Current definitions and eligibility criteria for Belgian services and research in the global Orphanet directory of services and resaerch for rare diseases

Intro:
The Orphanet database publishes data on services and research for rare diseases of around 40 countries in the world. Data collection, validation and publication is ruled by the Orphanet Standard Operating Procedures.

In Belgium, the national Orphanet team is hosted by the WIV-ISP. The team is responsible for the collection, registration, pre-release quality control and update of Belgian information on services and research in the database.
> A request for registration of data can be filed **here (NL)** or **here (FR)**.

The present document enlists definitions, selection criteria and the responsible experts or institutes that perform the post-release quality control for the different types of data. Experts or institutes responsible for the post-release quality control are appointed by the Belgian Health Authorities.
> Only after post-release quality control the data are considered validated.

Post-release quality control or PRQC consists of having a comprehensive overview of the data content by expert resource (expert centres, diagnostic tests and labs, patient organisations, research, registries….) in order to identify inaccuracies, non relevant data, out of date data and to make recommendations on how to correct those. PRQC is an iterative process that should be performed at regular intervals of time.

The aim is to have the Belgian information in the Orphanet database validated by the end of the current Joint Action (April 2014).

Types of data on services and research registered with Orphanet:
1. Diagnostic tests & Quality data of laboratories
2. Patient organisations
3. Rare disease consultations/centers
4. Clinical trials
5. Registries (patient & mutation) and biobanks
6. Research projects

1. Diagnostic tests & Quality data of laboratories

A diagnostic test in Orphanet **is:**
- A biological analysis performed in a clinical setting to diagnose or confirm the diagnosis of a rare disease or a group of rare diseases (rare technical competence).
- A constitutional genetic test, whatever the disease prevalence.

.
>> General inclusion criteria for tests:
A test should be specific for one disease or one group of diseases (and in that case, apply to all diseases of this group) and should require a high level expertise. Tests should be performed by the medical/diagnostics laboratory itself.

>> Specific inclusion criteria depending on the type of test:
Molecular genetics : All constitutional genetic testing analyses are collected, even for non-rare diseases and pharmacogenetics.
Constitutional cytogenetics: Conventional cytogenetic analyses (karyotypes, G-banding, etc) are not registered in Orphanet (but laboratories offering such a service can be registered. In that case, we collect only information on lab contact details). Molecular cytogenetic analyses like FISH as well as molecular genetics such as MLPA or array-CGH… are registered in Orphanet esp if designed for specific microdeletion/microduplication

Remark: These definitions and criteria have been largely agreed upon by the European consortium of Orphanet partners and have been further adapted to the Belgian situation. This document will be updated as necessary. Comments or questions with regard to this document are welcome: elfriede.swinnen@wiv-isp.be

syndromes. Tests for chromosome number anomalies and ring chromosomes done by FISH (e.g. Trisomy 11) are not registered in Orphanet, as their detection does not require a specific expertise in molecular cytogenetics.
Biochemical genetics : Only tests requiring special metabolic investigation are considered (enzyme assays, key metabolites analyses, or functional assays).
Microbiology (bacteriology/virology/mycology): Belgium has recognized laboratories of reference for a list of rare infectious diseases, for these diseases only their tests will be registered.

!!: Laboratory quality assessment data is also entered in the Orphanet database, and can be consulted as it is shown for the corresponding laboratories or to specific diagnostic tests. These data concern information on the accreditation status of the laboratory or on its participation in "external quality assessment" (EQA) schemes. EQA participations can be declared by the laboratory by providing a certificate. Since 2011 four EQA providers (CEQA, CF Network, UKNEQAS cytogenetic and EMQN) supply their lists of the former year EQA participations directly to Orphanet. So for these providers (and only since 2011), the laboratory does not have to send in certificates.

Update2012: All molecular genetic testing laboratories updated their information at least once in 2012.

