseases are **very heterogeneous, both in terms of symptoms and prevalence.** Consequently, 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, **if we consider them globally, rare diseases are numerous.** A study[6] 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 at any point in time. If we transpose this figure on the Belgian population, it is equivalent to a **conservative estimate of 500,000 people suffering from a rare disease in our country** (not taking into account rare tumours, infectious diseases and poisonings). The large number of rare diseases, their rarity when taken individually, but also the different medical disciplines involved in ensuring appropriate medical care make the organization of health policy in this area particularly complex.

Around 6,200 rare diseases[7] **have been clinically defined to date** 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 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[6]. 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: in Belgium, it takes an average of 4.9 years from the onset of the first symptoms for a person with a rare disease to receive a confirmed diagnosis[8]. 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 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 difficulties encountered.

The burden of rare diseases on patients, but also on their families, carers, healthcare systems and society overall merits greater visibility. Among the key players seeking to provide a better understanding and recognition of rare diseases and therefore, ultimately, to guarantee better care for people living with a rare disease, is the Orphanet network. **Orphanet was established in 1997 by the 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**[9] within Europe and across the globe. Belgium was one of the first countries to join the Orphanet consortium in 2001. 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. On the Orphanet website, the information is currently available in nine languages including French, Dutch and German, the three official languages in Belgium. Every month, more than a million pages of the Orphanet website are consulted from over 200 countries and **Belgium is among the top ten countries of the website's audience**[10].

Belgium's contribution to the international database Orphanet makes it possible to collect data related to the 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, 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 **Belgian Plan for Rare Diseases**[11] 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 has been actively participating since 2022 in the “Orphanet Data for Rare Disease” project (OD4RD)**, co-funded by the European Union. The **OD4RD project** (pilot-phase) has been launched in January 2022 for a 15 months period. It aims to advance the implementation of ORPHAcodes in hospitals of numerous European countries hosting the European Reference Networks (ERNs) and to use the expertise of the ERNs to further improve the Orphanet nomenclature. Our team participates in Work Package 4 which intends to provide support for the local implementation of ORPHAcodes by national healthcare providers through the establishment of **Orphanet nomenclature national support hubs.** This should facilitate the implementation (from a technical point of view) and use (from a coding and data exploitation point of view) of ORPHAcodes and thus increase the visibility and recognition of people living with a rare disease in our health information systems.

MAIN ACTIVITIES IN 2022

1. Belgian contribution to the Orphanet database [January– December 2022]

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 team and validated by 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 data (called “expert resources” by Orphanet) are registered:

- **Patient-centered 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, mutation registries and biobanks.

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

For most types of Belgian expert resources, there has been **a global increase in the amount of data collected over the past year** (Figure 2). However, it is possible that there is no variation or even a decrease in the total number of data collected, because of update work. Increasing the quantity of collected data improves the value of a database, but at the same time ensuring a good 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.

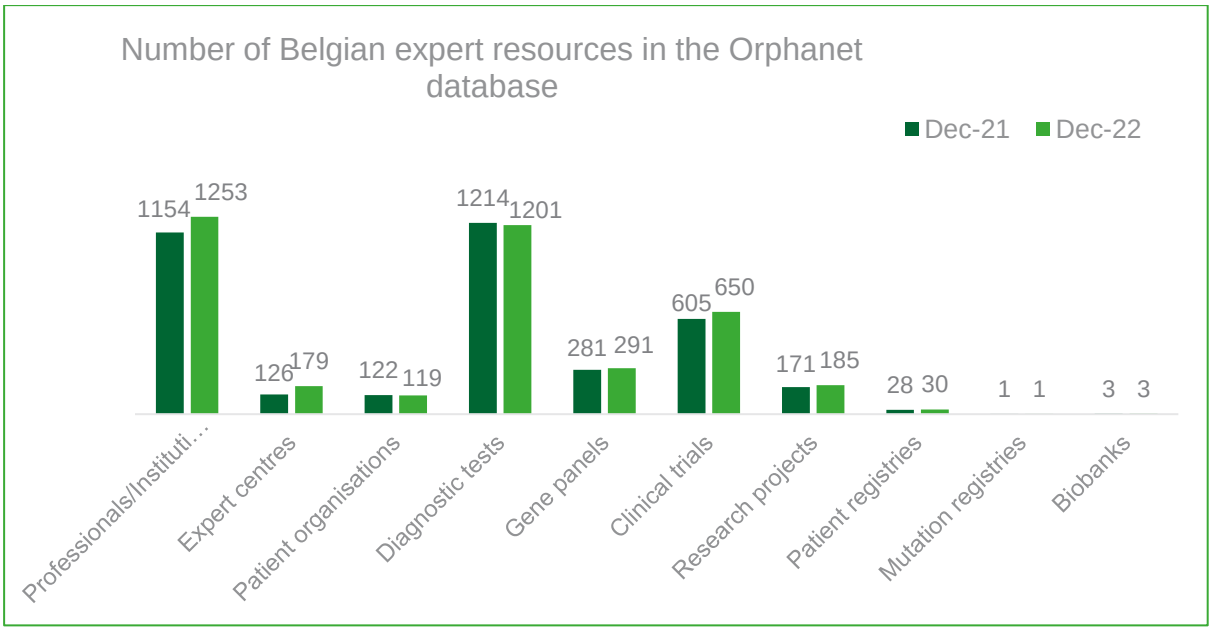


Fig. 2. Evolution of the number of Belgian expert resources registered in the Orphanet database between December 2021 and December 2022

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 3). 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).

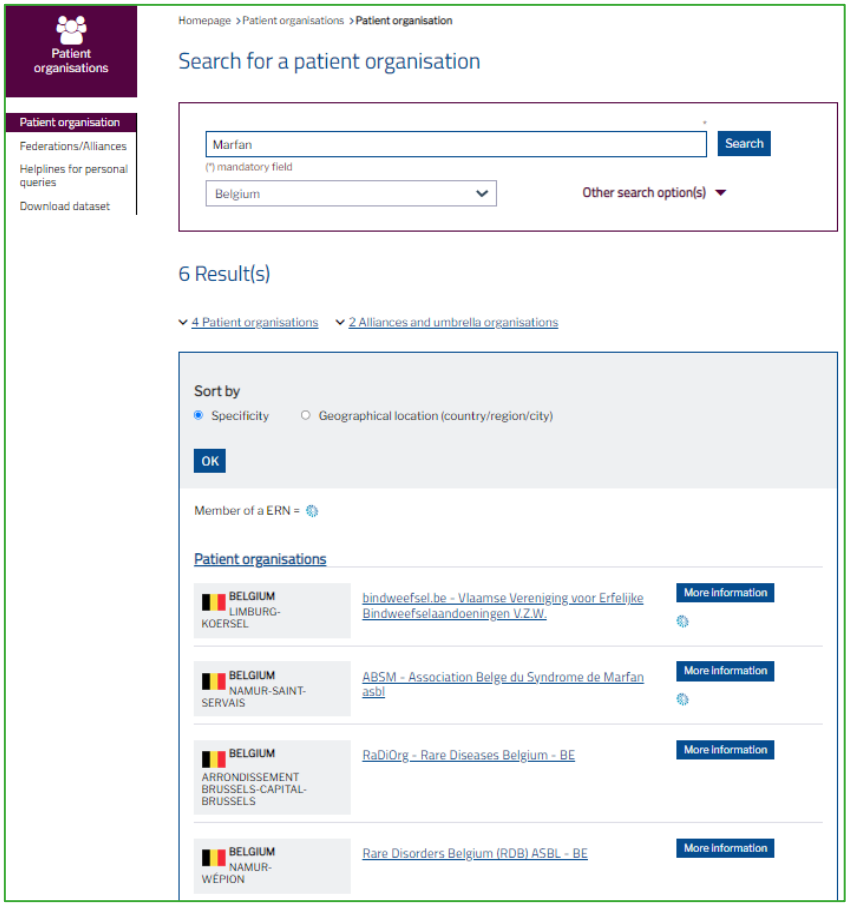


Fig 3. Example of a search in Orphanet for a Belgian patient organisation dedicated to Marfan syndrome

1.2. IMPROVEMENT OF THE COMPLETENESS AND QUALITY OF THE DATABASE

In 2022, 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, either by phone, email or via our online registration tool (Collector). 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 (usually every three months) 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 also 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. In 2022, these tasks concerned, among others, the registration of the EQA data from the CF-Network for 2021 and 2022, the correction of the clinical trials phase following the implementation of the "Not Applicable" phase, the deletion of data (patient organisations and expert centres) that has not been updated for more than 7 years (i.e. a “purge” task), etc.;

- **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 putting in place 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.**

1.3. ANNUAL UPDATE CAMPAIGN

Professionals registered in the database and linked to patient-centered activities are contacted yearly by a mailing launched at the Inserm level in which they are invited to review and, if needed, to update 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.

In Belgium, the annual update campaign was launched on June, 30 2022 and involved 851 professionals registered in the Orphanet database with a non-terminated expert resource linked. Unfortunately the **answer rate from professionals in charge of activities listed on Orphanet is very low:** only 31 Belgian professionals responded (3.6 % of the professionals contacted), either to request changes or to confirm that their data is still valid. All requests for modifications received as a result of this action have been processed and the date of last update has been adapted on the Orphanet website.

This low response rate was also observed in previous update campaigns and we can see from the graph below (Figure 4) that this is also the case in other countries of the Orphanet network. However, the collaboration 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 was provided. Delays are defined for each type of resource before removing them from the database if the delay since the last update is considered too long (e.g.: 7 years for diagnostic tests and experts centres).

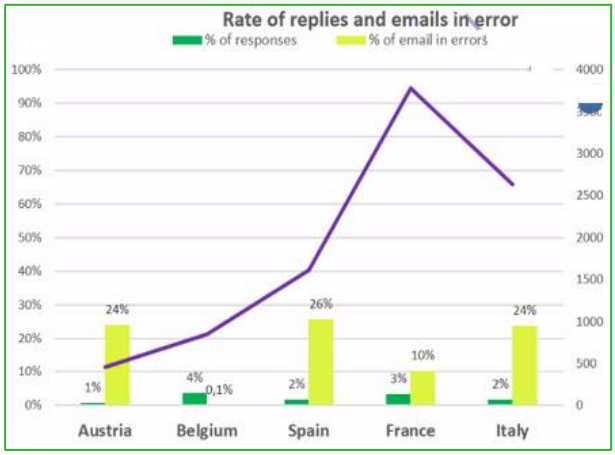


Fig.4. Rate of replies and emails in error received following the 2022 update campaign, in some countries of the Orphanet network (including Belgium)

Mailing therefore does not seem to be the best way to reach professionals, but it is the only way to keep traceability of the contact. The pro-active approach of calling professionals to review their data could be more effective but is difficult to put into practice, especially in large countries. The Orphanet collaborators will therefore have to think about other strategies in order to guarantee an effective exchange with professionals.

