orphanet

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LINEARIZATION RULES FOR ORPHANET CLASSIFICATIONS

Procedural document

Table of contents

Table of contents **2**
Introduction **3**
I. Purpose 3
II. Disclaimer 3
III. Range of application 3
IV. Archiving 3

General principles **4**
I. Compatibility with typing and hierarchy 4
II. Default rule 5

Priority rules between classifications **6**
I. Developmental anomalies 6
II. Neoplasms of specified sites 7
III. Infectious diseases 7
IV. Inborn errors of metabolism 7
V. Multisystem diseases 7

Decisions for specific diseases and groups **8**
I. Linearized as developmental anomalies 8
II. Linearized as systemic and rheumatologic diseases 9
III. Linearized as endocrine diseases 9
IV. Linearized as neurologic diseases 9
V. Linearized as skin diseases 9

Introduction

I. Purpose

All Orphanet disorders in the database are included in the Orphanet classification of rare diseases. This classification follows a principle of polyhierarchy: a disorder is set in all classifications corresponding to medical specialties to which it is relevant. Entities can have as many parents as needed.

Nevertheless, in order to sort out rare diseases by medical specialty and to avoid multiple countings, it is necessary to have a monohierarchical view available – *a linearization* – in which a disease belongs to one medical specialty only.

The purpose of this document is to formalize the rules for this linearization. It describes how to select for every rare disease included in the Orphanet database a medical specialty which has precedence.

The Orphanet linearization is distinct from the linearizeations of the World Health Organization's 11th International Classification of Diseases (ICD-11).

II. Disclaimer

There is no firm scientific ground to ascribe many of the rare diseases to a specialty rather than another. It is acknowledged that the linearization in such instances can be somewhat arbitrary. The linearization must be regarded as a conventional framework, not as a scientific statement.

III. Range of application

The linearization of Orphanet diseases is managed by a dedicated information scientist, under responsibility of the scientific direction.

IV. Archiving

Document archived on the Reggae\maladies server

Path: P:\PROCEDURES\Linearization rules

General principles

I. Compatibility with typing and hierarchy

The Orphanet classification of rare diseases has three kinds of entities (*phenomes*):

- **group of phenomes:** a collection of different types of phenomes, sharing a given characteristic and therefore being classified together
- **disorder**: a specific level of description among the following possibilities:
  - *biological anomaly*: An alteration of the normal values of biological entities. Example: hypertransferrinemia.
  - *clinical syndrome*: A set of manifestations resulting from the alteration of a physiological state and that can be present in several diseases. Examples: nephrotic syndrome, hepatic failure.
  - *disease*: An alteration of health status resulting from a physiopathological mechanism, and having a homogeneous clinical presentation and evolution and homogeneous therapeutic possibilities. Excludes developmental anomalies.
  - *malformation syndrome*: A set of morphological anomalies resulting from a developmental anomaly involving more than one morphogenetic field, regardless of the cause. Includes sequences and associations.
  - *morphological anomaly*: A set of anomalies resulting from a developmental anomaly involving only one morphogenetic field. Includes isolated anomalies and anatomical variants.
- **subtype**: a subset of a disorder among the following possibilities:
  - *clinical subtype*: defined by a distinct clinical presentation.
  - *etiological subtype*: defined by causes, and clinically indistinguishable from other etiological subtypes.
  - *histological subtype*: defined on the basis of its histological aspect.
  - *particular clinical situation in a disease or syndrome*: a set of manifestations presenting as a subset of a disease under particular circumstances.

Linearization parents must be attributed to ensure a strict top-to-bottom and bottom-to-top compatibility.

- Primary decisions are made at the disorder level.
- Subtypes inherit the linearization of their parent at the disorder level.
- Groups of phenomes are not linearized.

II. Default rules

Linearization parents are selected among the topmost entities in the classification.

ORPHA57146	Rare hepatic disease
ORPHA68329	Rare maxillo-facial surgical disease
ORPHA68367	Inborn errors of metabolism
ORPHA68416	Rare infectious disease
ORPHA89826	Rare skin disease
ORPHA93419	Rare bone disease
ORPHA93626	Rare renal disease
ORPHA93890	Rare developmental defect during embryogenesis
ORPHA96344	Rare gynecologic and obstetric disease
ORPHA97929	Rare cardiac disease
ORPHA97935	Rare gastroenterologic disease
ORPHA97955	Rare respiratory disease
ORPHA97962	Rare surgical thoracic disease
ORPHA97965	Rare surgical cardiac disease
ORPHA97966	Rare eye disease
ORPHA97978	Rare endocrine disease
ORPHA97992	Rare hematologic disease
ORPHA98004	Rare immune disease
ORPHA98006	Rare neurologic disease
ORPHA98023	Rare systemic and rheumatologic disease
ORPHA98026	Rare odontologic disease
ORPHA98028	Rare circulatory system disease
ORPHA98033	Rare psychiatric disease
ORPHA98036	Rare otorhinolaryngologic disease
ORPHA98047	Rare infertility disease
ORPHA98050	Rare allergic disease
ORPHA101433	Rare urogenital disease
ORPHA108999	Rare intoxication
ORPHA165711	Rare abdominal surgical disease
ORPHA250908	Rare neoplastic disease
ORPHA280879	Rare particular clinical situation

Rare genetic disease (ORPHA98053) must not used as a linearization parent.

When a disease is included in multiple classifications corresponding to various medical specialties, the priority is given to the specialty:

- corresponding to the most severely affected body system;
- corresponding with the most determining involvement for the prognosis;
- corresponding with the specialist most likely to be relied on for the management of the disease.

Priority rules between certain classifications are described in the following section.

