orphadata science

WHAT IS THE ORPHANET RARE DISEASE ONTOLOGY (ORDO)?

V4.2

June 2025

GLOBAL CORE BIODATA RESOURCE

elixir Core Data Resource

IRDiRC RECOGNIZED RESOURCES

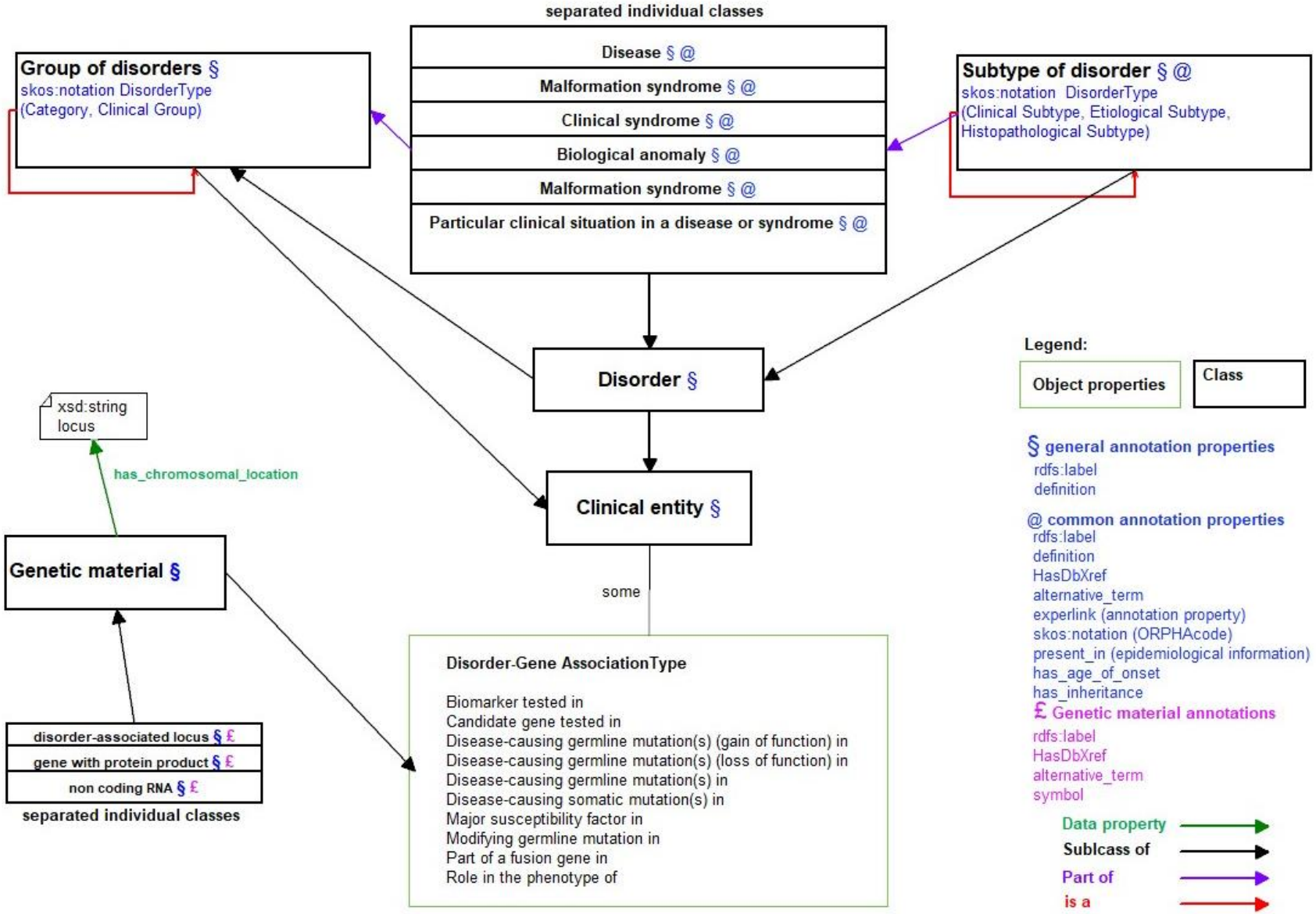
orphanet

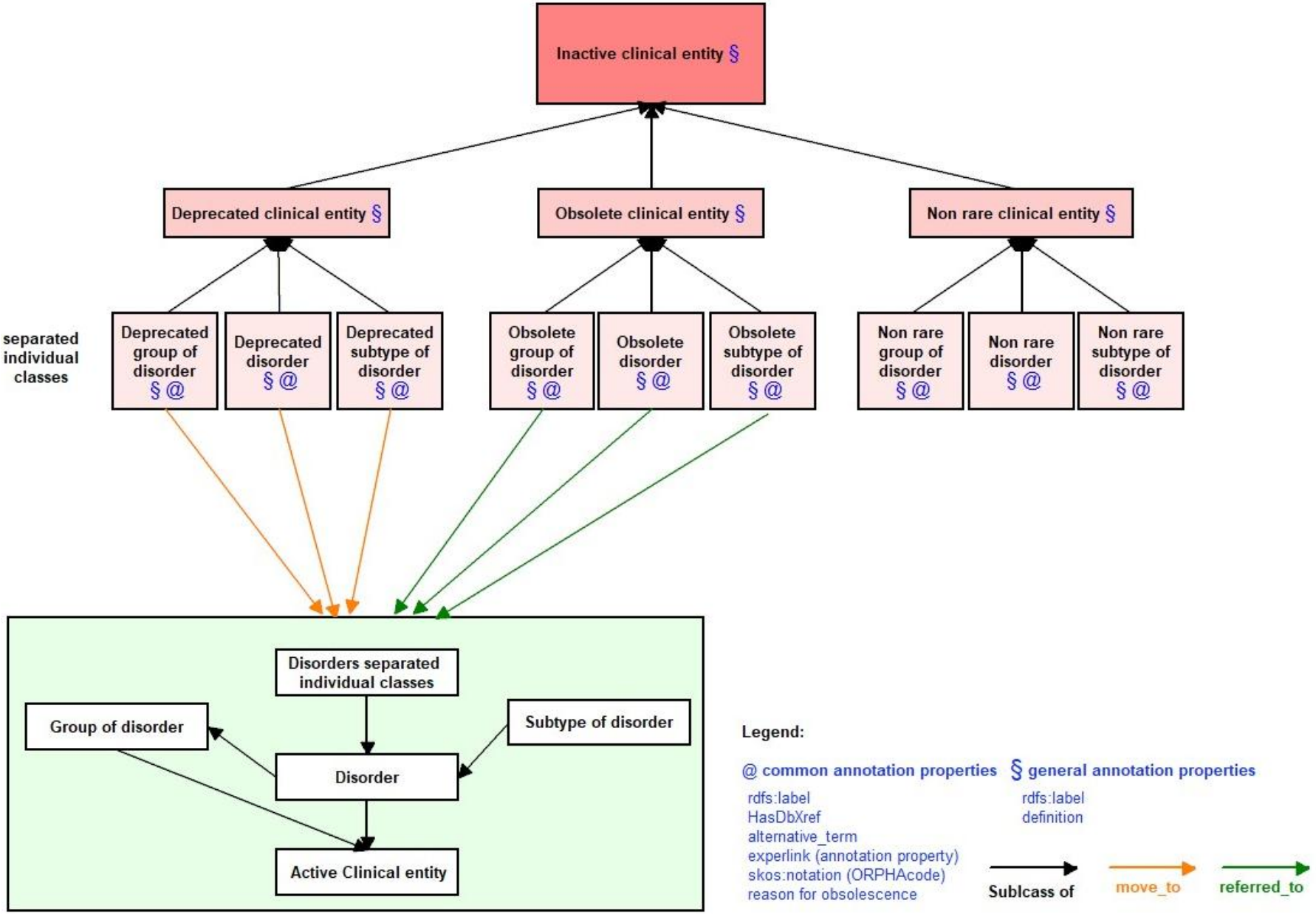
INTRODUCTION

The Orphanet Rare Disease ontology (ORDO) was jointly developed by Orphanet and the EBI to provide a structured vocabulary for rare diseases capturing relationships between diseases, genes and other relevant features which will form a useful resource for the computational analysis of rare diseases. It derived from the Orphanet database (www.orpha.net), a multilingual database dedicated to rare diseases populated from literature and validated by international experts. It integrates a nosology (classification of rare diseases), relationships (gene-disease relations, epidemiological data) and connections with other terminologies (MeSH, UMLS, MedDRA, Gard), databases (OMIM, UniProtKB, HGNC, ensembl, Reactome, IUPHAR, Genatlas, Mondo) or classifications (ICD-10, ICD-11). The ontology is maintained by Orphanet. Orphanet classifications can be browsed in the OLS view. The Orphanet Rare Disease Ontology is updated every six months and follows the OBO guidelines on deprecation of terms. It constitutes the official ontology of rare diseases produced and maintained by Orphanet (INSERM, US14).