Two possibilities could be considered:

- Each national team conducts its own annual update mailing campaign. This could work better as the email is coming from a known (trusted) institution and the email is in local language (the efficacity of this proposal should be assessed after one year);
- Establishment of new partnerships with official sources of data for collection and update.

The selection of the proposal to be implemented will be done by a vote by the Orphanet Management Board before being put in place.

1.4. REGISTRATION AND UPDATE OF EXPERT CENTRE

The possibility to register an expert centre on Orphanet depends on the specific situation in the different countries. **In Belgium, eligibility criteria are appraised by the Orphanet Belgium management board.** The country-specific inclusion criteria taken into account during the selection process are indicated in a document published on the Orphanet Belgium website[12], in order to be transparent on how the data selection is determined. **Our objective is that 100% of the rare disease centres which meet the criteria established by the Belgian Management Board are listed in Orphanet.**

Registration in Orphanet is not compulsory because there is no legislative framework, which results in the fact that the professional in charge of a certain activity can refuse the publication of their personal 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 it 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 authorized to be registered in Orphanet, as agreed by the Orphanet Belgium Management Board. A clear visual distinction between these two categories is established on the Orphanet website thanks to the use of specific flags (logos):

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 that have a convention with the NIHDI:** these centres are focused on a specific (group of) rare diseases (neuromuscular diseases, cystic fibrosis, haemophilia, hereditary metabolic diseases, paediatric nephrology, refractory epilepsy and spina bifida);
- **genetic centres officially recognized by the health authorities** for their diagnostic and counselling activities;
- **hospitals recognized by the health authorities to have a "rare disease function"**.

In 2019, a consultation of the NIHDI website was carried out by the Belgian IS, in order to determine which centres having a convention with the NIHDI were not yet listed on Orphanet. Subsequently, the missing reference centres were created on Orphanet. Once the information was accessible on the Orphanet website, the IS informed the involved professionals that the activity had been published and asked them for a final validation. No new conventions have been established since then. **Post-release quality controls of all Belgian reference centres already registered are conducted regularly over the years** to keep the data up-to-date.

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

These centres appear on the Orphanet website with the "Member of a ERN" flag .

The centres belonging to these two categories are represented by two flags (Figure 5).

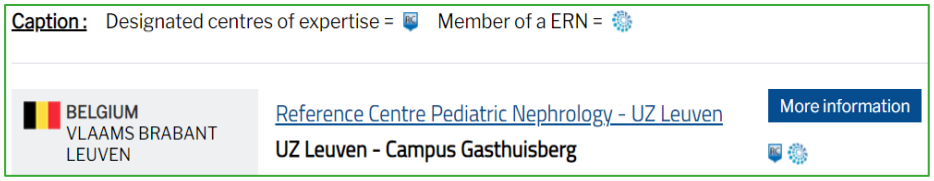


Fig.5. Example of a centre which is both officially-designated at national level and member of an ERN

Belgian centres participating in an ERN are registered on Orphanet since 2019. ERNs are virtual networks that bring together centres from across the European Union. 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 MS. A second call for healthcare providers to join existing ERNs was launched in 2019. At the end of 2021, the ERN Board of Member States, 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 the 24 existing ERNs.**

A **list of the ERNs and the participating Health Care Providers per country** can be consulted on the Orphanet international portal[13]. 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[14].

The registration of the ERN-Belgian centres approved following the second call was done during the first months of 2022. In the context of the Ukraine crisis, the EC asked Orphanet to urgently register all the expert centres belonging to an ERN. The information provided by the EC to Orphanet was limited (name of the hospitals and list of diseases for which the expertise is recognized). Each national team was in charge of checking and completing the dataset through the validation of the diseases associated with the centres, adaptation of the name of the centres, translation of the label into local language(s), creation of location specifications (department, service, contact details), name of the medical coordinator, name of the members of the medical team, addition of the website link (if any), creation of the link with the ERN concerned, etc. A cleaning process (identification and deletion of duplicates) was also carried out. In order to perform this task, many contacts by emails and/or phone have been made with the clinicians involved, as well as with the managers of the ERNs when uncertainties remained at the disease level (ORPHAcodes) to be associated with the centres.

Special attention was given to the links to be established with (groups of) diseases for which the centres have a recognized expertise within the ERN. A correct choice of ORPHAcodes must be done, 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,...) to a list of 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 ERNs websites or of the application forms for membership (when available) but 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 (Excel file) to determine with them, as precise as possible, the rare diseases (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.

In all cases, the identification of the specific expertise of the national centres belonging to an ERN 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: https://health.ec.europa.eu/consultations/2019-call-membership-existing-european-reference-networks-erns_en *in the following section: "**The scope, criteria and thresholds of the diseases covered by each of the 24 ERNs**". However, this file is under construction (missing or incomplete data). Moreover, some ERNs still use terminologies other than the ORPHAcodes (such as ICD-10, OMIM, etc.) to provide information on the recognised expertise of the centres. A full revision of the Belgian ERN-centres will be considered on the basis of this document, once it is finalized.*

100% of Belgian centres that joined an ERN as full members following the two calls are registered in Orphanet. This represents **95 Belgian centres from 10 different hospitals** (Table 1). However, the number of Belgian ERN-centres created in Orphanet (i.e. having a unique identifier) is much higher. This is due to the fact that many centres have asked to separate the paediatric section from the adult section, or have requested to create separate centres specific to each group of approved diseases (with different coordinators, team members and contact details). This increases the workload related to this task for the Orphanet collaborators, but it makes it easier for patients to identify the expert centres taking care of their specific condition.

	NAME OF THE ERN	NUMBER OF PARTICIPATING CENTRES IN BELGIUM (calls 1 and 2)
1	**VASCern:** European Reference Network on Rare Multisystemic Vascular Diseases	5
2	**Endo-ERN:** European Reference Network on Rare Endocrine Conditions	7
3	**ERN LUNG:** European Reference Network on respiratory diseases	6
4	**EuroBloodNet:** European Reference Network on Rare Hematological Diseases	6
5	**EURO-NMD:** European Reference Network for Rare Neuromuscular Diseases	5
6	**ITHACA:** European Reference Network on Rare Congenital Malformations and Rare Intellectual Disability	5
7	**ERN-Skin:** European Reference Network on Rare and Undiagnosed Skin Disorders	3
8	**ERN-RND:** European Reference Network on Rare Neurological Diseases	4
9	**EURACAN:** European Reference Network on Rare Adult Cancers (solid tumors)	6
10	**ERN-PaedCan:** European Reference Network for Paediatric Cancer (haemato-oncology)	4
11	**ERN-BOND:** European Reference Network on Rare Bone Disorders	2
12	**MetabERN:** European Reference Network for Rare Hereditary Metabolic Disorders	6
13	**GUARD-HEART:** Gateway to Uncommon And Rare Diseases of the HEART	3
14	**ERN-EYE:** European Reference Network on Rare Eye Diseases	3
15	**EUROGEN:** European Reference Network on urogenital diseases and conditions	4
16	**ERN GENTURIS:** European Reference Network on GENetic TUmour RIsk Syndromes	4
17	**RARE-LIVER:** European Reference Network on Rare Hepatological Diseases	4
18	**ReCONNET:** Rare Connective Tissue and Musculoskeletal Diseases Network	3
19	**ERKNet:** European Rare Kidney Diseases Reference Network	3
20	**EpiCARE:** European Reference Network on Rare and Complex Epilepsies	2
21	**RITA:** Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases Network	2
22	**ERNICA:** European Reference Network on Rare inherited and congenital anomalies	3
23	**TransplantChild:** European Reference Network on Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	2
24	**ERN CRANIO:** European Reference Network on Rare craniofacial anomalies and ENT disorders	3
Total		95

Call 1 (2017):
67 Belgian centres belonging to 23 ERNs.

Call 2 (Dec 2021):
28 Belgian centres belonging to 19 ERNs.

Belgium (95 centres) participates in the 24 existing ERNs

Table 1. Number of Belgian centres recognized as full members in each of the 24 existing ERNs

Some difficulties are currently encountered with regard to the designation of RD expertise in Belgium and therefore with the publication of centres listed as "expert centres" in Orphanet:

1) The number of Belgian centres that are full members of an ERN may seem high (n=95) for a small country like Belgium. Some professionals and patients consider that the selection processes applied by ERNs are not rigorous and homogenous enough to recognize “real” expertise. The high number of Belgian centres being members of one or more ERNs is partly explained by the fact that during the first call, there was no legislation put in place to regulate the application of centres. This regulation was only implemented at the time of the second call: only centres belonging to a RD function could apply for membership of an ERN. This will also be the case for the next calls. It should nevertheless be noted that Orphanet has a commitment with the EC to register the ERN centres in the different countries of the network. It is therefore mandatory to publish all Belgian ERN centres on Orphanet;

2) The Belgian criteria to register a centre in Orphanet (NIHDI convention or participation in an ERN) do not fully meet the expectations of some patients and healthcare professionals. Indeed, Orphanet Belgium quite often receives feedback from end-users who are not satisfied with the way expertise is currently represented in Orphanet. According to some, the current criteria do not provide a correct representation of the best national expertise available for a given rare disease. In addition, they believe that by only considering these two criteria for our selection, we reject applications for registration from centres that are legitimate to be considered experts in their field.

A discussion was initiated at the end of 2022 with the FPS Public Health to report complaints received by the Orphanet Belgium team and to look for solutions for a better representation of the “real” Belgian expertise in Orphanet, so that the patient is able to identify the centres offering the best diagnostic and treatment possibilities for a given rare disease (see page 40 for more information on this topic).

