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Procedures: Orphanet inventory of rare diseases

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I. Introduction

1. Purpose/objectives

This document aims to describe how the Orphanet inventory of rare disorders is updated and maintained.

2. Disclaimer

- This publication is part of the joint action RD-Action which has received funding from the European Union's Health Programme (2014-2020).
- The content of this publication represents the views of the author only and is his sole responsibility; it can not be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

3. Range of application

The Orphanet inventory of rare disorders includes rare disorders and their subtypes but also the groups that are used to organise the Orphanet classification system. This procedure applies to every modification of the inventory. The inventory is maintained by data managers with a scientific and/or medical background.

The inventory of rare disorders is accessible through the "Rare diseases" tab on the Orphanet website, through the Orphanet Report Series "List of rare diseases and synonyms in alphabetical order », through the Orphadata website and through the Orphanet Rare diseases Ontology (ORDO).

4. References

- Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products

Procedural documents :

- Disease naming rules in English
- Linearizations rules for Orphanet classifications

5. Definitions

The Orphanet inventory of rare disorders is organised via a classification system that is based on a spectrum of entities defined by the typology below:

A Group of phenomes is a collection of clinical entities, sharing a given characteristic and are therefore classified together. Groups of phenomes can be clinically homogeneous or, on the contrary, can be used to put together clinically heterogeneous disorders for the needs of organizing the classification. In that case they are called "categories"
Example: Clinically homogeneous group of phenomes: ORPHA216 Neuronal ceroid lipofuscinosis, Category: ORPHA68385 Neurometabolic disease.

Disorders are a set of entities including diseases, syndromes, anomalies and particular clinical situations. Disorders are clinically homogeneous entities described in at least two independent individuals, confirming that the clinical signs are not associated by fortuity.

- A disease is an alteration of health status resulting from a physiopathological mechanism, and having a homogeneous clinical presentation and evolution and homogeneous therapeutic possibilities. It excludes developmental anomalies.
  Example : ORPHA313 Lamellar ichthyosis
- A malformation syndrome is a set of morphological anomalies resulting from a developmental anomaly involving more than one morphogenetic field, regardless of the cause. It includes sequences and associations.
  Example : ORPHA808 Seckel syndrome
- A clinical syndrome is a set of manifestations resulting from the alteration of a physiological state and that can be present in several diseases.
  Example : ORPHA95409 Acute adrenal insufficiency
- A morphological anomaly is a set of anomalies resulting from a developmental anomaly involving only one morphogenetic field. It includes isolated anomalies and anatomical variants.
  Example : ORPHA3384 Truncus arteriosus
- A biological anomaly is an alteration of the normal values of biological entities.
  Example: ORPHA209893 Congenital isolated thyroxine-binding globulin deficiency
- A particular clinical situation is a set of manifestations presenting as a subset of a disease under particular circumstances.
  Example: ORPHA90066 Pneumonia caused by Pseudomonas aeruginosa infection

Subtypes are a set of sub-forms of a disorder that could be clinical, aetiological or pathological, histopathological.

- A clinical subtype is a subset of a disorder defined by a distinct clinical presentation.
  Example: ORPHA314911 Severe Canavan disease
- An aetiological subtype is a subset of a disorder defined by its causes, and is clinically indistinguishable from other aetiological subtypes.
  Example: ORPHA98794 Angelman syndrome due to maternal 15q11q13 deletion
- A histopathological subtype is a subset of a disorder defined on the basis of its histological aspect.
  Example: ORPHA251601 Fibrillary astrocytoma

This typology is available only via Orphadata and ORDO.

A rare disorder is defined according to the European legislation defining a prevalence threshold of not more than five affected persons per 10’000 (Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products)

Every entity of the inventory is defined by:

- An ORPHA number: unique identifier attributed randomly by the database and stable through time.
- A preferred term: the most generally accepted name in the medical community.
- Synonyms: perfect equivalents in the scope of the preferred term they are attached to. As many synonyms as necessary are added to a preferred term.