ORDO is accessible on several websites:

- Link to ORDO on Orphadata website
- Link to SPARQL Endpoints for ORDO on Orphadata website
- Link to ORDO on Bioportal
- Link to ORDO on EBI website


separated individual classes
Disease § @
Malformation syndrome § @
Clinical syndrome § @
Biological anomaly § @
Malformation syndrome § @
Particular clinical situation in a disease or syndrome § @
Group of disorders §
skos:notation DisorderType
(Category, Clinical Group)
Subtype of disorder § @
skos:notation DisorderType
(Clinical Subtype, Etiological Subtype, Histopathological Subtype)
Disorder §
Clinical entity §
xsd:string
locus
has_chromosomal_location
Genetic material §
some
Disorder-Gene AssociationType
Biomarker tested in
Candidate gene tested in
Disease-causing germline mutation(s) (gain of function) in
Disease-causing germline mutation(s) (loss of function) in
Disease-causing germline mutation(s) in
Disease-causing somatic mutation(s) in
Major susceptibility factor in
Modifying germline mutation in
Part of a fusion gene in
Role in the phenotype of
disorder-associated locus § £
gene with protein product § £
non coding RNA § £
separated individual classes
Legend:
Object properties
Class
§ general annotation properties
rdfs:label
definition
@ common annotation properties
rdfs:label
definition
HasDbXref
alternative_term
experlink (annotation property)
skos:notation (ORPHAcode)
present_in (epidemiological information)
has_age_of_onset
has_inheritance
£ Genetic material annotations
rdfs:label
HasDbXref
alternative_term
symbol
Data property
Subclass of
Part of
is a


Inactive clinical entity §
Deprecated clinical entity §
Obsolete clinical entity §
Non rare clinical entity §
separated individual classes
Deprecated group of disorder § @
Deprecated disorder § @
Deprecated subtype of disorder § @
Obsolete group of disorder § @
Obsolete disorder § @
Obsolete subtype of disorder § @
Non rare group of disorder § @
Non rare disorder § @
Non rare subtype of disorder § @
Disorders separated individual classes
Group of disorder
Subtype of disorder
Disorder
Active Clinical entity
Legend:
@ common annotation properties
rdfs:label
HasDbXref
alternative_term
experlink (annotation property)
skos:notation (ORPHAcode)
reason for obsolescence
§ general annotation properties
rdfs:label
definition
Sublcass of
move_to
referred_to

Briefly, In ORDO, there are 3 SuperClass : "**Clinical entity", which is central, "Genetic material" and "Inactive clinical entity"**.

SuperClass	Definition
clinical entity	A generic term used to describe the clinical items included in the Orphanet nomenclature of rare diseases.
genetic material	DNA or RNA sequence (gene with protein product, non-coding RNA and disorder-associated locus).
Inactive clinical entity	A clinical entity that has been excluded from the Orphanet nomenclature. This includes obsolete entities, deprecated entities, and entities that have been inactivated because they are not rare in Europe.

Note that "Group of disorders", "Disorder" and "Subtype of disorder" are subclasses of **"Clinical entity" SuperClass**, all of them representing the classification of rare diseases. These classes have poly-parental relations.

SubClassOF "Clinical Entity"	Definition
SubClassOF "Group of disorders"	Group of disorders (A collection of clinical entities sharing a set of common features.)
Category	A group of clinically heterogeneous disorders sharing one general feature, used to organise the classification
Clinical group	A group of clinically homogeneous disorders that share a similar etiology, course, outcome, and/or management
SubClassOF "Disorder"	Disorder (A clinical entity characterised by a set of homogeneous phenotypic abnormalities and evolution allowing a definitive clinical diagnosis.)
disease	A disorder with homogeneous therapeutic possibilities and an identified pathophysiological mechanism. Developmental anomalies are excluded.
biological anomaly	A disorder defined by a set of physiological abnormalities without clearly associated clinical manifestations.
clinical syndrome	A disorder with homogeneous therapeutic possibilities, regardless of the pathophysiological mechanism involved.