The table 2 shows the Belgian centres participating in ERNs for rare or complex diseases, listed by hospital:

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)	VASCern (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
	Endo-ERN (Rare Endocrine Conditions)	CALL 2 (2021)
	ERN-LUNG (Respiratory Diseases)	CALL 1 (2017)
	EuroBloodNet (Rare Hematological Diseases)	CALL 2 (2021)
	EURO-NMD (Rare Neuromuscular Diseases)	CALL 1 (2017)
	ITHACA (Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders)	CALL 1 (2017)
	ERN-RND (Rare Neurological Diseases)	CALL 2 (2021)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 2 (2021)
	ERN-BOND (Rare Bone Disorders)	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
	GUARD-HEART (Gateway to Uncommon And Rare Diseases of the HEART)	CALL 2 (2021)
	ERN-EYE (Rare Eye Diseases)	CALL 2 (2021)
	eUROGEN (Rare urogenital diseases and complex conditions)	CALL 2 (2021)
	RARE-LIVER (Rare Hepatological Diseases)	CALL 2 (2021)
	CRANIO (Rare craniofacial anomalies and ear, nose and throat disorders)	CALL 2 (2021)
University Hospital Brussels (UZ Brussel) (4)	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN-LUNG (Respiratory Diseases)	CALL 2 (2021)
	GUARD-HEART (Gateway to Uncommon And Rare Diseases of the HEART)	CALL 1 (2017)
	ERN GENTURIS (GENetic TUmour RIsk Syndromes)	CALL 2 (2021)
AZ Sint-Maarten (Mechelen) (1)	VASCern (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
Cliniques universitaires Saint-Luc (UCLouvain) (15)	VASCern (Rare Multisystemic Vascular Diseases)	CALL 1 (2017)
	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	ERN-LUNG (Respiratory Diseases)	CALL 2 (2021)
	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 (2021)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 2 (2021)
	ERN-PaedCan (Paediatric Cancer (haemato-oncology))	CALL 2 (2021)
	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)
	ERKNet (Rare Kidney Diseases)	CALL 1 (2017)
	EpiCARE (Rare and Complex Epilepsies)	CALL 2 (2021)
	ERNICA (Rare inherited and congenital anomalies)	CALL 2 (2021)
	TransplantChild (Transplantation in Children (incl. HSCT, heart, kidney, liver, intestinal, lung and multiorgan)	CALL 1 (2017)

NAME OF THE BELGIAN HOSPITAL	NAME OF THE EUROPEAN REFERENCE NETWORK (ERN)	DATE OF APPROVAL
University Hospital Erasme (ULB) (8)	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)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
Liège University Hospital (Centre Hospitalier Universitaire de Liège) (6)	Endo-ERN (Rare Endocrine Conditions)	CALL 1 (2017)
	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 1 (2017)
	MetabERN (Rare Hereditary Metabolic Disorders)	CALL 1 (2017)
	eUROGEN (Rare urogenital diseases and complex conditions)	CALL 1 (2017)
	ERN GENTURIS (GENetic TUmour RIsk Syndromes)	CALL 1 (2017)
Jules Bordet Institute (2)	EuroBloodNet (Rare Hematological Diseases)	CALL 1 (2017)
	EURACAN (Rare Adult Cancers (solid tumors)	CALL 1 (2017)
Hôpital Universitaire des Enfants Reine Fabiola - HUDERF (1)	ERN-PaedCan (Paediatric Cancer (haemato-oncology))	CALL 1 (2017)

Table 2. Belgian hospitals participating in ERNs for rare or complex diseases (results of calls 1 and 2)

A **list of all the Belgian centres participating in ERNs for rare or complex diseases** (n=95, 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**.

1.5. 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[15] (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[16], 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 early 2022, an update of registered patient associations was carried out. All associations whose last update dated back to more than 2 years (n=94) have been contacted by email (and if necessary, also by phone) to ask them to update their data. When possible, the data was always proactively updated on the basis of consultation of the websites, Facebook pages and publications in the Belgian Official Journal. Only confirmation of the relevance of published data was requested from the associations. Following the COVID-19 outbreak, many associations have encountered difficulties, particularly financial ones, which unfortunately led to a stop in activity for some of them. Conversely, other organizations have been created.

In 2022, 8 Belgian patient organisations were created in Orphanet :

- “Association Syndrome de Cornelia de Lange (point de contact pour la Belgique francophone)”;
- “Vereniging Cornelia de Lange syndroom (aanspreekpunt voor Nederlandstalig België)”;
- “BePOPI - Belgische organisatie van en voor PID-patiënten/Organisation belge de et pour les patients DIP”;
- “BorstkankerMAN vzw”;
- “Donner des ailes asbl - Association belge du syndrome d'Angelman”;
- “Mymu Wallonie-Bruxelles asbl”;
- “Rare Disorders Belgium (RDB) asbl” (previously published only as an alliance);
- “Ring14 Belgium vzw”.

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

- “Can Cé-Tu? asbl”;
- “Prader-Willi Belgium asbl”;
- “Association belge des Victimes du Syndrome Valproate/Belgische Vereniging van Slachtoffers van Valproaat Syndroom”.

A **list of the Belgian associations active in the rare disease field published on Orphanet** (n=119, data from December 2022, specifying the associated (groups of) diseases identified via the ORPHAcodes) can be found in **Annex 2**.

1.6. REGISTRATION AND UPDATE OF DIAGNOSTIC TESTS

For patients affected by a rare disease, obtaining a timely and accurate diagnosis is key in accessing appropriate medical expertise. **Orphanet is the reference database in the framework of the European Commission Expert Group on Rare Diseases (CEGRD) Recommendation on Cross Border Genetic Testing of Rare Diseases in the European Union**[17]. Our database offers, amongst a range of expert resources on rare diseases, a directory of diagnostic tests. 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.

About 1,200 tests performed in Belgium laboratories are currently registered in Orphanet. The registration and update of the Belgian genetic tests registered in Orphanet is a task performed in collaboration with the **Belgian Genetic Tests Database** (BGTD)[18]. This database is developed by Sciensano, in close 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.

An automated system for transferring information from BGTD to Orphanet, following modifications that can be made at any time by the geneticists at the level of BGTD, has yet to be set up. The conclusion of agreements and the development of Application Programming Interfaces (APIs) between the BGTD and the Orphanet-Inserm platform should allow regular transfers of Belgian diagnostic tests to Orphanet in the future. However for the moment, the communication of information is done manually, on the basis of Excel files updated regularly and shared between the manager of the BGTD and the manager of the Orphanet Belgium database.

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 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 dataset currently related to diagnostic tests is often considered too complex by clinicians and by 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 launched in Q3 2022 by the Orphanet coordinating team. The Orphanet Belgium IS 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. The decisions taken during these meetings will be submitted to the vote of the Orphanet Management Board at the end of 2022 and a lot of data adaptation work will have to be done in 2023 according to the new business rules which will be put in place for the registration of diagnostic tests in Orphanet.

A **similar reflection concerning the registration process for non-DNA tests** (in particular biochemical tests) should be carried out in the course of 2023.

1.7. 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), supported by the World Health Organization. The ICTRP database centralizes data on clinical trials provided by national and international registries such as:
- the **European Clinical Trials Database** (EudraCT)
- **Clinical trials.gov** (searchable registry and results database of clinical trials conducted in the United States and around the world).

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 35 national clinical trials in 2022.** The dataset of each clinical trial (title, phase, date of first enrolment, 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 (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 41 multinational clinical trials in 2022.** 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 principal investigator and on the location of the investigation centres, in order to create the corresponding national clinical entry.

ICTRP 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. An **online database of Belgian clinical trials** was created in 2018 by the Federal Agency for Medicines and Health products (FAMHP). This is a helpful source of information, in particular to identify details on the investigation centres in our country. However it holds information on all the clinical trials approved in Belgium by the FAMHP, and not only clinical trials conducted on rare diseases.

1.8. REGISTRATION AND UPDATE OF RESEARCH PROJECTS

The Orphanet coordinating team collects projects funded by the International Rare Diseases Research Consortium (IRDiRC) members at the European level. IRDiRC 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.

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"** that gathers all the research data collected by:

- the French-speaking Community (http://www.cref.be/);
- the Flemish Community on the FRIS Research portal (https://www.researchportal.be/nl);
- the Federal Authorities (http://www.belspo.be/).

There is no Belgian 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 RD. 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, they can be obtained via professionals declaring their activity through our online registration tool or by email.

In 2022, new ongoing Belgian research projects related to several rare diseases (e.g. ORPHA:293987 Rapid-onset childhood obesity-hypothalamic dysfunction-hypoventilation-autonomic dysregulation syndrome, ORPHA:805 Tuberous sclerosis complex, etc.) **have been registered.**

Polaris (Figure 6**), a Web interface for visualization, curation and analysis of rare disease research landscape is being developed** in the frame of the IRDiRC roadmap. It is developed by *MyScienceWork* and funded through the Support-IRDiRC project and currently by the European Joint Co-fund programme for rare diseases (EJP RD). This new tool should be officially launched in the beginning of 2023 for the funders members of IRDiRC and for the Orphanet network members.

The main goals of the Polaris platform are:

- to facilitate the data capture of research projects;
- 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;
- to provide a web analysis interface to both Orphanet and IRDiRC members.

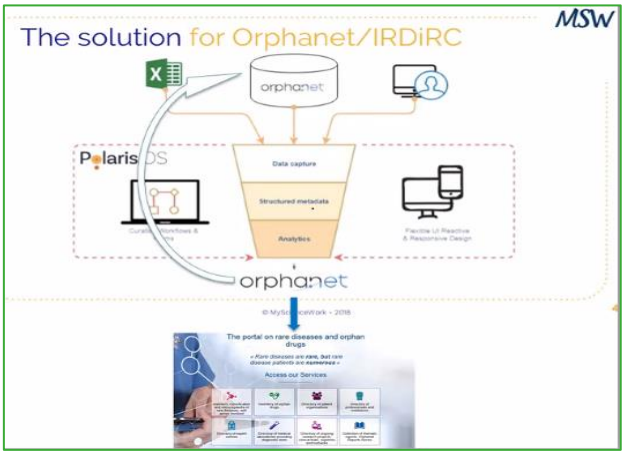


Fig.6. Illustration of how the future Polaris platform will work

1.9. REGISTRATION AND UPDATE OF REGISTRIES

There is no Belgian 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 2022, a few new Belgian patient registries related to rare diseases (e.g. ORPHA:89936 X-linked hypophosphatemia, etc.) **have been registered** in the Orphanet database.

2. Monitoring of the Orphanet Belgium team's activity

A "**National team's Quality Monitoring Dashboard**" has been developed by the Orphanet coordinating team based on a series of indicators (e.g. carrying out quality tasks in terms of content and timeliness, regular update of the registered data, treatment of the forms submitted via the online registration tool, participation in internal trainings, presence at the Orphanet Management Board meetings, etc.) to define the minimum activity requirements of a national team.

The **latest analysis was carried out for the period July 2021-July 2022** for all national teams belonging to the Orphanet consortium. **For Belgium, all the indicators are in green**, meaning that the quality of the activities carried out by the Orphanet Belgium team is equal to or above the expected threshold.

