Criteria for registration of Dutch activities in the Orphanet database

Orphanet's mission is to increase awareness and knowledge on rare disorders (RD) and ultimately contribute to improve the diagnosis, care and treatment of patients with rare diseases. One of the ways to contribute to this mission is to provide information on rare disease expertise in Europe and beyond. Therefore Orphanet provides a catalogue of expert resources in member countries. This catalogue contains information on the following activities:

1. **Expert centers**
2. **Patient organizations/Alliances**
3. **Diagnostic tests and laboratories**
4. **Clinical trials**
5. **Research projects**
6. **Patient registries**
7. **Variant Registries**
8. **Biobanks**

To determine if activities are eligible for registration in the Orphanet database a set of inclusion and exclusion criteria exist per activity. Most criteria are for general use in the entire Orphanet network, some criteria however are specific for certain countries. Underneath you can find the Orphanet inclusion and exclusion criteria per activity and, in dark red, the criteria specific for Dutch activities.

If an activity is eligible for registration and not yet present in the database, the activity can be declared via the Orphanet online registration tool, or by contacting the Dutch Orphanet team via an e-mail to orphanet@radboudumc.nl.

1. Expert centers

Definition:
An expert center is a specialized center for a rare disease or a group of rare diseases organized for the medical management and, when applicable, genetic counselling of patients.

Inclusion criteria:
- Only expert center for rare diseases officially designated by the Dutch Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport; VWS) are registered

Official source of information:
- List of officially designated expert centers for rare diseases provided by the Dutch Ministry of Health, Welfare and Sport

2. Patient organizations/alliances

Definition:
A patient organization/alliance is a non-for profit organization providing support for patients living with a rare disease, a group of rare diseases or rare forms of common diseases.

Inclusion criteria:
- Having a designated head and/or a contact person
- Being contactable by telephone and/or e-mail

Exclusion criteria:

- Fund-raising trust / foundation that helps one or several patients with no real advice or help given to others
- Research funding trust / foundation
- Blog and/or forum only

3. Diagnostic tests and laboratories

Definition:
A diagnostic tests is a test performed by a medical laboratory in a clinical setting.

General Inclusion criteria:
- Only tests requiring specific technical competence should be included

Specific inclusion criteria:
- Molecular genetics:
  - Only tests offered by medical laboratories that are part of the Vereniging Klinisch Genetische Laboratoriumdiagnostiek (VKGL) are registered
- Cytogenetics:
  - Molecular cytogenetic analyses like FISH, MLPA or array-CGH are registered only if they are designed for specific microdeletion/microduplication syndromes. Tests for chromosome number anomalies and ring chromosomes done by FISH (e.g. Trisomy 11) are not registered as their detection does not require a specific expertise in molecular cytogenetics
- Biochemical genetics:
  - Only tests requiring special metabolic investigation and allowing for establishing a diagnosis of a rare disease should be considered: enzyme assays, key metabolite analyses or functional assays when required
- Bacteriology, virology, parasitology and mycology:
  - If the country has centers/laboratories of reference for infectious diseases, only their tests should be listed for a given disease

4. Clinical trials

Definition:
A clinical trial is an interventional study evaluating a drug, medical device, protocol, gene therapy, cell therapy or a vaccine, explicitly focused on a rare disease or a group of rare diseases and authorized by the national regulatory authorities.

Exclusion criteria:
- Non-interventional/observational study or pre-clinical study
- Clinical trial on a common disease which has rare forms
- Clinical trial evaluating an intervention other than a drug, medical device, protocol, gene therapy, cell therapy or a vaccine (e.g. surgery or behavioral therapy)
- Clinical trials not authorized by the national regulatory authorities

Official sources of information:
- List of clinical trials funded by the Dutch IRDiRC consortium member The Netherlands Organisation for Health Research and Development (ZonMw) – list provided by ZonMW
- List of clinical trials present in the WHO's International Clinical Trials Registry Platform (ICTRP) database – list provided by ICTRP

5. Research projects

Definition:
A research project is an ongoing and unpublished project explicitly focused on a rare disease or a group of rare diseases, either funded by a funding body (public/private and for profit/not for profit) with a scientific committee performing a competitive selection of research projects, or by the regular national research funding.

Inclusion criteria:

- Terminated research projects that started after ZonMW joined the IRDiRC consortium (2012) are also registered for analyses purposes
- Observational clinical trial

Exclusion criteria:

- Studies on general aspects of a common disease which has rare forms (e.g. Parkinson disease, Alzheimer disease, Breast cancer)
- Studies that are too fundamental: no specific disease or a general title including some rare diseases
- Studies that could one day be applicable in the field of rare diseases but don't have that focus currently

Official sources of information:

- List of research projects funded by the Dutch IRDiRC member The Netherlands Organisation for Health Research and Development (ZonMw) – list provided by ZonMW
- List of research projects funded by the European Joint Programme on Rare Diseases (EJP RD) – list provided by EJP RD

6. Patient registries

Definition:
A patient registry is a collection of standardized information (medical and other, entered by clinicians and/or patients) about individual persons, collected in a systematic and comprehensive way for clear purposes and objectives to facilitate clinical and epidemiological research and the monitoring of care provision and therapeutic interventions for a particular rare disease, a group of rare diseases, or a rare form of a common disease, and that serves one or more predetermined scientific, clinical, or policy purposes.

Exclusion criteria:

- A study performed by recruitment of patients of a registry
- A patient registry for common disease(s)
- The clinical data collection was not performed in a systematic way (e.g. single-center database, private clinical data collection)

7. Variant registries

Definition:
A variant registry is a systematic data collection on gene variants described as responsible for a rare disease or group of rare diseases with on online interface, governed by an identified person.

Exclusion criteria:

- A collection of gene variants without associated phenotype

8. Biobanks

Definition:
A biobank is a collection of human biological samples (e.g. tissues, blood and derivatives, other body fluids, cells, DNA) and associated data such as clinical and research data, whose donors have been diagnosed with a rare disorder, a rare form of a common disorder, or can be defined by a group of rare disorders and that is to be used for research to contribute to the understanding of the physiology and diseases of humans.

Exclusion criteria:

- A collection of biological material with no specificity but that might be useful in the field of rare diseases.
- A private collection, except if it is open for collaboration