malformation syndrome	A disorder resulting from a developmental anomaly involving more than one morphogenetic field. Malformative sequences and associations are included.
morphological anomaly	A disorder characterised by a morphological alteration resulting from a development anomaly involving a single morphogenetic field.
particular clinical situation in a disease or syndrome	A set of phenotypic abnormalities presenting in a subset of patients under particular circumstances.
SubClassOF "Subtype of disorder"	Subtype of a disorder (Subdivision of a disorder according to a positive criterion.
clinical subtype	Subdivision of a disorder according to distinct clinical characteristics (severity, age of onset, particular clinical signs, etc.).
etiological subtype	Subdivision of a disorder according to distinct causes resulting in a similar clinical Presentation.
histopathological subtype	Subdivision of a disorder according to characteristic histological pattern.

The SuperClasse **“Genetic material”** has 3 SubClass. There are describe below.

SuperClass	SubClasseOf	Definition
genetic material	disorder-associated locus	Chromosomal region associated with a hereditary disorder but without any precision on the possible associated gene.
	gene with protein product	DNA sequence translated into protein.
	non coding RNA	RNA transcript not translated into protein.

The SuperClasse **“Inactive clinical entity”** is dedicated to gathering all clinical entities that has been excluded from the Orphanet nomenclature. This includes obsolete entities, deprecated entities, and entities that have been inactivated because they are not rare in Europe. Note that superclass keeps itself the same structure as the classification of rare diseases.

SubClassOF "Inactive clinical entity"	**Definition**
SubClassOF "deprecated clinical entity"	A clinical entity that was initially considered as an independent diagnosis, but is now considered as part of another diagnosis as a result of the evolution of knowledge, and is therefore removed from the Orphanet nomenclature
deprecated group of disorder	A group of disorder that was initially considered as an independent diagnosis, but is now considered as part of another diagnosis as a result of the evolution of knowledge, and is therefore removed from the Orphanet nomenclature.
deprecated disorder	A disorder that was initially considered as an independent diagnosis, but is now considered as part of another diagnosis as a result of the evolution of knowledge, and is therefore removed from the Orphanet nomenclature.
deprecated subtype of disorder	A subtype of disorder that was initially considered as an independent diagnosis, but is now considered as part of another diagnosis as a result of the evolution of knowledge, and is therefore removed from the Orphanet nomenclature.
SubClassOF "non rare clinical entity"	A clinical entity that does not meet the European definition of a rare disease (less than 5 affected individuals per 10,000 in Europe) in light of current epidemological knowledge, and has therefore been removed from the Orphanet nomenclature.
non rare group of disorder	A group of disorder that does not meet the European definition of a rare disease (less than 5 affected individuals per 10,000 in Europe) in light of current epidemological knowledge, and has therefore been removed from the Orphanet nomenclature.
non rare disorder	A disorder that does not meet the European definition of a rare disease (less than 5 affected individuals per 10,000 in Europe) in light of current epidemological knowledge, and has therefore been removed from the Orphanet nomenclature.
non rare subtype of disorder	A subtype of disorder that does not meet the European definition of a rare disease (less than 5 affected individuals per 10,000 in Europe) in light of current epidemological knowledge, and has therefore been removed from the Orphanet nomenclature.
SubClassOF "obsolete clinical entity"	A clinical entity that has been removed from the Orphanet nomenclature for one of the following reasons: exact duplicate of another existing clinical entity; unclear clinical entity that cannot be precisely characterised; only one published case in the literature; organisational category that is no longer in use.

obsolete group of disorder	A group of disorder that has been removed from the Orphanet nomenclature for one of the following reasons: exact duplicate of another existing clinical entity; unclear clinical entity that cannot be precisely characterised; only one published case in the literature; organisational category that is no longer in use.
obsolete disorder	A disorder that has been removed from the Orphanet nomenclature for one of the following reasons: exact duplicate of another existing clinical entity; unclear clinical entity that cannot be precisely characterised; only one published case in the literature; organisational category that is no longer in use.
obsolete subtype of disorder	A subtype of disorder that has been removed from the Orphanet nomenclature for one of the following reasons: exact duplicate of another existing clinical entity; unclear clinical entity that cannot be precisely characterised; only one published case in the literature; organisational category that is no longer in use.