Post-release Quality Control (PRQC) of Belgian data on diagnostic tests:
Microbiology (bacteriology/virology/mycology): PRQC was performed by Dr Gaetan Muyldermans and Dr Sophie Quoilin of the Belgian Institute for Public Health [Dec2012]
Molecular genetics & PGx: PRQC is being done by the Belgian College of Human Genetics [Jun2013]
Constitutional cytogenetics: PRQC is being done by the Belgian College of Human Genetics [Jun2013]
Biochemical genetics : Experts for PRQC have not been appointed yet

2. Patient organisations

A patient organisation on rare diseases **is**:
- An active patient organisation or foundation which provides support for a rare disease or a group of rare diseases.
- Patient organisations on non-rare diseases also dealing with rare forms of common diseases, or with disabilities, are to be included if there is no specific organisation. Furthermore, Orphanet makes exceptions regarding a few more prevalent diseases, when these diseases are viewed as orphans by affected persons who expect to find information on these diseases on Orphanet (although these diseases are indeed non rare based on prevalence). So for these diseases it provides lists of patient organisations (and minimal information on the disease).
- Orphanet lists national patient organisations as well as European and international organisations based in Europe. Regional patient organisations may also be registered in the database if there is no national equivalent or if they are independent. Also rare-disease-specific sub-sections/contactgroups of general organisations are registered. Organizations not based in Europe but covering a disease or a group of diseases not covered by a European organisation are also registered including European contact points.

A patient organisation on rare diseases **is not:**
- A fund-raising trust/foundation that helps one/few patients with no real advice or help given to others
- A research-funding trust/foundation
- A learned society
- A blog or/and forum only

Criteria for data selection:
- In Belgium, patient organisations may be vzw/asbl, private or public foundations or contactgroups
- The organisation has to be responsive; can be contacted by telephone, e-mail, etc
- The organisation should have a designated head and/or a contact person.

Remark: These definitions and criteria have been largely agreed upon by the European consortium of Orphanet partners and have been further adapted to the Belgian situation. This document will be updated as necessary. Comments or questions with regard to this document are welcome: elfriede.swinnen@wiv-isp.be

- For an organisation with an official contact point in Belgium, the official contact point is also registered
- Umbrella organizations and national alliances, as well as patient organizations able to support and advocate for patients with any rare disease are also registered.

Update2012: All Belgian patient organisations currently in the database have been contacted and their data and scope of diseases were updated. Non-responsive organisations were removed.

Post-release Quality Control (PRQC) of Belgian patient organisations:
Representatives of RaDiOrg, the Observatorium for Chronic Diseases and the Fund of Rare Diseases and Orphan Drugs will perform this task.

3. Rare disease consultations/centers [under discussion at national & European level]

A medical management expert centre on rare diseases **is:**
A specialised or multidisciplinary centre for a rare disease (or a group of rare diseases) organised for medical management of patients or recognised as an expert centre for consultation. Centres of expertise mentioned in Orphanet should deliver a service of indisputably higher quality than a standard hospital service in the relevant speciality. This data is intended to contribute to appropriate referrals of patients to expert centres, to ease the process of second opinions between professionals, and to establish reference networks.

A medical management expert centre on rare diseases **is not:**
- A conventional specialised medical dpt without specific focus on rare diseases, even if it is a reputed one.
- A self-declared centre.

A genetic counselling centre **is**:
It is a clinic either for all genetic diseases or for a genetic disease/group of diseases

A network of expert centres **is:**
- A network of expert centres specialised in a disease (or group of diseases) with an official designation by health authorities in a country or specific funding from a well-established body
- It can be national, European or International

A network of expert centres **is not**:
- A self-declared network (same hospital or same disease without any funding)
- Clinical centres participating in the same clinical trials
- Clinical centres with expert knowledge in the same field but without official recognition.

>> At this moment, the Belgian health authorities only recognize the data on Belgian centers for rare diseases that work under a convention with the RIZIV-INAMI as validated data in Orphanet. These are the centers for cystic fibrosis, neuromuscular disorders and hereditary metabolic diseases. Also the 8 genetic centres in Belgium have official recognition for their diagnostic and counselling activities.

