Coding Rare Disorders: Introduction to the Orphanet nomenclature

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European Rare Kidney Disease Network
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Why code Rare Disorders?

• **Make RD visible** in order to:
  – Have sound epidemiological data
  – Produce evidence for public health & health economics
  – Document the natural history of RD
  – Identify patients from health records for clinical research

• Different systems are using **different terminologies**
  – Need for inter-operability

• Need **to have a common language** to allow for sharing clinical data between health care centres and databases and registries:
  – Patients are rare and scattered
  – Significant amounts of data are necessary to perform research
How does the Orphanet nomenclature respond to RD coding needs?
Orphanet RD nomenclature

 Around 6,000 Rare Disorders

<table>
<thead>
<tr>
<th>ORPHA number</th>
<th>Preferred label</th>
<th>Synonyms</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORPHA:98672</td>
<td>Autosomal dominant optic atrophy</td>
<td>ADOA</td>
</tr>
<tr>
<td>ORPHA:893</td>
<td>WAGR syndrome</td>
<td>Del(11)(p13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deletion 11p13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Monosomy 11p13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wilms tumor-aniridia-genitourinary anomalies-intellectual disability syndrome</td>
</tr>
<tr>
<td>ORPHA:231169</td>
<td>Usher syndrome type 1</td>
<td>USH1</td>
</tr>
</tbody>
</table>

- The only nomenclature **specific for RD**
- **Unique, stable ORPHA number**
- **Definitions**
- 9 languages (En, Es, De, Fr, It, Nl, Pt, Pl, Cz)
- Cross-referenced with medical terminologies/databases (ICD-10, SNOMED-CT, OMIM...)
- Peer-reviewed publications only (2 cases<RD<1/2000)
Orphanet RD classification

- **Why?**
  - Representation of knowledge
  - Epidemiology and statistics studies

- **How?**
  - Organized by medical specialties

**Multi-dimensional**

**Multi-hierarchical**

**Stickler syndrome**

- Orphanet classification of rare developmental anomalies during embryogeny
- Classification of sucking/swallowing disorders
- Orphanet classification of rare genetic diseases
- Orphanet classification of rare eye diseases
- Orphanet classification of rare bone diseases
- Orphanet classification of rare otorhinolaryngological diseases
- Orphanet classification of rare surgical maxillo-facial diseases

**Orphanet classification of rare otorhinolaryngological diseases**

- Rare otorhinolaryngologic disease ORPHA:98036
  - Syndrome or malformation associated with head and neck malformations ORPHA:156237
    - Rare disease with Pierre Robin syndrome ORPHA:138044
      - Pierre Robin syndrome associated with collagen disease ORPHA:138041
        - Stickler syndrome ORPHA:828
  - Rare otorhinolaryngologic disease ORPHA:98036
    - Rare deafness ORPHA:68361
      - Syndromic genetic deafness ORPHA:90642
        - Stickler syndrome ORPHA:828
Logical structure

Group

**Disorder:** statistical reporting

- Disease, clinical syndrome, malformation syndrome, morphological anomaly, biological anomaly, particular clinical situation

Subtype:

- Etiological, clinical, histopathological
More information
How Orphanet nomenclature can be used for coding?
Coding a patient with the nomenclature

**First option**
Search in the nomenclature just like in a dictionary

- Several results
- Level of precision is unknown
- Relationships between ORPHA are unknown
Coding a patient with the classification

Second option
Search in the nomenclature and confirm your choice within the classification

Rare neurological disease
Leukodystrophy

Alexander
- Type 1
- Type 2

Canavan
- Severe
- Mild

Krabbe
- Infantile
- Late-infantile
- Adult

Pelizaeus-Merzbacher
- Connatal
- Classic
- Transitional
- Carriers

Pelizaeus-Merzbacher-like
Coding a patient with the classification

Second option
Search in the nomenclature and confirm your choice within the classification