Priority rules between classifications

I. Developmental anomalies

Generally, the classification as developmental anomaly has priority over the classification as disease of the affected body system. The linearization parent is *ORPHA93890 Rare developmental defect during embryogenesis.*

In particular:

- **Developmental anomalies of the heart**: to be linearized under *ORPHA93890 Rare developmental anomalies during embryogenesis*, rather than under *ORPHA97965 Rare surgical cardiac disease.*
- **Developmental anomalies of the circulatory system,** including angiomas : to be linearized under *ORPHA93890 Rare developmental anomalies during embryogenesis*
- **Rare teratologic diseases**: both included in their own classification and in the classification of developmental anomalies. To be linearized under *ORPHA93890 Rare developmental anomalies during embryogenesis.*

Exceptions:

- **Developmental anomalies of the teeth**: to be linearized under *ORPHA98026 Rare odontologic disease.*
- **Bone disorders**:
  - Primary morphological anomalies of bones (*Dysostoses, ORPHA364559*) are linearized as developmental anomalies: the linearization parent is *ORPHA93890 Rare developmental defect during embryogenesis.*
  - Diseases of the bone tissue (*Primary bone dysplasias, ORPHA364526*) are linearized as bone diseases: the linearization parent is *ORPHA93419 Rare bone disease.*

II. Neoplasms of specified sites

For malignant tumours, the classification as neoplasm has priority over the classification as disease of the relevant body system. The linearization parent is *ORPHA250908 Rare oncologic disease.*

For benign tumours, the classification as disease of the relevant body system has priority.

For endocrine tumours, formerly known as carcinoid tumours, the classification as neoplasm has priority over the classification as endocrine disease. The linearization parent is *ORPHA250908 Rare oncologic disease.*

III. Infectious diseases

The classification as infectious disease has priority over the classification as disease of the relevant body system. The linearization parent is *ORPHA68416 Rare infectious diseases.*

IV. Inborn errors of metabolism

When the disease affects only one specific organ, it is linearized as a disease of this specific organ.

When the disease affects several organs, it is linearized as a metabolic disease under *ORPHA68367 Inborn errors of metabolism.*

V. Multisystem diseases

They are linearized under *ORPHA98023 Rare systemic or rheumatologic disease.*

Decisions for specific diseases and groups

In the following list, decisions made for a group apply to all disorders included in it, unless specified otherwise.

I. Linearized as developmental anomalies

Linearization parent: *Rare developmental defects during embryogenesis (ORPHA93890)*

- Congenital vascular bone syndromes (ORPHA235832)
  - e.g. Angio-osteohypertrophic syndrome (ORPHA2346)
- Disorders of sex development (ORPHA90771)
- Ectodermal dysplasias (ORPHA79373)
- Immuno-osseous dysplasias (ORPHA169349)
- Joubert syndrome and related disorders (ORPHA140874)
- Malformation syndromes with hamartosis (ORPHA98196)
- Neurofibromatosis type 1 (ORPHA636)
- Syndromes with deafblindness
  - e.g. Usher syndrome (ORPHA886)
- Syndromes with deafness associated with pigmentary anomalies
  - Albinism - deafness syndrome (ORPHA998)
  - Ermine phenotype (ORPHA999)
  - Ocular albinism - late-onset sensorineural deafness (ORPHA1000)
  - Waardenburg syndrome (ORPHA3440)
  - Deafblind hypopigmentation syndrome, Yemenite type (ORPHA3214)
  - Deafness - white hair - contractures - papillomas (ORPHA3215)
  - Deafness - vitiligo - achalasia (ORPHA3239)
  - Tietz syndrome (ORPHA42665)
  - Ocular albinism with congenital sensorineural deafness (ORPHA352740)
- Syndromic intellectual disabilities, included in the Orphanet database in the group *Rare intellectual disabilities with developmental anomaly* (ORPHA102369). (Non-syndromic intellectual disabilities on the other hand are linearized as neurologic diseases.)

II. Linearized as systemic and rheumatologic diseases

Linearization parent: *Rare systemic and rheumatologic disease (ORPHA98023)*

- Amyloidoses (ORPHA69) when multisystemic. On the other hand, localized amyloidoses are linearized at the relevant body system.
- Ehlers-Danlos syndromes (ORPHA98249)
- Langerhans cell histiocytoses (ORPHA389)
- Non-histaminic angioedemas (ORPHA658)
- Vasculitides (ORPHA52759)

III. Linearized as endocrine diseases

Linearization parent: *Rare endocrine disease (ORPHA97978)*

- Primary lipodystrophies (ORPHA90970)
- Rare dyslipidemias (ORPHA101953)
- Rare parathyroid diseases and phosphocalcic metabolism disorders (ORPHA68415)

IV. Linearized as neurologic diseases

Linearization parent: *Rare neurologic disease (ORPHA98006)*

- Leukodystrophies (ORPHA68356)
- Non-syndromic intellectual disabilities, included in the database in the group *Rare intellectual disability without developmental anomaly* (ORPHA101685). (Syndromic intellectual disabilities on the other hand are linearized as develomental anomalies.)
- Non-infectious myosites. On the other hand, infectious myosites, included in the database in the group *Infectious, fungal or parasitic myopathies (ORPHA206988)* follow the general rule giving priority to the classification as infectious disease.
- Neurovascular diseases, except malformations

V. Linearized as skin diseases

Linearization parent: Rare skin disease (ORPHA89826)

- Cutis laxa (ORPHA209)
- Inherited epidermolysis bullosa (ORPHA79361)
- Ichthyoses (ORPHA79354)
- Oculocutaneous albinisms (ORPHA55)
- Trichothiodystrophy (ORPHA33364)

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