Definition of properties in ORDO

Property	Definition
biomarker tested in	A gene in which a variation is used to monitor disorder activity and/or patient outcome.
candidate gene tested in	A gene in which a mutation is suspected, but not yet proven, to be responsible for a disorder, but for which a genetic test (s) is (are) available
disease-causing germline mutation(s) (gain of function) in	A mutation of a gene in a germ cell that results in a new function of the corresponding protein is sufficient to cause the disorder and can be transmitted to the offspring.
disease-causing germline mutation(s) (loss of function) in	A mutation of a gene in a germ cell that alters the function of the corresponding protein is sufficient to cause the disorder and can be transmitted to the offspring.
disease-causing germline mutation(s) in	A mutation of a gene in a germ cell that is sufficient to cause the disorder and can be transmitted to the offspring.
disease-causing somatic mutation(s) in	A mutation of a gene in a somatic cell that is sufficient to cause the disorder but can not be transmitted to the offspring.
major susceptibility factor in	A gene mutation in a germ cell that predisposes to the development of a disorder, and that is necessary but not sufficient to develop the disorder.
part of a fusion gene in	A coding or regulatory DNA sequence from a gene that has fused with another coding and/or regulatory DNA sequence from a different gene.
role in the phenotype of	A gene included in a chromosomal rearrangement, and proved to have a major influence in the phenotype of the chromosomal rearrangement.

modifying germline mutation in	A gene mutation in a germ cell that modifies the clinical presentation of the disorder and that can be passed on to offspring.
part_of	Relation between two clinical entities, one being included in the other. Ex : clinical subtype part_of disease.
moved_to	In some cases, “Deprecated clinical entities” have a “Moved to” association, for appropriate redirection towards the active clinical entity that must be used instead of the deprecated entity.
Referred_to	The majority of “Obsolete clinical entities” have a “Referred to” association, as a suggestion inviting the user to consult the Orphanet classification in order to identify the most appropriate active clinical entity of replacement according to the diagnosis information.
has_chromosomal location	Relationship between a gene with protein product, non-coding RNA or disorder-associated locus and its cytogenetic location on the chromosome.
present_in	Relationship between a clinical entity and the geographical area for which epidemiological data (Epidemiology) is available.
has_age_of_onset	Relationship between clinical entity and age of onset.
has_inheritance	Relationship between a clinical entity and modes of inheritance.
‘Historical entity’	Historical entity: a clinical entity for which no new information has been published in the literature since the advent of the genetic era in the 1990s, but is considered as a distinct phenotype and is therefore kept in the Orphanet nomenclature
Expertlink	Stable URL pointing to the specific page of a given disease on the Orphanet website.

Categories of properties in ORDO

Has_age_of_onset	
adolescent	From 12 to 18 years.
adult	From 19 to 65 years.
all ages	From birth to adulthood without peak of onset.
antenatal	Before birth.
childhood	From 2 to 11 years.
ederly	After 65 years.
infancy	From the end of the fourth week to the 23rd month of life.

neonatal	From birth to the fourth week of life.
no age of onset data available	No information is available in the scientific literature on the age of onset of the first clinical manifestations.

Has_inheritance	
autosomal dominant	Pattern of inheritance in which a single mutated allele located on one of the 22 autosomes (non-sex chromosomes) is sufficient to express the phenotype.
autosomal recessive	Pattern of inheritance in which two mutated alleles of the same gene located on one of the 22 autosomes (non-sexual chromosomes) are needed to express the phenotype.
mitochondrial	Pattern of inheritance in which a mutation in one of the mitochondrial genes is sufficient to express the phenotype. The transmission is exclusively maternal.
multigenic/multifactorial	The combination of one or more genes and/or environmental factors contributes to the expression of the phenotype.
no inheritance data available	No information is available in the scientific literature on heredity of the clinical entity.
not genetically inherited	clinical entity without genetic inheritance.
oligogenic	The combination of mutated alleles of two or more genes is necessary to express the phenotype.
semi-dominant	Pattern of inheritance in which a single mutated allele located on one of the 22 autosomes (non-sex chromosomes) suffices to express the phenotype, the phenotype of the homozygous individual being more severe, when both alleles are mutated.
unknown inheritance	Hereditary clinical entity whose mode of inheritance is unknown.
X-linked dominant	Pattern of inheritance in which a single mutated allele on the X chromosome is sufficient to express the phenotype. The phenotype is more consistently and severely expressed in hemizygous boys (having only one copy of the gene) than in heterozygous girls.
X-linked recessive	Pattern of inheritance in which two mutated alleles on the X chromosome are needed to express the phenotype. The phenotype is expressed in hemizygous boys (having only one copy of the gene) and homozygous girls.
Y-linked	Pattern of inheritance in which a single mutated allele on the Y chromosome is sufficient to express the phenotype. The transmission is exclusively paternal.