Rare neurological disease

Leukodystrophy

Pelizaeus-Merzbacher

Pelizaeus-Merzbacher-like

Alexander

Canavan

Krabbe

Type 1

Type 2

Severe

Mild

Infantile

Infantile

Late-infantile

Adult

Connatal

Classic

Transitional

Carriers
Refine the diagnosis

Rare neurological disease

Leukodystrophy

- Alexander
  - Type 1
  - Type 2
- Canavan
  - Severe
  - Mild
- Krabbe
  - Infantile
  - Late-infantile
  - Adult
- Pelizaeus-Merzbacher
  - Connatal
  - Classic
  - Transitional
  - Carriers
- Pelizaeus-Merzbacher-like

Allow for improvement in the precision of diagnosis
Diagnosis pathway

Rare neurological disease

Leukodystrophy

Alexander
- Type 1
- Type 2

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- Infantile
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Carriers
Rare neurological disease

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Diagnosis pathway

Rare neurological disease

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Allow for assessment of the diagnosis pathway
Unsolved cases

Rare neurological disease

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Pelizaeus-Merzbacher-like

Allow for identification of patients even without a confirmed diagnosis
Aggregation of data: from local to European level

Rare neurological disease

Leukodystrophy

- Pelizaeus-Merzbacher
- Pelizaeus-Merzbacher-like

Alexander
- Type 1
- Type 2

Canavan
- Severe
- Mild

Krabbe
- Infantile
- Late-infantile
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Sound data for epidemiological estimate of the 6,000 RD 
Independently of the precision of the diagnosis
Aggregation of data: from local to European level

Rare neurological disease

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  - Carriers

Answer *many and varied questions in different settings*

How many patients suffering from leukodystrophy are seen within a European network?
Where can you find the Orphanet nomenclature?
Dissemination media

- Information on a specific disorder
- Computational use nomenclature, alignments, classification
- Computational analysis logical inference
Orphadata: Rare diseases and cross referencing file

Here are XSD (XML Schema Definitions) and JPEG representations for this product.

<table>
<thead>
<tr>
<th>Language</th>
<th>Files</th>
<th>Number</th>
<th>Size</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>German</td>
<td><a href="http://www.orphadata.org/data/xml/de_product1.xml">http://www.orphadata.org/data/xml/de_product1.xml</a></td>
<td>9663</td>
<td>25.82 MB</td>
<td>3 Oct 18</td>
</tr>
</tbody>
</table>

Xml and Json files in 9 languages

**Updates:** 1st Monday of every month

**Content:** 9,000 groups, disorders and sub-types

<table>
<thead>
<tr>
<th>ORPHA numbers</th>
<th>Names &amp; syn</th>
<th>Typology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitions</td>
<td>Alignments</td>
<td>(group, disease, malformation syndrome, ...)</td>
</tr>
<tr>
<td></td>
<td>(exact or nearby)</td>
<td>Attributes</td>
</tr>
<tr>
<td></td>
<td>ICD10, OMIM, UMLS, MeSH, MedDRA</td>
<td>Historical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deprecated (with referrals)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Categories</td>
</tr>
</tbody>
</table>
Orphadata differentials
https://github.com/Orphanet/Orphadata.org
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https://github.com/Orphanet/Orphadata.org
In the near future...
Provide a **unique server** to give access to

- the Orphanet nomenclature (ORPHA numbers, names and definitions)
- the classification
- the mappings with ICD10/ICD11
- versionning AND differentials

Develop tools to help coding process

- visualise and **browse the classification**
- help to identify the ORPHA for statistical reporting
How can ERNs contribute to the nomenclature

disease.orphanet@inserm.fr

**ERNs:**
- Identify a coordinator for the task
- Identify the scope
  - Which groups?
  - Organization of the classification?
  - ICD-10 alignements?
  - Production of definitions?
- Identify the capacity of work
- Identify the timeframe

**Orphanet:**
- Introduce the nomenclature principles
- Assess the extent of the demand
- Propose methodology/tools
- Propose a timeline
Thank you for your attention