INDICATORS ON THE ORPHANET ONLINE REGISTRATION SERVICE ACTIVITY

Collector is the back-office tool of the online Orphanet registration service[19]. It is used by information scientists, national validators and the international coordinating team to process the professionals' requests for registering or updating their activities related to rare diseases in Orphanet. This online registration service was launched in the beginning of 2014.

In 2022, 35 forms were submitted by Belgian professionals and completely processed. 13 forms concerned new data and 22 were update requests to data already registered. This number has fallen sharply compared to the previous years, with Orphanet users seeming to favour communication by emails. However this figure needs to be put into perspective. Firstly, individual requests usually involve changes to many different related types of data. Moreover, Collector is not the only source available for registration/update requests. Although we encourage the use of this online registration tool for traceability issues, many requests are submitted to the Orphanet Belgium team by emails or phone calls. In this case, the requests are processed but not counted in Collector.

It is always possible to **check when the published data was last updated** (either following a contact with the person in charge of the activity or following the last verification by the IS of the reliable official/legitimate source of information), as shown in the screenshot below (Figure 7).

Fig.7. Screenshot of the Orphanet website: the Orphanet Belgium team updated information about a patient organisation (mention of its participation in an international network, addition of diseases for which the association provides information and support) following email exchanges. The date of the last update is visible.

MANAGEMENT OF THE ORPHANET BELGIUM WEBSITE

The Orphanet Belgium team ensures the maintenance and update of a **national Orphanet website**[20] **available in two languages, French and Dutch**. The Orphanet national website contains information specific to Belgium. A **new Orphanet Belgium website has been in preparation since the end of 2022** and will be **officially launched no later than the next Rare Disease Day in February 2023.** The objective is to offer our users a site with a new look that is more catchy and user-friendly (Figure 8).

Fig.8. Screenshot of the homepage of the new Orphanet Belgium website

The following topics are covered:

- **Contact:** on this page the contact details of the Orphanet Belgium team can be found;
- **Team/Board/ Partnerships:** short description of the Orphanet Belgium team and Management Board with mention of the sponsors (FPS Public Health, Sciensano and INAMI-RIZIV) and partners (BGTD, RaDiOrg, etc.);
- **Historical background of the Orphanet network;**
- **National news and events**. This can include 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;
- **General information:** information about the Orphanet network, rare diseases and orphan drugs (explanations on the activities, 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.) are available, as well as information on the Orphanet quality commitment;
- **Criteria for Belgian Expert Resources:** document mentioning the definitions, sources of information and inclusion/exclusion criteria for expert resources. Documenting inclusion criteria for expert resources in each country is of great relevance for the end-users of Orphanet to know how data is collected at the national level, as well as the selection criteria used. Therefore a pdf document[12] listing each type of data (expert centres, medical laboratories and diagnostic tests, patient organisations, research projects, clinical trials, registries and biobanks) and our sources of information (i.e. public or private institutions, funding bodies, national umbrella patient organisation, clinical trial databases, etc.) as well as their inclusion/exclusion criteria can be found in the “Documents” section of our national website.

PARTICIPATION IN THE OD4RD PROJECT

Rare diseases are still poorly represented in the medical terminologies in use. There is no terminology specific to rare diseases with the exception of the nomenclature of rare diseases developed by Orphanet (based on ORPHAcodes). One of the main objectives of the **Orphanet Data for Rare Disease project** (OD4RD), co-funded by the EU4Health program of the European Commission, is to **advance the implementation of ORPHAcodes in hospitals hosting the ERN-centres of many European countries** and to **use the expertise of ERNs to further improve the Orphanet nomenclature.** This should allow to establish a **common language**, with codes specifically for rare diseases, in order to effectively monitor and report on rare diseases (including undiagnosed cases) at European level.

The OD4RD project has been launched in January 2022 for a 12 months period, and has been extended until March 31st 2023. During the pilot year, 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 (Figure 9).

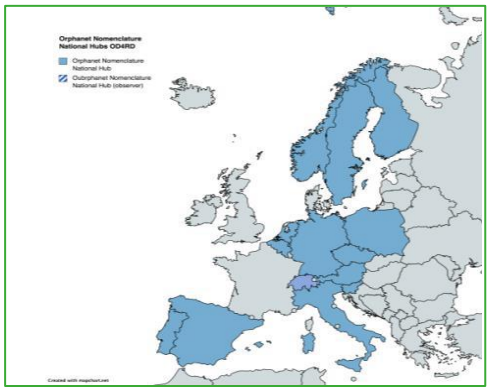


Fig.9. Network of OD4RD nomenclature and codification national hubs

This **European project builds 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 which participates in work package 4. The main objective of WP4 is to ensure support for the local implementation of ORPHAcodes into routine coding systems of national HCPs hosting ERNs (or linked to ERNs). Orphanet national nomenclature support hubs must facilitate a 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 **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. This revealed that the **overall picture of RD coding with ORPHAcodes is very different between WP4 participating countries.** The range extends from already implemented ORPHAcodes with linkage to ICD-10 in national coding systems used in all hospitals to not yet using ORPHAcodes at all. In Belgium, the situation is complex because a transition to SNOMED CT® as the common national reference terminology in all electronic health records is underway. Moreover no legislative framework and no incentive (i.e. 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.

Taking into consideration the different situation and needs of end users in regards to ORPHAcodes implementation in the WP4 participating countries, it has been necessary to develop individual **national action plans** to achieve the project goals. The coordinating partners of WP4 (BfArM and Inserm) developed a template that enabled the participating countries to document the development of their measures to ensure support for the local implementation of ORPHAcodes in national HCPs. This template was divided into four sections: trainings/workshops, networking, helpdesk implementation and further activities. These topics were discussed during the **monthly WP4 conference calls** and experiences of the different countries were shared in order to benefit from each other and to address common topics in a coordinated manner.

All **OD4RD project deliveries** can be accessed here: **https://od4rd.eu/03-deliverables**

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. The following table (Table 3) shows the list of Belgian hospitals that received training in 2022. Flexibility in the types of training is offered: there are various possibilities in terms of methods (online, on site), duration (from 2 hours to a day, depending on availability and needs) and testing of knowledge autonomously via online quizzes. The training sessions have been recorded in order to distribute the course to people who could not attend the training (Figure 10).

NAME OF THE HOSPITAL	DATE	HOW?	REMARK
UCL Saint-Luc, Brussels	April 29, 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	August 29, 2022	Online, in French/English	Based on the advanced quiz developed by the Orphanet coordinating team (Inserm). Participant: RD coordinator (n=1).
Ghent University hospital	September 19, 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	October 21, 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).
Other hospitals with a RD function: UZ Brussel, UZ Antwerpen, UZ Leuven, HUB (Erasme, HUDERF, Bordet), GHdC-IPG	To be planned in 2023 with the healthcare professionals	Online or on site. In French/Dutch or English.	/
Non-university hospitals, ERN-centres and any institutions involved in the RD field	To be planned in 2023-2025 with the healthcare professionals	Online or on site. In French/Dutch or English.	/

Table 3. Trainings on Orphanet nomenclature and classification delivered to Belgian hospitals in 2022

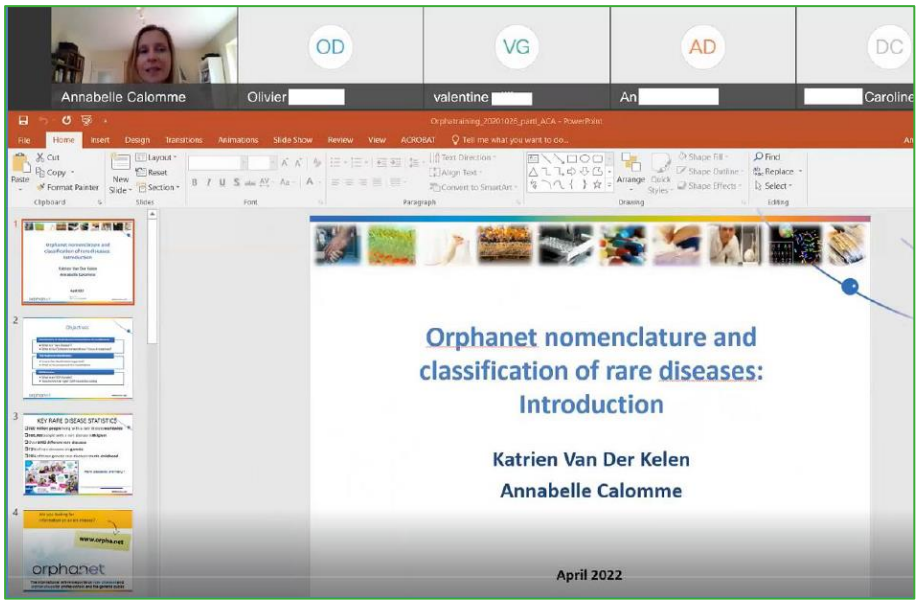


Fig 10. Screenshot of the online training session organised on April 29, 2022 for clinicians and coders from the Cliniques universitaires Saint-Luc's Rare Disease Institute

Furthermore, 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.

Finally, the national hubs are in charge of **establishing an ORPHAcodes helpdesk** in local languages. This helpdesk is dedicated to answering questions related to the Orphanet nomenclature content and the implementation of ORPHAcodes in Health Information Systems. It will provide guidance for both implementing the nomenclature and using the nomenclature and classification for statistical aggregation analysis for coded data.

For this purpose, a **central OD4RD Github** has been set up: it is an online ticketing system that allows requests to be stored, tracked and made available to others. This system facilitates a simple and interactive workflow. After creating an account, issues can be posted.

A **FAQ section within the GitHub** has been developed by the Orphanet coordinating team based on users' questions. It provides standardised and generalised reference answers among 7 main topics: alignments with other terminologies, coding recommendations, education and communication, epidemiology of RD, ORPHAcodes and nomenclature, Orphanet classification and Orphanet tools. It is open access to any end users.

In Belgium, a process is also in place to manage questions addressed by emails (**Orphacodes.Belgium@sciensano.be**) by ORPHAcodes users.

The project has been renewed until the end of 2025 (OD4RD2). During this next phase (April 2023-December 2025) the network will be expanded to 6 new national hubs (Bulgaria, Ireland, Estonia, Latvia, Lithuania and Romania) with the objective to have 19 + 1 observer fully autonomous National Hubs. The OD4RD2 project will capitalize on the pilot phase and has the ambition to increase the number of ERNs collaborations and develop material to better explain how to deal with coding-related issues.

Ultimately, the OD4RD project will contribute to better diagnosis and care of RD patients, as it will allow comparability of data, and therefore assessment of current practices and results against gold standards of care, necessary for taking actions and improvement in the RD field.