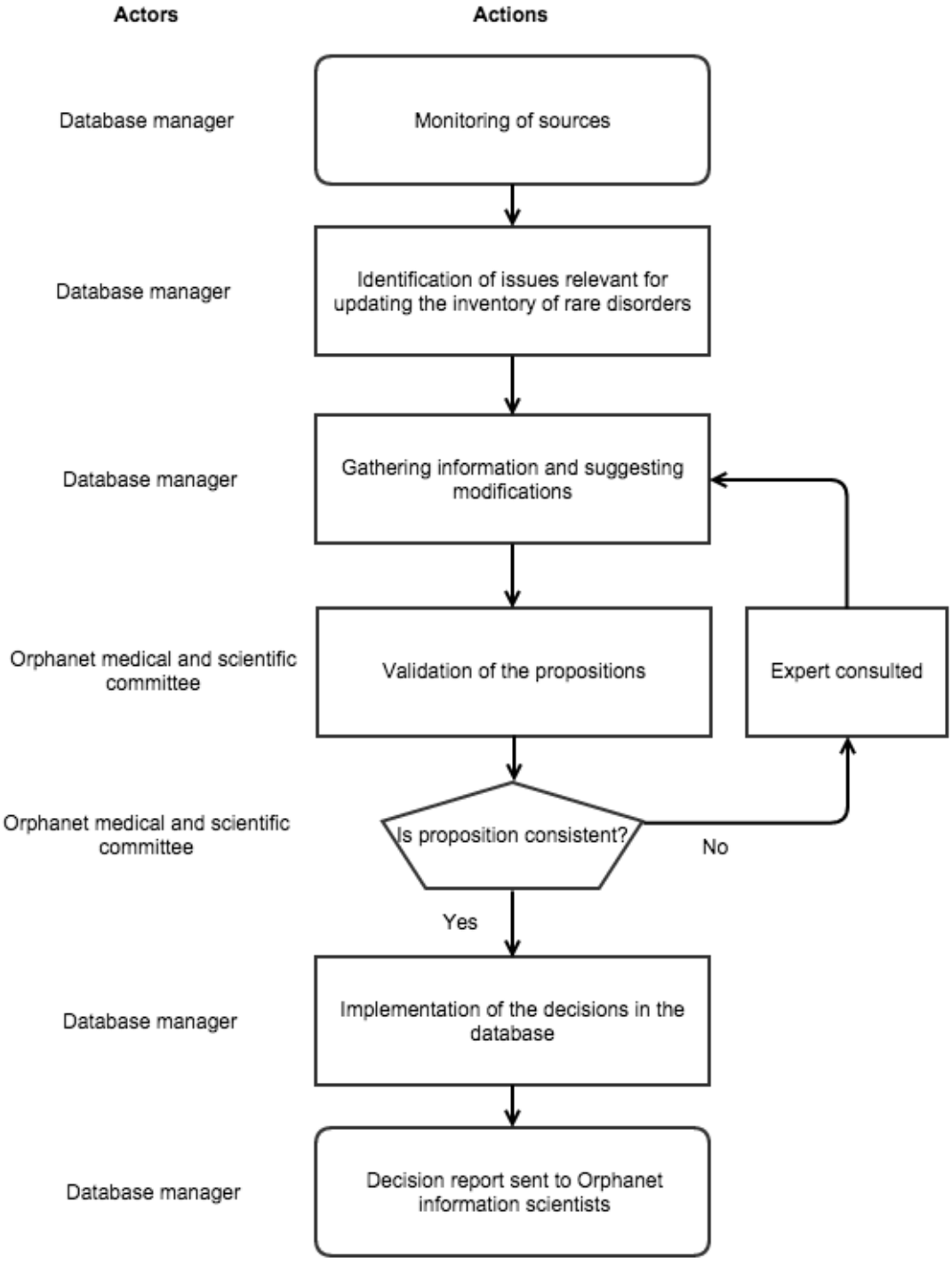
- Acronyms: included only when actually used in literature. Convenience acronyms used in Orphanet summaries that have no use in the scientific community are not included. Several entities can share the same acronym.
- Keywords : significant terms for a disease or group of disease that are usefully retained for redirecting users to relevant diseases, but do not fit the defining criteria of a preferred name, a synonym or an acronym.

6. Filing and updates

This procedure is updated annually and as often as necessary by one of the data managers. The most up-to-date version is available on the Orphanet website:
http://www.orpha.net/orphacom/cahiers/docs/GB/eproc_Orphanet_inventory_rare_diseases_PR_R1_Nom_04.pdf

II. METHODOLOGY

1. Flowchart



2. Description

The Orphanet inventory of rare disorders is updated on a monthly basis. Sources for update are:

- International scientific literature (peer-reviewed publications);
- Advice from experts consulted for the revision of the Orphanet encyclopaedia for professionals and of the Orphanet classification system;
- Existing resources in the field of rare diseases collected by Orphanet (medical laboratories, expert centers, research projects, clinical trials, orphan drugs...);
- Suggestions from users of the Orphanet database.
- Internal quality control.

Every source is monitored in order to identify:

- Newly described disorders;
- New information modifying the medical definition of an already listed disorder;
- New consensual medical classifications.

Decisions on any modification of the inventory are agreed upon at a monthly meeting held by a medical and scientific committee within Orphanet, constituted by medical doctors and scientists.

The data managers gather material about every issue identified by the sources above in order to suggest modifications to the inventory. All material is submitted to the medical and scientific committee. When the material gathered is not sufficient to formulate a consistent proposal, experts are identified and consulted to complete the dossier. Decisions are made case by case and actions include:

- Creation of a new entity (newly described entities/lacking entities);
- Modification of an entity already in the database (e.g. nomenclature, hierarchical relationships with its subtypes and/or the group of disorders it belongs to);
- Identification of a historical entity (e.g. an entity described before the advent of the genetic era (the 90's) for which there have been no further publications);
- Obsolete erroneous entries (e.g. duplicated entities) or groups that are not used anymore. In the case of duplicates, a "referred to" relationship is created between the obsoleted entity and its duplicate kept in the inventory of rare disorders.
- Deprecated entities when they no longer exist per se but have been recognised by the scientific community as being another entity. In this case, a "moved to" relationship is established between both entities in order to redirect users on the targeted entity.

For each new entity, decisions are made on:

- The typology of the entity (group, disease, syndrome, subtype, etc.);
- The classifications it belongs to, including the classification in which it is linearised (see in references

the procedural document on linearisation rules for Orphanet classifications);

- Nomenclature (the main name of the disease in English and in French, all its synonyms, acronyms and key words if needed).

A meeting report is published internally after each meeting. Every information scientist in Orphanet implements the decisions made with regards to his own activity in order to attain completeness and coherence of the database.

The minutes of the meeting are also sent to the Orphanet national teams along with a summary table and a ready-to-translate table in order to inform them and to obtain translations of the names of the new entries in the languages in which the inventory of rare disorders is translated (English, French, German, Italian, Spanish, Portugese, Polish and Dutch).

For any questions or comments, please contact us: contact.orphanet@inserm.fr

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