Like in the other Orphanet-participating member states of the EU, Belgium need to design a procedure allowing to decide on the validaty of data on expert consultations for other rare diseases. Belgium will do so by collecting and analysing data from the Belgian hospitals through an online survey. All hospitals will be contacted and all professionals already registered with Orphanet will be informed when the mapping starts. Professionals that have expressed their interest to be included in the database will also be informed in person.
At the moment no new data on rare disease *consultations* is registered in the database, certain updates to the already registered information can be done.

>> However, data on all other aspects can already be registered such as research projects, diagnostic testing, counselling, collaboration with a patient organisation, clinical trials, registries, participation in networks, ... We kindly invite you to do so.

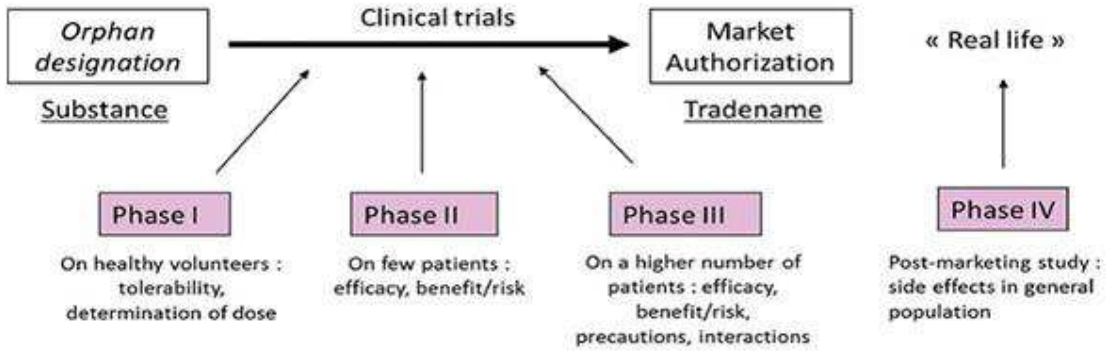
Remark: These definitions and criteria have been largely agreed upon by the European consortium of Orphanet partners and have been further adapted to the Belgian situation. This document will be updated as necessary. Comments or questions with regard to this document are welcome: elfriede.swinnen@wiv-isp.be

4. Clinical trials

A clinical trial on rare diseases **is:**
An interventional study aiming to evaluate a drug (or a combination of drugs or a biological product, etc) as treatment (or prevention…) of a rare disease (or rare form of a common disease). A clinical trial is defined nationally as it has to be regulatorily registered in each country involved.

A clinical trial on rare diseases **is not:**
A non-therapeutic clinical study, a therapeutic pre-clinical study (on animals for example).
Observational clinical studies that could be identified are registered as research projects (except for Phase IV studies that could be observational clinical trials).

Selection criteria of clinical trials:
Only ongoing or "to-be-ongoing" clinical trials that concern a rare disease/group of rare diseases or rare forms of common diseases are collected. Clinical trials conducted by both industry and research institutions are eligible. Priority is given to the international multicentric clinical trials. The phase I clinical trials are collected but not published online, unless the sponsor or the investigator expressly requires it. Clinical trials can only be registered if a protocol or brief description of the trial's objectives are available.



Update2012: Quality control updates for existing data have been done and missing trials have been identified. Pre-release quality control and registration of these trials (to work towards completeness) is planned *after* update and PRQC of existing data is finished.

Post-release Quality Control (PRQC) of data on clinical trials:
PRQC will be performed by the FAMPH, but no official experts have been appointed yet.

5. Registries and biobanks in Orphanet

A patient registry (or disease registry) on rare diseases **is:**
Any kind of systematic registry of clinical data for clinical research on a rare disease or a group of rare diseases, governed by an identified body.
The concept of coverage (regional, national, European or international) that is associated with patient registries reflects the area of collection of a single physical database, to which several clinical entities contribute.