TRAINING ACTIVITIES

1. Orphanet Information Scientist trainings

As part of the continuous development of its collaborators, the members of the Orphanet Belgium team participated in various training courses organised by the Orphanet-Inserm coordinating team. Following public health measures due to the COVID-19 crisis, the annual training usually held in Paris (Orphanet headquarters) could not take place. **Online trainings** for Information Scientists were organized from March to April 2022 (11 sessions of approximatively 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 tools** (Figure 11) : **Arbor** to explore all the classifications of diseases produced by Orphanet; **Collector** (collection of requests for registration or updates submitted by professionals in **Professor**), **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.11. Orphanet tools overview

Here are some examples of **topics covered by the 2022 IS Orphanet trainings**:

- General presentation of the Orphanet network and portal;
- 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;
- Presentation of the Orphanet tools;
- 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, data workflow;
- Genes: how are genes registered in the database and what is needed to register them.

2. OD4RD “Train the trainers” program

For the OD4RD project endeavors to be successful, **well-trained National Nomenclature hubs are needed to support local implementation of ORPHAcodes.** During the summer of 2022, basic and advanced sessions were organised by the Orphanet nomenclature project manager and the national hubs scientific coordinator in order to train the collaborators involved in the Orphanet nomenclature trainings and in the dissemination of the Orphanet Nomenclature and Classification at the national level.

The main purpose of these trainings is to ensure that all hubs can fully explain the benefits of ORPHAcoding versus other general terminologies as well as the alignments methodology with other terminologies and the different services and tools available, so that they can discuss at the hospital level what solution can be implemented to ease the burden of the coders regarding rare diseases.

Each national hub acts as a **national helpdesk** and a contact point for all questions related to ORPHAcodes. It promotes ORPHAcoding to the different stakeholders and organizes trainings in local language(s) for clinicians, geneticists and coders to ensure accurate and standardized coding practices.

3. National Orphanet website trainings

At the end of 2022, Inserm developed a **new version of the national Orphanet websites**, based on the **content management system Grav**. All national Orphanet websites have been fully updated, including the Belgian Orphanet websites. Subsequently, the structural web pages have been translated into French and Dutch and the content has been adapted to the Belgian context.

To become familiar with this new system, the Belgian Orphanet team participated in training courses organized by the Orphanet coordinator (3 sessions of about two hours organised in November and December 2022).

From February 2023, the new Belgian Orphanet websites will be publicly accessible at the following addresses:

- **https://orphanet.site/belgique** for the French-language website;
- **https://orphanet.site/belgie** for the Dutch-language website.

NATIONAL AWARENESS AND NETWORKING

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 were carried out to this end by the Orphanet Belgium team in 2022.

1. Meeting with the CHU Liège RD coordinator on the implementation of ORPHAcodes

An online meeting was organized with the rare disease coordinator of CHU Liège, Ms. Sylvie Taziaux, on February 07, 2022. She leads a project that contributes to the use of ORPHAcodes in the medical records of rare disease patients at CHU Liège. She explained her experience concerning the creation of a specific tool designed for rare diseases coding in computerized patient files. Following its creation in 2018, the adoption of this tool was a long and difficult process, not only because of technical obstacles but also because of the resistance of a part of the clinicians, although the Orphanet website is generally already well known and appreciated in this hospital. The fact is that clinicians are not always convinced of the importance and benefits of making the RD patients particularly visible by means of a specific code. Moreover, the search for the correct ORPHAcodes is sometimes considered tedious and time-consuming.

Based on this experience, our team could anticipate that **a lot of awareness-raising, both on the level of the local project manager and on the level of the heads of hospital departments, will be necessary to convince the Belgian specialists** (clinicians, as well as coders, hospital information managers, IT services and other stakeholders involved) **to improve their knowledge of ORPHAcodes and generalize their use in hospitals.** In this sense, the organisation of national trainings planned within the framework of the OD4RD project is particularly relevant.

2. Participation in the 2022 Rare Disease Day

Rare Disease Day is a global initiative which takes place every year on the last day of February. **In Belgium, this is the opportunity for RaDiOrg[15], the umbrella association for people living with a rare disease, to present its awareness campaign.** This year, the main idea of this campaign was to make the expectations of all people living with rare diseases concrete and visible in terms of diagnosis and care, by setting up a physical waiting room in the heart of Brussels (Figure 12). Starting from February 28 for three subsequent days, rare disease patients, healthcare providers, loved ones and supporters took turns to draw attention to this important public health issue. Meetings with decision-makers and politicians were organized in the waiting room in order to find solutions to end the waiting time for diagnosis setting and care.

A **petition was also launched by RaDiOrg** on this occasion in order to ask political decision-makers to work in favor of more appropriate care for people living with rare diseases.

As every year, the Rare Disease Team of Sciensano participated in this awareness-raising action. We contributed to the promotion of the RaDiOrg campaign, both online (e.g. by sharing information on the Orphanet Belgium website, on the Sciensano website and on social networks; using banners in the email signatures, etc.) and offline (by sticking up posters containing key information on the issues of rare diseases in our country).

Fig.12. Visuals of the awareness campaign launched by RaDiOrg in 2022 for the International Rare Disease Day

3. Oral presentation at the OD4RD Final Meeting

The Final OD4RD meeting was a hybrid event organised by the Orphanet Network Coordinating team (Inserm) on October 6, 2022. It was held at the Cité Universitaire in Paris and online, and gathered **83 participants including all project partners as well as ERNs and other stakeholders.** The main objectives of this meeting were allowing ERNs and the external partners to learn about the project and its current and planned outcomes and to discuss on potential improvements, additional tasks and challenges to be addressed in the next months of the project and in its next phase ("OD4RD2" project).

Part of the Sciensano RD team was present in Paris. On this occasion, an **oral presentation of the Belgian action plan and the achievements of the Belgian hub** was given by the Orphanet Belgium IS (Figure 13).

Fig.13. Presentation of the Belgian action plan of the European OD4RD project by Annabelle Calomme (Orphanet Belgium, Sciensano) during the final OD4RD meeting in October 2022 in Paris

4. Participation in the Orphanet annual meeting

The **2022 Orphanet Annual meeting was held as a satellite event of the OD4RD Final meeting** organised by the Orphanet Network Coordinating team (Inserm). The meeting was held in Paris and online on the 7th October 2022 and gathered **65 participants**.

The objectives of this meeting were multiple:

- assess what has been done in the past year by the coordinating team, by each single National Team and by the Network as a whole;
- agree on the strategic annual action plan;
- discuss on potential improvements, additional tasks and challenges to be addressed in 2023.

A **poster summarizing the main activities and achievements of the Orphanet Belgium team in 2022** was presented on this occasion (Figure 14).

Fig.14. Poster of activities and achievements of the Orphanet Belgium team in 2022

5. Meetings with the FPS Terminology Centre

In Belgium, the **Terminology Center** within the 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 and a transition to SNOMED CT® as the national reference terminology in all Belgian electronic health records (EHR) is underway (planned for 2027).

The Orphanet Belgium team actively promotes the use of ORPHAcodes in EHRs as one of our missions as a participant in the OD4RD project. ORPHAcodes are indeed the *sine qua non* condition for RD data interoperability, for RD patients' visibility and for linking healthcare and research settings. However, **the implementation of ORPHAcodes remains a big challenge in Belgium knowing that the national health authorities support the use of only one coding system (SNOMED CT®) in the EHRs.**

To discuss this topic, **the Sciensano RD team organized two meetings with the Terminology Center in November and December 2022.** Our main objective was to demonstrate why the use of ORPHAcodes is a crucial need for the RD community by presenting a list of strong arguments validated by the Orphanet coordinating team in charge of these aspects (Figure 15). The Terminology Center agreed that for the RD field, the ORPHAcoding system has clear advantages compared to a generic medical terminology. However, **they confirmed their decision to keep only one coding system - SNOMED CT® - in the Belgian EHRs.**

Fig.15. PowerPoint presentation on the importance of the implementation of ORPHAcodes in the Belgian HIS

Several advances have nevertheless been achieved:

- If a RD is missing or not sufficiently accurately represented in SNOMED CT® at the moment that the mapping between SNOMED CT® and ORPHAcodes can be considered as complete as possible, **Sciensano can ask the Terminology Center to add the missing entity to the "national extension of SNOMED CT"** in which concepts specific to Belgium can be added;

- The Terminology Center agreed that a flag (logo) to indicate rarity based on a SNOMED ID that maps to an ORPHAcode in a patient file would be very useful to make these patients more visible and to improve their chances of good clinical management (especially in emergency situations). They therefore proposed to work on **a system that will add a flag in the EHR when a SNOMED CT® ID for a RD (i.e. corresponding to an ORPHAcode) is used to diagnose a RD patient**;

- The Terminology Center proposed to start a **working group with Sciensano** (from 2023), in order to share our needs in the field. Ideally, this working group should include representatives from hospitals (e.g. representatives from the RD functions) for validation, in order to check the usability of the rarity flag in the electronic patient files.

Orphanet considers that the solutions proposed by the Terminology Center are not optimal, since it involves the creation of an additional system ("SCT BE extension", National Extension including Dutch and French translations) that should be maintained. This option will be more costly and less accurate than using directly the Orphanet nomenclature system that is up-to-date and free.

6. Meeting with the FPS Public Health and the Ministry of Health regarding the designation of RD expertise in Belgium

In Belgium, the Orphanet Management Board composed of representatives of Sciensano, as well as members of the national health authorities (FPS Public Health) and members of the National Institute for Health and Disability Insurance (NIHDI) decides on the criteria for registration of Belgian activities, while respecting the European Orphanet eligibility criteria.

Currently, two categories of Belgian expert centres are authorized to be registered in Orphanet:

- the officially-designated centres (i.e. the reference centres having a convention with the NIHDI with a specific focus on rare diseases, the genetic centres and the hospitals recognized by the regional health authorities to have a "rare disease function");
- the centres participating in a European Reference Network (ERN).

The Belgian criteria don't fully meet the expectations of some patients and healthcare professionals. Indeed, in Orphanet Belgium, we quite often receive feedback from patient organisations and professionals who are dissatisfied with the way expertise in the RD field is currently represented in Orphanet. To discuss this subject, we requested a meeting with our national health authorities (FPS Public Health), in the presence of a representative of the Ministry of Health.

During this online meeting held in December 2022, **the Sciensano RD team proposed a new model based on the creation of a national designation committee and the use of questionnaires developed by Orphanet** (adapted if necessary). The Orphanet Quality Criteria Questionnaires[21] aim to assess the appropriateness of registering in Orphanet an expert centre that is not officially-designated. They are based on the EUCERD recommendations on quality criteria for expert centres for rare diseases.