To exploit ORDO, SPARQL queries can be use on SPARQLendpoint, virtuoso, blazegraph or other tools who permit SPARQL queries.

These are examples of queries that you can use:

Example 1:

Getting a concept label from Orphanumber.

```
PREFIX ordo:<http://www.orpha.net/ORDO/>
PREFIX w3: <http://www.w3.org/2000/01/rdf-schema#>
SELECT ?label
WHERE {
ordo:Orphanet_558 w3:label ?label
}
```

Example 2:

Getting a concept label and alternative term from Orphanumber.

```
PREFIX ordo:<http://www.orpha.net/ORDO/>
PREFIX ebi: <http://www.ebi.ac.uk/efo/>
PREFIX w3: <http://www.w3.org/2000/01/rdf-schema#>
SELECT ?label ?alternativeterm
WHERE {
ordo:Orphanet_1187 w3:label ?label.
ordo:Orphanet_1187 ebi:alternative_term ?alternativeterm
}
```

Example 3:

Getting the genetic material linked to more than 10 disorders

```
PREFIX ordo:<http://www.orpha.net/ORDO/>
PREFIX w3: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX owl: <http://www.w3.org/2002/07/owl#>

SELECT ?gene ?geneLab ?nbD
WHERE{
  {
    SELECT ?g  (COUNT(?d) as ?nbD)
```

```
    WHERE {
      ?r owl:onProperty ?rel.
      ?g w3:label ?gLabel.
      ?g w3:subClassOf ?r.
      ?g w3:subClassOf ?class.
      ?class w3:subClassOf ?sc.
      filter (?sc = ordo:Orphanet_C010)
      ?r owl:someValuesFrom ?d.
    }
    GROUP BY ?g
  }
  filter (?nbD > 10)
  BIND (?g as ?gene)
  ?gene w3:label ?geneLab.
}
ORDER BY DESC(?nbD)
```

Example 4:

Getting the label and mapping information about a concept.

```
PREFIX owl: <http://www.w3.org/2002/07/owl#>
PREFIX obo: <http://purl.obolibrary.org/obo/>
PREFIX dc: <http://purl.org/dc/elements/1.1/>
PREFIX xsd: <http://www.w3.org/2001/XMLSchema#>
PREFIX rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
PREFIX oboInOwl: <http://www.geneontology.org/formats/oboInOwl#>
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX Orphanet_: <http://www.orpha.net/ORDO/Orphanet_#>
PREFIX ORDO: <http://www.orpha.net/ORDO/>
select ?s ?p ?o WHERE {
?s ?p ?o.
optional {?o ?m ?v.
?v rdfs:label ?e}.
```

```
filter (?s = ORDO:Orphanet_558)

}

ORDER BY ?o)
```

LEXICON

EMBL-EBI: European Bioinformatics Institute

HGNC: *HUGO Gene Nomenclature Committee*

HIPBI-RD: Harmonising phenomics information for a better interoperability in the RD field

ICD-10: International Classification of Diseases 10th

ICD-11: International Classification of Diseases 11th

INSERM: Institut national de la santé et de la recherche médicale

IUPHAR: International Union of Basic and Clinical Pharmacology

MedDRA: Medical Dictionary for Regulatory Activities

MeSH: Medical Subject Headings

Mondo: The Mondo Disease Ontology

OBO: OBO format is the text file format used by OBO-Edit, the open source, platform-independent application for viewing and editing ontologies.

OLS: Ontology Lookup Service

OMIM: *Online Mendelian Inheritance in Man*

ORDO: Orphanet Rare Disease Ontology

RD-Action: Rare Diseases Action

UMLS: *Unified Medical Language System*

UniProtKB: UniProt Knowledgebase

Authors : Orphadata Team

WHAT IS THE ORPHANET RARE DISEASE ONTOLOGY (ORDO) ? V4.2, June 2025

https://www.orphadata.com/docs/WhatIsORDO.pdf

Co-Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HADEA. Neither the European Union nor the granting authority can be held responsible for them

Inserm

MINISTÈRE
DU TRAVAIL, DE LA SANTÉ,
DES SOLIDARITÉS
ET DES FAMILLES
Liberté
Égalité
Fraternité

Co-funded by
the European Union