I.   Rare diseases and functional consequences

The Orphanet inventory of rare diseases is annotated with activity limitation/participation restriction (functional consequences), using the Orphanet Functioning Thesaurus, derived and adapted from the International Classification of Functioning, Disability and Health – Children and Youth (ICF-CY, WHO 2007).

The information provided is assessed taking into account the whole patient population affected by the disease, receiving standard care and management (specific and/or symptomatic management, prevention and prophylaxis, devices and aids, care and support). Functioning is divided into different abilities, tasks and activities.. Disability therefore involves limitation of activity or restriction of participation, described as functional consequences.

Each functional consequence is annotated with the following:

- Frequency in the patient population:
    - Very frequent: more than 80%
    - Frequent: between 30% and 80%
    - Occasional: fewer than 30%

- Temporality:
    - Permanent limitation/restriction: the functional consequence is present throughout the life of the patient. It can be congenital, secondary to loss of a skill or a participation. It can be a direct or indirect consequence of the disease or of its treatment.
    - Transient limitation/restriction: the functional consequence occurs during acute episodes, periodic crises or relapses. It resolves or reduces spontaneously or by the action of a treatment or care.
    - Delayed acquisition: a skill or a participation is performed later than by a healthy person.

- Degree of severity:
    - Low: activity or participation can be carried out with little difficulty by the patient alone.
    - Moderate: activity or participation can be carried out with some technical and/or human assistance
    - Severe: activity or participation cannot be carried out without substantial technical and/or human assistance.
    - Complete: activity or participation cannot be carried out, even with technical and/or human assistance.
    - Unspecified: limitation/restriction is difficult to quantify or highly variable between patients (ranging from 'Low' to 'Complete').

- Loss of ability when relevant, defined by the progressive and definitive loss of a skill or participation over the course of the disease.

A functional limitation is stated to be « undefined » when the current knowledge does not enable information about the extent of the consequences on daily life to be provided.

The unaffected activities and participation are not listed.

Environmental factors that may have an impact on the daily activities of the patients are also identified and listed when possible.

Description of the XML tags

- **DisorderDisabilityRelevanceList count**: total number of clinical entities (disorders, group of disorders or subtypes) in the Xml file.
- **Orphanum**: unique identifying number assigned by Orphanet to a given clinical entity.
- **ExpertLink**: stable URL pointing to the specific page of the given clinical entity on the Orphanet website.
- **Disorder_Name:** preferred name of a given clinical entity.
- **Lang:** ISO 639 code for language names.
- **DisorderGroup**: can be either Group of disorders, Disorder or Subtype of disorder *(see definitions in annex).*
- **DisorderType**: can be either Disease, Clinical syndrome, Malformation syndrome, Biological anomaly, Morphological anomaly, Category, Clinical group, Etiological subtype, Clinical subtype, Histopathological subtype or Particular clinical situation in a disease or syndrome *(see definitions in annex).*
- **DisabilityDisorderAssociationList count:** total number of functional consequences or environmental factors identified for a given clinical entity.
- **DisabilityCategory:** the category can be either "Activity limitation/participation restriction", "No functional disability" or "Not applicable". Functional consequences are identified only if the category "Activity limitation/participation restriction" is relevant for the given clinical entity. If the category "Not applicable" is indicated, see the "ReasonForNotApplicable" field.
- **ReasonForNotApplicable:** for a given disease, if the category is "Not applicable", a reason is identified and can be either "Hypervariable functioning", "Early death-causing disease" or "Not applicable for another reason".
- **DisabilityID**: unique identifying number assigned to a functional consequence or an environmental factor.
- **AnnotationDate:** date of the annotation of the given clinical entity.
- **StatusDisability:** status of the validation of the given clinical entity's annotation. Can be either Validated or Not yet validated.
- **FrequenceDisability:** frequency of the functional consequence in the given population. Can be either "very frequent", "frequent" or "occasional".
- **TemporalityDisability:** temporality of the functional consequence in the given population. Can be either "permanent limitation/restriction", "transient limitation/restriction" or "delayed acquisition".
- **SeverityDisability:** severity of the functional consequence in the given population. can be either "low", "moderate", "severe", "complete" or "Unspecified".
- **LossOfAbility:** defined as a progressive and definitive loss of a skill or ability over the course of the disease. Can be either **"**yes" or "no".
- **SourceOfValidation:**source of validation of the given clinical entity's annotation.
- **SpecificManagement:** can be either **"**yes" or "no". The functional consequences or

environmental factors are evaluated based on the average limitation of all patients (infants, children, adolescents, adults) receiving standard care and management (specific treatment, symptomatic treatment). If specific management protocol is known for the given disease, this field will indicate "y" for yes and all the annotations will have been conducted considering this specific management protocol.