Our proposal was built on:

- a "survey" (emails exchanges) conducted among our colleagues in the other countries of the Orphanet consortium to find out how RD expertise is designated in their own country;
- reading legislative documents (reference frameworks, national action plans, procedures, etc.) that are applicable in other countries;
- reports and exchanges with clinicians and patient organizations (mainly RaDiOrg, the umbrella organization for rare disease patients in Belgium).

This proposal was not retained, mainly for reasons related to the difficulty of implementing such a solution with regard to legal aspects: in Belgium, the distribution of responsibilities between the federal and regional levels has the consequence that the FPS Public Health is not empowered to define and use a list of criteria to attribute the "expert" label to a centre. Therefore for the moment, **the criteria related to the identification and registration of expert centres in Orphanet will not be reassessed.**

The work carried out with regard to new RD conventions established with the NIHDI and with the launch of the "Joint Action on the integration of ERNs into national healthcare systems" supported by the European Commission could help to better define where the optimal expertise can be found in our country. A mobilization of the national competent authorities, as well as regional health ministries, should be considered, with the support of experts in the field (clinicians, patients, etc.), to move forward on this complex issue. One option could be the creation of a national mirror group composed of all relevant stakeholders which is one of the activities that is proposed in the "**European Rare Disease Partnership**". The draft of the proposal for the Rare Disease Partnership is currently being written and should be submitted by September 2023.

7. Contribution to the OrphaNetWork News

OrphaNetWork News is an **internal newsletter published by Orphanet approximately every 3 months** (Figure 16)**.** 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 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 OrphaNetWork newsletter, to systematically read every issue and to carry out the action points posted in this document. **The Orphanet Belgium team published information on their activities in the 4 issues published during the year 2022** (communication about meetings, conferences, congresses, trainings, etc.).

Fig.16. Cover page of the November-December 2022 issue of the OrphaNetWork internal newsletter

8. Creation of documents to facilitate the registration of Belgian patient associations

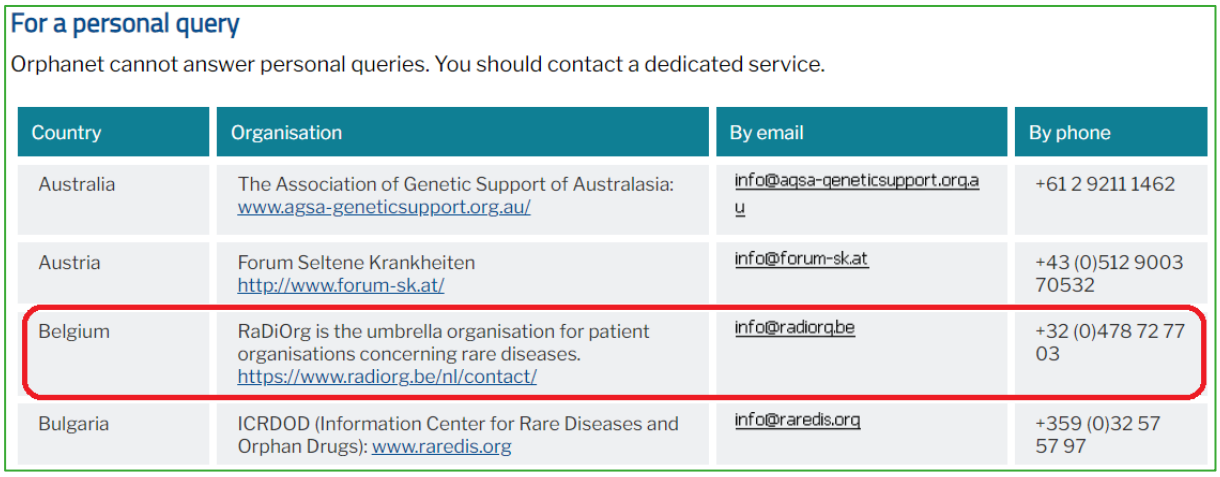
An article[22] (currently only available in French) describing the **registration procedure and the advantages for a patient association of being referenced in the Orphanet database** was written in June 2022 by the Orphanet Belgium Information Scientist at the request of RaDiOrg. The list of patient organisations registered in Orphanet at that time is provided. This document is available on the Orphanet Belgium website.

In addition, **guidelines in local languages (French, Dutch) for patient organizations registration** in Orphanet were created. This aims to help patients to use the Orphanet's online registration tool (only available in English) to submit a request for registration of their association.

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, 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 portal (Figure 17). 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 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.17. 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 required form 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 quite 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 each request 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 inclusion criteria currently defined by the Orphanet Belgium MB).
- 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 given RD diagnosis.
- For clinicians/coders: provide (online or on-site) Orphanet nomenclature and classification trainings.

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.

CONCLUSION AND PERSPECTIVES

Since its creation in 1997, Orphanet has become a well-established and internationally recognized portal dedicated exclusively to rare diseases and orphan drugs. Orphanet is the reference source for the nomenclature and classification of rare diseases, both for healthcare and for research. Its freely-accessible website and associated tools contribute to help all audiences access high quality expert-reviewed information, to provide 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 about 40 countries within Europe and beyond, is coordinated by the Inserm in Paris. National teams are located in each participating country of the network and Belgium is part of it for more than 20 years. The sustainability of the Orphanet national teams in the long-term is essential to meet the challenges arising from a rapidly evolving political, scientific and informatics landscape.

In 2022, 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 listed in Orphanet (expert centres, patient organisations, medical laboratories and diagnostic tests, clinical trials, research projects, registries and biobanks). 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 has been made in 2022 to **register expert centres that have joined a European Reference Network (ERN) following the second call launched by the EU**. These networks allow the generation and promotion of best practices for rare disease healthcare in Europe, providing data and resources that contribute to avoiding of duplicating efforts and making better use of available resources. **Belgium now participates in all 24 existing ERNs** and **100% of the Belgian centres that joined an ERN following the two calls for membership are registered in Orphanet**. For some of the ERN-centres registered since 2019, a data update has already been necessary in 2022.

In 2023, we plan to devote time to the **adaptations that will be necessary following the adoption of a new model for recording diagnostic tests in Orphanet**. Training to learn how to use the Polaris platform will also be required. This **new tool for registration, curation and analysis of research projects** will be available for the funders, for the members of IRDiRC and for the Orphanet network members. It should facilitate the identification of projects not yet registered in the Orphanet database as well as the analysis of our research national data, for example in terms of disease coverage.

In addition, we will continue to **carry out our service activities**, such as providing assistance and information to people living with a rare disease or health professionals who contact us regularly via email or phone. We will also **participate in national awareness-raising activities** concerning rare diseases in general but also related to the Orphanet database and associated tools.

The Orphanet Belgium team will **continue to actively participate in the European project OD4RD** (“Orphanet Data for Rare Diseases”) whose main objective is to contribute to the generation of accurate and standardized data related to rare diseases through the implementation and maintenance of ORPHAcodes in the routine coding information systems of national healthcare providers. This project involves the delivery of trainings in the two national languages (or in English depending on demand), online or on site, to people involved in the field of rare diseases in a clinical context (clinicians, coders, people in charge of registries, IT managers, etc.). This also includes the promotion of ORPHAcodes to key players in the field of rare diseases (national health authorities, hospital managers, experts, etc.).

REFERENCES

1. Orphanet Belgium activity report 2017-2019: DOI : https://doi.org/10.25608/4d5z-2q16

2. Orphanet Belgium activity report 2020: DOI : https://doi.org/10.25608/72vb-ay88

3. Orphanet Belgium activity report 2021: DOI : https://doi.org/10.25608/5bev-y998

4. Orphanet Reports Series / Procedures: https://www.orpha.net/consor/cgi-bin/Education_Home.php?lng=EN

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

6. Wakap, S., Lambert, D.M., Olry, A. et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. Eur J Hum Genet 28, 165–173 (2020). https://doi.org/10.1038/s41431-019-0508-0

7. “Prevalence and incidence of rare diseases: Bibliographic data”, Orphanet Report Series, Rare Diseases collection, January 2022, Number 1, : Diseases listed in alphabetical order : https://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf ; The number of rare diseases listed in Orphanet is also available at the bottom of the Orphanet website homepage: https://www.orpha.net/consor/cgi-bin/index.php

8. Figures obtained following "The Journey to Diagnosis for People Living with Rare Diseases. A Rare Barometer Survey" launched in March 2022 by EURORDIS. For Belgium, 882 respondents, 341 rare diseases represented. No official report/communication was yet available at the time of this report. A scientific article should be published in 2023 by EURORDIS and RaDiOrg will publish a report/outcome in early 2024.

9. 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: https://www.orpha.net/orphacom/cahiers/docs/GB/Orphanet_Network_MB_members.pdf

10. Orphanet – 2021 Activity report, Orphanet Report Series, Reports Collection, October 2022 (V1) http://www.orpha.net/orphacom/cahiers/docs/GB/ActivityReport2021.pdf

11. Belgian Plan for Rare Diseases, Brussels, December 2013, French version; Dutch version.

12. Orphanet evaluation criteria for Belgian expert resources, version 2, 08 October 2021: http://www.orpha.net/national/data/BE-FR/www/uploads/Belgian-criteria-document_version-08OCT2021_4.pdf

13. European reference networks description on the Orphanet website: https://www.orpha.net/consor/cgi-bin/Clinics_ERN.php?lng=EN

14. European reference networks description on the official website of the European Union: https://health.ec.europa.eu/european-reference-networks/networks_en

15. RaDiOrg, Rare Diseases Belgium website: https://www.radiorg.be/

16. EURORDIS website: https://www.eurordis.org/

17. Recommendation on Cross Border Genetic Testing Of Rare Diseases in the European Union (2015): https://ec.europa.eu/health/sites/health/files/rare_diseases/docs/2015_recommendation_crossbordergenetictesting_en.pdf

18. Belgian Genetic Tests Database (BGTD): https://gentest.healthdata.be/

19. Orphanet online registration service: https://www.orpha.net/professor/htdocs/

20. Orphanet Belgium national website (2023 version): https://orphanet.site/belgium

21. Orphanet Quality Criteria Questionnaires: see annexes of the “Procedural document on data collection and registration of expert centres in Orphanet, Orphanet, February 2019, Version 1”: https://www.orpha.net/orphacom/cahiers/docs/GB/eproc_expert_centres_R2_PatCar_Cns_EP_02.pdf

22. “Etre référencé sur le site Orphanet: un pas vers plus de visibilité pour les associations de patients belges”: https://orphanet.site/user/env/belgique/themes/orphanet/files/POs-publication_Orphanet_Annabelle_June-2022.pdf