A patient registry on rare diseases **is not:**
A study performed by recruitment of patient of a registry, i.e. clinical trial or clinical study.

Remark: These definitions and criteria have been largely agreed upon by the European consortium of Orphanet partners and have been further adapted to the Belgian situation. This document will be updated as necessary. Comments or questions with regard to this document are welcome: elfriede.swinnen@wiv-isp.be

Selection criteria of patient registries:
Patient registries on a rare disease (or group of rare diseases) should be governed by an identified body.
Cancer registries are listed only if they focus on (a) rare form(s) of cancer.

A mutation registry on rare diseases **is:**
A systematic data collection on gene mutations described as responsible for a rare disease (or group of rare diseases) with an online interface, governed by an identified body.
Mutation registries are tools for medical laboratories as well as research laboratories.

A mutation registry on rare diseases **is not:**
A collection of gene mutations without an associated phenotype.
An empty database associated with a project of data collection on gene mutations.

A biobank on rare diseases **is:**
Any kind of systematic, open-for-collaboration register of biological specimen for clinical research with a clear orientation toward the field of rare diseases.

A biobank on rare diseases **is not:**
A collection of biological material with no specificity but that might be useful in the field of rare diseases.
A private, not open for collaboration, collection.

Selection criteria of biobanks
In Orphanet, biobanks and collections of biological samples (DNA, cells, tissues, serum/plasma) produced by the scientific community conducting research on rare diseases, and who are willing to share their resources with the scientific community are listed. This excludes private collections, except if they are open for collaboration (samples available to third parties).

Post-release Quality Control (PRQC) of data on registries:
PRQC will be performed by the Institute of Public Health and the College of Human Genetics

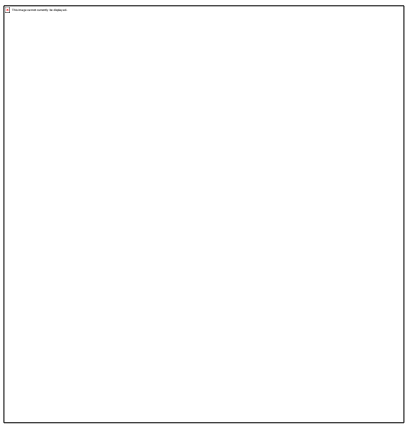
6. Research projects in Orphanet

A research project in Orphanet **is:**
An ongoing and unpublished research project explicitly focusing on a rare disease or a group of rare diseases. It is either funded by a funding body (public or private, for or not-for-profit) with a scientific committee (after competitive evaluation) or by the regular funding of a research institution.

A research project on rare diseases **is not:**
- A study on general aspects of a common disease which has rare forms (Parkinson disease, Alzheimer disease, or breast cancer, etc)
- A study on non rare diseases
- A study that could one day be applicable in the field of rare diseases but without explicit intention
- A study that has already been published e.g. with the label of the study being the title of the article in PubMed.

Selection criteria of research projects:
Research projects can only be put online if a website, a link to a protocol or a brief description of the research purpose is provided.
Projects from the following research categories can be registered.

Remark: These definitions and criteria have been largely agreed upon by the European consortium of Orphanet partners and have been further adapted to the Belgian situation. This document will be updated as necessary. Comments or questions with regard to this document are welcome: elfriede.swinnen@wiv-isp.be



A network of research projects **is:**
A collaborative research project funded by the Framework Programme of DG Research or E-Rare, clinical networks funded by DG Sanco, a multinational non-therapeutic clinical research study, a network of experts (such as Treat-NMD, ECORN-CF, PRINTO), or a network of clinical investigation centers.

A network of research projects **is not:**
An informal network, a network not funded.

Post-release Quality Control (PRQC) of data on research projects:
To be decided

Remark: These definitions and criteria have been largely agreed upon by the European consortium of Orphanet partners and have been further adapted to the Belgian situation. This document will be updated as necessary. Comments or questions with regard to this document are welcome: elfriede.swinnen@wiv-isp.be