- **Type:** can be either "Disability" (functional consequence) or "Environmental factor".
- **Defined:** If the relationship between the given clinical entity and the functional consequences or the environmental factor is defined by a severity, temporality and frequency then the value given will be "y" (for yes). If the relationship is not defined, the value will be "n" (for no).

Example

<DisorderDisabilityRelevanceList count="**XXXX**">

    XXXX is the total number of clinical entities in this XML file

<OrphaNumber>**893**</OrphaNumber>
 <Name lang="**en**">**WAGR syndrome**</Name>

    The main name of the clinical entity is "WAGR syndrome" with 893 as its ORPHA number

<DisorderGroup id="**36547**">
<Name lang="**en**">**Disorder**</Name></DisorderGroup>

    The entity is a disorder, not a group, not a subtype.

<DisorderType id="21401">
<Name lang="**en**">**Malformation syndrome**</Name></DisorderType>

    The entity is a malformation syndrome, not a Disease, Clinical syndrome, Malformation syndrome, Biological anomaly, Morphological anomaly or Particular clinical situation in a disease or syndrome.

<SourceOfValidation>Expert</SourceOfValidation>
   <SpecificManagement>n</SpecificManagement>
   <Online>y</Online>
   <AnnotationDate>2018-06-29 00:00:00.0</AnnotationDate>
   <StatusDisability id="27327">
    <Name lang="en">Validated</Name>
   </StatusDisability>
   <DisabilityCategory id="27278">
    <Name lang="en">Activity limitation/participation restriction</Name>
   </DisabilityCategory>
   <ReasonForNotApplicable/>
  </DisorderDisabilityRelevance>

    The entity was annotated on 29/06/2008. The annotation was validated by an expert and described as an "Activity limitation/participation restriction" for the given disease.

<DisabilityDisorderAssociationList count="91">

    The entity was annotated with 91 functional consequences and/or environmental

factors.

```xml
<DisabilityDisorderAssociation id="74963">
    <Disability id="4">
     <Name lang="en">Seeing/watching</Name>
    </Disability>
    <FrequenceDisability id="27201">
     <Name lang="en">Very frequent</Name>
    </FrequenceDisability>
    <TemporalityDisability id="27180">
     <Name lang="en">Permanent limitation</Name>
    </TemporalityDisability>
    <SeverityDisability id="27236">
     <Name lang="en">Moderate</Name>
    </SeverityDisability>
    <LossOfAbility>n</LossOfAbility>
    <Type>Disability</Type>
    <Defined>y</Defined>
</DisabilityDisorderAssociation>
```

The given entity has been annotated with a functional consequence (disability) named "Seeing/watching". This limitation appears to be very frequent, of moderate severity and of permanent temporality in the given entity. It is not progressive (the loss of capacity is indicated as "no").

```xml
<DisabilityDisorderAssociation id="74964">
    <Disability id="5">
     <Name lang="en">Hearing/listening</Name>
    </Disability>
    <FrequenceDisability id="27208">
     <Name lang="en">Frequent</Name>
    </FrequenceDisability>
    <TemporalityDisability id="27187">
     <Name lang="en">Acquisition delay</Name>
    </TemporalityDisability>
    <SeverityDisability id="27271">
     <Name lang="en">Unspecified</Name>
    </SeverityDisability>
    <LossOfAbility>n</LossOfAbility>
    <Type>Disability</Type>
    <Defined>y</Defined>
</DisabilityDisorderAssociation>
```

The given entity has been annotated with a functional consequence (disability) named " Hearing/listening". This limitation appears frequent, of unspecified severity and leads to a delay in acquisition in the given entity. It is not progressive (the loss of capacity is indicated as "no").