ANNEXES

1. Belgian centres participating in ERNs for rare or complex diseases (as recorded in Orphanet in December 2022)

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
	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
	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
	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
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)	Liège University Hospital (Centre Hospitalier Universitaire de Liège)	CALL 1 (2017)	ORPHA:3027 Caudal regression syndrome ORPHA:237 Duplication of urethra ORPHA:322 Exstrophy-epispadias complex ORPHA:289365 Familial vesicoureteral reflux ORPHA:435365 Fetal lower urinary tract obstruction ORPHA:2795 Fowler urethral sphincter dysfunction syndrome ORPHA:84085 Hinman syndrome ORPHA:49041 IgG4-related retroperitoneal fibrosis ORPHA:37202 Interstitial cystitis ORPHA:140949 Low-flow priapism ORPHA:398043 Malignant tumor of penis ORPHA:600952 Non-syndromic anorectal malformation with perineal fistula ORPHA:600961 Non-syndromic anorectal malformation with rectourethral fistula ORPHA:601028 Non-syndromic anorectal malformation with rectovaginal fistula ORPHA:600984 Non-syndromic anorectal malformation with rectovesical fistula ORPHA:600993 Non-syndromic anorectal malformation with vestibular fistula ORPHA:95706 Non-syndromic posterior hypospadias ORPHA:180205 Rare non-malformative uterovaginal or vulvovaginal disease ORPHA:3176 Spina bifida-hypospadias syndrome ORPHA:887 VACTERL/VATER association
	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 December 2022)

NAME OF THE BELGIAN PATIENT ORGANISATION/SUPPORT GROUP REGISTERED IN ORPHANET	(GROUP(S) OF) RARE DISORDER(S)
ABeFAO-Association Belge des Familles Touchées par l'Atrésie de l'Oesophage Belgische Vereniging voor Families Getroffen door Slokdarmatresie	ORPHA:1199 Esophageal atresia
ABFPI - Association Belge contre la Fibrose Pulmonaire Idiopathique A.S.B.L.	ORPHA:2032 Idiopathic pulmonary fibrosis
ABMM - Association Belge contre les Maladies neuro-Musculaires A.S.B.L.	ORPHA:166 Charcot-Marie-Tooth disease/Hereditary motor and sensory neuropathy ORPHA:2103 Guillain-Barré syndrome ORPHA:685 Hereditary spastic paraplegia ORPHA:68381 Neuromuscular disease
ABN-BVN A.S.B.L. - Association Belge de Narcolepsie - Cataplexie Belgische Vereniging voor Narcolepsie	ORPHA:33208 Idiopathic hypersomnia ORPHA:2073 Narcolepsy type 1 ORPHA:83465 Narcolepsy type 2
ABSM - Association Belge du Syndrome de Marfan asbl	ORPHA:284963 Marfan syndrome type 1 ORPHA:284973 Marfan syndrome type 2 ORPHA:284979 Neonatal Marfan syndrome
ABT- Association Belge de Thalassémie A.S.B.L.	ORPHA:846 Alpha-thalassemia ORPHA:848 Beta-thalassemia ORPHA:231230 Beta-thalassemia associated with another hemoglobin anomaly ORPHA:231386 Beta-thalassemia with other manifestations ORPHA:232288 Syndrome with alpha-thalassemia as a major feature
AccessAndGo-ABP asbl	ORPHA:2912 Poliomyelitis ORPHA:2942 Postpoliomyelitis syndrome
Action Parkinson A.S.B.L.	ORPHA:2828 Young-onset Parkinson disease
AFBOI - Association Francophone Belge de l'Ostéogenèse Imparfaite A.S.B.L.	ORPHA:666 Osteogenesis imperfecta
AHOSA vzw - Anders HOren Samen Aanpakken	ORPHA:637 Full NF2-related schwannomatosis ORPHA:90641 Mitochondrial non-syndromic sensorineural deafness ORPHA:87884 Non-syndromic genetic deafness ORPHA:648 Noonan syndrome
AHVH- Association de l'hémophilie, von Willebrand et autres pathologies de la coagulation Vereniging van hemofilie-, von Willebrand en andere stollingsstoornissen	ORPHA:68334 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 Rare genetic renal disease
AKABE- Association syndrome Kabuki Belgium asbl	ORPHA:2322 Kabuki syndrome
ALICE ASBL - Association Libre d'Informations sur la Croissance des Enfants « Silver Russell »	ORPHA:813 Silver-Russell syndrome
Alpha-1 Plus Belgium A.S.B.L./V.Z.W.	ORPHA:60 Alpha-1-antitrypsin deficiency
ALS Liga België V.Z.W./ Ligue SLA Belgique A.S.B.L.	ORPHA:803 Amyotrophic lateral sclerosis ORPHA:275872 Frontotemporal dementia with motor neuron disease
Alzheimer Liga Vlaanderen vzw	ORPHA:89043 Rare dementia
Angelman Syndroom België V.Z.W.	ORPHA:228402 2q23.1 microdeletion syndrome ORPHA:72 Angelman syndrome ORPHA:85278 Christianson syndrome
Angioedema Belgium A.S.B.L./V.Z.W.	ORPHA:658 Non-histaminic angioedema
Anna Timmerman vzw - Belangenvereniging omtrent doofblindheid	ORPHA:90641 Mitochondrial non-syndromic sensorineural deafness ORPHA:87884 Non-syndromic genetic deafness ORPHA:886 Usher syndrome
APEDAF - Association des Parents d'Enfants Déficients Auditifs Francophones A.S.B.L.	ORPHA:90641 Mitochondrial non-syndromic sensorineural deafness ORPHA:87884 Non-syndromic genetic deafness
APK - Association Parkinson A.S.B.L.	ORPHA:2828 Young-onset Parkinson disease
APSB - Association des Patients Sclérodermiques de Belgique A.S.B.L.	ORPHA:801 Scleroderma
ASBBF - Association Spina Bifida Belge Francophone ASBL	ORPHA:3388 Neural tube defect
Association Belge de Lutte contre la Mucoviscidose A.S.B.L. Belgische Vereniging voor Strijd tegen Mucoviscidose V.Z.W.	ORPHA:586 Cystic fibrosis
Association belge du Syndrome de Williams [Section de l'A.S.B.L. INCLUSION]	ORPHA:904 Williams syndrome
Association Lupus Erythémateux ASBL	ORPHA:300345 Autosomal systemic lupus erythematosus ORPHA:464343 Catastrophic antiphospholipid syndrome ORPHA:93552 Pediatric systemic lupus erythematosus ORPHA:535 Rare cutaneous lupus erythematosus
Association Neurofibromatose Belgique (ANB) ASBL	ORPHA:636 Neurofibromatosis type 1
Association Syndrome de Cornelia de Lange - BE (point de contact pour la Belgique francophone)	ORPHA:199 Cornelia de Lange syndrome
Association X fragile Belgique ASBL	ORPHA:908 Fragile X syndrome ORPHA:93256 Fragile X-associated tremor/ataxia syndrome
B.R.S.V. - Belgische Rett Syndroom Vereniging vzw	ORPHA:778 Rett syndrome
Belgische Vereniging voor Dystoniepatiënten V.Z.W. - Association Belge des Patients Dystoniques A.S.B.L.	ORPHA:68363 Rare dystonia
Belgische Vereniging voor Longfibrose vzw	ORPHA:2032 Idiopathic pulmonary fibrosis
Belgische Vereniging Ziekte van Hirschsprung/Association belge de la maladie de Hirschsprung	ORPHA:388 Hirschsprung disease
BePOPI - Belgische organisatie van en voor PID-patiënten/Organisation belge de et pour des patients DIP	ORPHA:101997 Primary immunodeficiency
be-TSC V.Z.W./ be-STB A.S.B.L.	ORPHA:805 Tuberous sclerosis complex
bindweefsel.be - Vlaamse Vereniging voor Erfelijke Bindweefselaandoeningen V.Z.W.	ORPHA:166100 Autosomal dominant otospondylomegaepiphyseal dysplasia ORPHA:284993 Marfan syndrome and Marfan-related disorders ORPHA:3164 Omphalocele syndrome, Shprintzen-Goldberg type ORPHA:251312 Overlapping connective tissue disease ORPHA:275798 Pulmonary arterial hypertension associated with connective tissue disease ORPHA:139030 Rare developmental defect with connective tissue involvement ORPHA:285014 Rare disease with thoracic aortic aneurysm and aortic dissection ORPHA:828 Stickler syndrome ORPHA:3377 Trismus-pseudocamptodactyly syndrome ORPHA:90002 Undifferentiated connective tissue syndrome ORPHA:166277 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 Allan-Herndon-Dudley syndrome ORPHA:68367 Rare inborn errors of metabolism
BorstkankerMAN vzw	ORPHA:227535 Hereditary breast cancer

NAME OF THE BELGIAN PATIENT ORGANISATION/SUPPORT GROUP REGISTERED IN ORPHANET	(GROUP(S) OF) RARE DISORDER(S)
CIB-Liga - Liga voor Chronische Inflammatoire Bindweefselziekten VZW	ORPHA:221 Dermatomyositis ORPHA:809 Mixed connective tissue disease ORPHA:732 Polymyositis ORPHA:289390 Primary Sjögren syndrome ORPHA:801 Scleroderma ORPHA:536 Systemic lupus erythematosus ORPHA:52759 Vasculitis
CLAIR ASBL - Contre Les Affections Inflammatoires Rhumatismales	ORPHA:300345 Autosomal systemic lupus erythematosus ORPHA:92 Juvenile idiopathic arthritis ORPHA:93552 Pediatric systemic lupus erythematosus ORPHA:535 Rare cutaneous lupus erythematosus ORPHA:801 Scleroderma ORPHA:536 Systemic lupus erythematosus
CMP-Vlaanderen vzw [Contactgroep Myeloom en Waldenström Patiënten Vlaanderen]	ORPHA:29073 Multiple myeloma ORPHA:33226 Waldenström macroglobulinemia
Collectif Drépanocytose asbl / Collectieve sikkelanemie vzw	ORPHA:232 Sickle cell anemia
Cum Cura VZW	ORPHA:223727 Bone sarcoma ORPHA:873 Desmoid tumor ORPHA:363976 Giant cell tumor of bone ORPHA:3394 Soft tissue sarcoma ORPHA:66627 Tenosynovial giant cell tumor
DEBRA Belgium A.S.B.L., Association d'entraide pour les patients atteints d'épidermolyse bulleuse DEBRA Belgium V.Z.W., Vereniging voor epidermolysis bullosapatiënten	ORPHA:79361 Inherited epidermolysis bullosa
Donner des ailes ASBL - Association belge du syndrome d'Angelman	ORPHA:72 Angelman syndrome
Duchenne Parent Project Belgium V.Z.W.	ORPHA:98896 Duchenne muscular dystrophy
Dyskinesia A.S.B.L.	ORPHA:244 Primary ciliary dyskinesia
Dysmelia A.S.B.L./V.Z.W.	ORPHA:93457 Non-syndromic limb reduction defect
ELA Belgique A.S.B.L. - Association européenne contre les leucodystrophies [Antenne Belgique]	ORPHA:68356 Leukodystrophy
Ensemble pour Lola et les Enfants de la Lune ASBL	ORPHA:910 Xeroderma pigmentosum
Epilepsie Liga VZW	ORPHA:101998 Rare epilepsy
FAPA - Familial Adenomatous Polyposis Association A.S.B.L./V.Z.W.	ORPHA:220460 Attenuated familial adenomatous polyposis ORPHA:733 Familial adenomatous polyposis ORPHA:443909 Hereditary nonpolyposis colon cancer
Fondation contre le Cancer / Stichting tegen Kanker	ORPHA:98057 Rare tumor
Fondation Lou - fondation privée	ORPHA:3157 Septo-optic dysplasia spectrum
Fragiele X Vlaanderen	ORPHA:908 Fragile X syndrome
GESED - Groupe d'Entraide des Syndromes d'Ehlers-Danlos A.S.B.L.	ORPHA:98249 Ehlers-Danlos syndrome
Groupe de soutien aux personnes atteintes du syndrome de Guillain-Barré et leur famille [Groupe de l'ABMM]	ORPHA:2103 Guillain-Barré syndrome
HME-MO Lotgenoten Contactgroep - België	ORPHA:321 Multiple osteochondromas
Hodgkin en non-Hodgkin VZW	ORPHA:98293 Hodgkin lymphoma ORPHA:547 Non-Hodgkin lymphoma
HTAP Belgique - Association des patients souffrant d'HyperTension Artérielle Pulmonaire en Belgique A.S.B.L.	ORPHA:422 Idiopathic/heritable pulmonary arterial hypertension
Huntington Liga V.Z.W.	ORPHA:399 Huntington disease
Ichthyosis België V.Z.W. - Ichthyosis Belgique A.S.B.L.	ORPHA:79354 Ichthyosis
IKAROS vzw - Epilepsie-contactgroep [Contactgroep Oost-Vlaanderen]	ORPHA:101998 Rare epilepsy
Imagene CAPS Association in Belgium asbl/vzw	ORPHA:575 Muckle-Wells syndrome
INCLUSION A.S.B.L.	ORPHA:87277 Rare intellectual disability
KIKOV-Leuven - Kinderkanker Oudervereniging Leuven vzw	ORPHA:98057 Rare tumor
LCH Belgium - Feitelijke vereniging/ Association de fait	ORPHA:389 Langerhans cell histiocytosis
Les Enfants de Salus Sanguinis, Fondation d'utilité publique	ORPHA:68347 Tumor of hematopoietic and lymphoid tissues
Les Services de l'APEM-T21 A.S.B.L.	ORPHA:870 Down syndrome
LFBE - La Ligue francophone belge contre l'Epilepsie ASBL	ORPHA:101998 Rare epilepsy
LHFB - Ligue Huntington Francophone Belge A.S.B.L. [Région Wallonne et Communauté Française]	ORPHA:399 Huntington disease
Liga Myasthenia Gravis vzw	ORPHA:589 Myasthenia gravis
Ligue Alzheimer ASBL	ORPHA:1020 Early-onset autosomal dominant Alzheimer disease
Ligue Belge du Sjögren ASBL	ORPHA:79078 IgG4-related dacryoadenitis and sialadenitis ORPHA:289390 Primary Sjögren syndrome
LVV - Lymfklierkanker Vereniging Vlaanderen V.Z.W.	ORPHA:391 Classic Hodgkin lymphoma ORPHA:168966 Composite lymphoma ORPHA:547 Non-Hodgkin lymphoma
msa-ams.be - Meervoudig Systeem Atrofie - Atrophie MultiSystématisée V.Z.W./A.S.B.L.	ORPHA:102 Multiple system atrophy
MRKH.be (België - Belgique - Belgium)	ORPHA:180068 Partial bilateral aplasia of the Müllerian ducts
Mymu Wallonie-Bruxelles ASBL	ORPHA:29073 Multiple myeloma
NET & MEN Kanker VZW België/Belgique	ORPHA:276161 Multiple endocrine neoplasia ORPHA:877 Neuroendocrine neoplasm
NF Kontakt - Vereniging voor patiënten met neurofibromatose vzw	ORPHA:637 Full NF2-related schwannomatosis ORPHA:137605 Legius syndrome ORPHA:636 Neurofibromatosis type 1

NAME OF THE BELGIAN PATIENT ORGANISATION/SUPPORT GROUP REGISTERED IN ORPHANET	(GROUP(S) OF) RARE DISORDER(S)
OSTC - Overdruksyndroom en Tarlov cysten VZW	ORPHA:238624 Idiopathic intracranial hypertension ORPHA:65250 Perineural cyst
Patienten Rat und Treff VoG: Informationen für alle Patienten der deutschsprachigen Gemeinschaft Belgiens	Rare diseases
Patiëntenvereniging Zeldzame Leverziekten vzw	ORPHA:2137 Autoimmune hepatitis ORPHA:186 Primary biliary cholangitis ORPHA:562639 Primary biliary cholangitis/primary sclerosing cholangitis and autoimmune hepatitis overlap syndrome ORPHA:171 Primary sclerosing cholangitis
P.H. België - Belgische Patiëntenvereniging voor Pulmonale Hypertensie vzw	ORPHA:422 Idiopathic/heritable pulmonary arterial hypertension
Postpolio België VZW	ORPHA:2942 Postpoliomyelitis syndrome
Prader-Willi Vlaanderen vzw	ORPHA:739 Prader-Willi syndrome
RaDiOrg - Rare Diseases Belgium - BE	Rare diseases *(see the Orphanet website for the 33 linked ORPHAcodes)*
Rare Disorders Belgium (RDB) ASBL - BE	Rare diseases *(see the Orphanet website for the 33 linked ORPHAcodes)*
Relais 22 asbl	ORPHA:567 22q11.2 deletion syndrome
RetinaPigmentosa asbl, association belge francophone de la rétinopathie d'origine génétique	ORPHA:71862 Inherited retinal disorder
Ring14 Belgium vzw	ORPHA:1440 Ring chromosome 14 syndrome
ROHHAD Association Belgium A.S.B.L.	ORPHA:293987 Rapid-onset childhood obesity-hypothalamic dysfunction-hypoventilation-autonomic dysregulation syndrome
Sang pour Sang asbl	ORPHA:232 Sickle cell anemia
Sclero'ken VZW	ORPHA:90291 Systemic sclerosis
Spierziekten Vlaanderen vzw	ORPHA:99 Autosomal dominant cerebellar ataxia ORPHA:1172 Autosomal recessive cerebellar ataxia ORPHA:166 Charcot-Marie-Tooth disease/Hereditary motor and sensory neuropathy ORPHA:337 Fibrodysplasia ossificans progressiva ORPHA:685 Hereditary spastic paraplegia ORPHA:68381 Neuromuscular disease ORPHA:98496 Rare peripheral neuropathy ORPHA:306577 Sodium channelopathy-related small fiber neuropathy
STAN Trefpunt VerSTANdelijke Handicap vzw	ORPHA:87277 Rare intellectual disability
Stichting PTEN België/Nederland - België contact	ORPHA:306498 PTEN hamartoma tumor syndrome
SUN CHILD - Prendre un enfant par la main A.S.B.L.	ORPHA:98057 Rare tumor
Syndrome Moebius Belgique ASBL - Moebius Syndroom België VZW	ORPHA:570 Moebius syndrome
Tous ensemble, main dans la main A.S.B.L.	ORPHA:68366 Lysosomal disease
Turnerkontakt vzw	ORPHA:881 Turner syndrome
URANUS - Contactgroep voor mensen met epilepsie [Contactgroep West-Vlaanderen]	ORPHA:101998 Rare epilepsy
VAGA - Vereniging voor Aangeboren GelaatsAfwijkingen vzw	ORPHA:141229 Facial cleft ORPHA:68329 Rare maxillo-facial surgical disease
VASCAPA (Vascular Anomaly Patient Association) A.S.B.L./V.Z.W.	ORPHA:68419 Vascular anomaly or angioma
VECARFA VZW - Vecarfa 22q11 Deletie Syndroom Vlaanderen	ORPHA:567 22q11.2 deletion syndrome
Vereniging Cornelia de Lange syndroom - BE (aanspreekpunt voor Nederlandstalig België)	ORPHA:199 Cornelia de Lange syndrome
Vereniging MED-SED Belgisch contactpunt	ORPHA:251 Multiple epiphyseal dysplasia ORPHA:253 Spondyloepiphyseal dysplasia and spondyloepimetaphyseal dysplasia
Vereniging voor sarcoïdosepatiënten VZW	ORPHA:90340 Blau syndrome ORPHA:797 Sarcoidosis
Vlaamse Parkinson Liga (VPL) vzw	ORPHA:2828 Young-onset Parkinson disease
von Hippel-Lindau België	ORPHA:892 Von Hippel-Lindau disease
VSH - Vereniging voor Spina Bifida en Hydrocephalus VZW	ORPHA:275543 L1 syndrome ORPHA:3388 Neural tube defect ORPHA:3176 Spina bifida-hypospadias syndrome
VVA - Vlaamse Vereniging Autisme VZW	ORPHA:168778 Rare pervasive developmental disorder
WBS - Williams-Beuren Syndroom VZW	ORPHA:904 Williams syndrome
Werkgroep Hersentumoren vzw	ORPHA:98062 Rare nervous system tumor
Wij Ook Belgium vzw	ORPHA:1331 Familial prostate cancer
XLH Belgium A.S.B.L.	ORPHA:89936 X-linked hypophosphatemia
Zebrapad VZW	ORPHA:98249 Ehlers-Danlos syndrome
ZOI - Zelfhulp Osteogenesis Imperfecta VZW	ORPHA:666 Osteogenesis imperfecta
Last update: 31Dec2022	

Many patients with rare diseases do not have a formal organisation. Please contact the **RaDiOrg helpline** ("Rare Diseases Belgium asbl/vzw") if you have non-medical questions on a specific disease:
FR: https://www.radiorg.be/fr/a-propos/helpline/
NL: https://www.radiorg.be/nl/over-ons/helpline/

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MORE INFORMATION

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