Rare Diseases
Nomenclature and classification

Annie Olry

ORPHANET - Inserm US14, Paris, France

annie.olry@inserm.fr

Using standards and embedding good practices to promote interoperable data sharing in ERNs

26 Apr 2017

Orphanet RD nomenclature

ORPHA number	Preferred label	Synonyms
ORPHA:93545	Renal or urinary tract malformation	CAKUT
		Congenital anomalies of kidney and urinary tract
ORPHA:216	Neuronal ceroid lipofuscinosis	NCL
ORPHA:586	Cystic fibrosis	CF
		Mucoviscidosis
ORPHA:355	Gaucher disease	Acid beta-glucosidase deficiency
		Glucocerebrosidase deficiency
ORPHA:77259	Gaucher disease type 1	Non-cerebral juvenile Gaucher disease

- The only clinical terminology specific for rare diseases
- Unique, stable ORPHA number
- Definitions
- 8 languages (En, Fr, Es, It, Nl, De, Pt, Pl)
- Peer-reviewed publications only (2 cases<RD<1/2000)

Search for a **rare disease**

Search
Search by sign
Classifications
Genes
Disability
Encyclopaedia for patients
Encyclopaedia for professionals
Emergency guidelines
Sources/procedures

Disease name *

Search

(*) mandatory field

- (●) Disease name
- ( ) OMIM
- ( ) Gene name or symbol
- ( ) Orpha number
- ( ) ICD-10

Usher syndrome

Suggest an update

Disease definition

Usher syndrome (US) is characterized by the association of sensorineural deafness (usually congenital) with retinitis pigmentosa and progressive vision loss.

ORPHA:886

Synonym(s):

Retinitis pigmentosa-deafness syndrome

USH

Prevalence: **1-9 / 100 000**

Inheritance: **Autosomal recessive**

Age of onset: **Infancy, Neonatal**

ICD-10: **H35.5**

OMIM: 276900 276901 276902 276904 500004 601067 602083 602097 605472 606943 611383 612632 614504 614869 614990

UMLS: **C0271097**

MeSH: **D052245**

GARD: 7843

MedDRA: **10063396**

RD classification

- **Why?** → Improve information
  Epidemiology and statistics studies
- **How?** → Organized by medical specialties
- **Particularity** → Systemic disorders

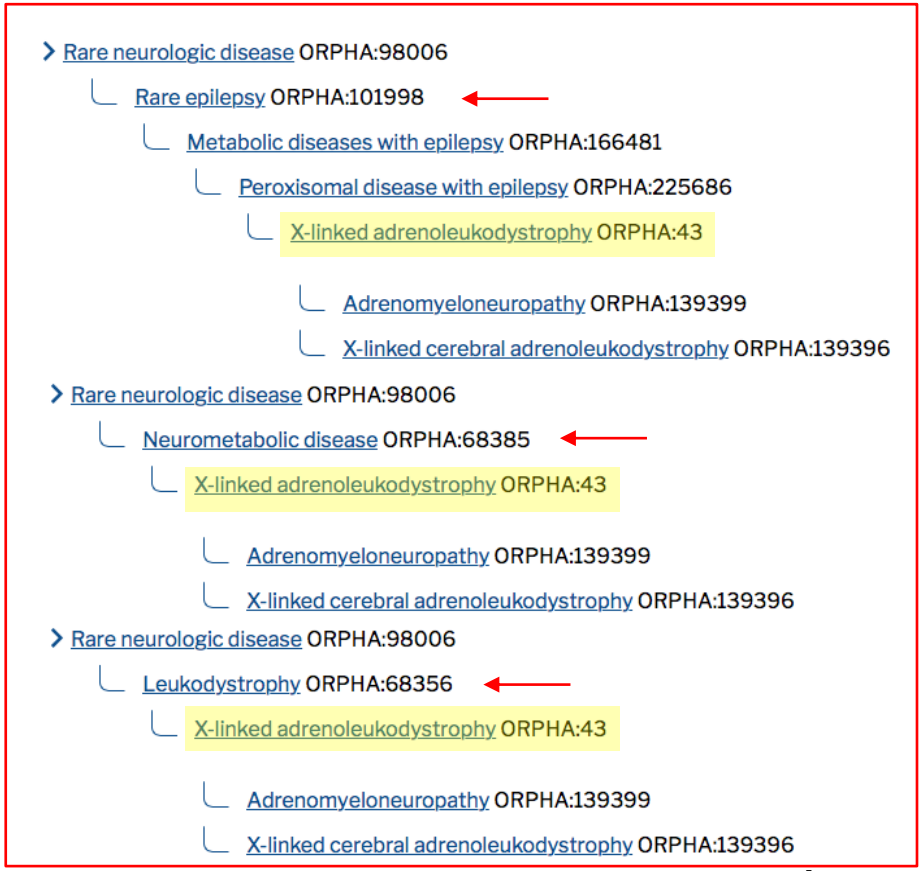
Multi- classification

Multi-dimensional

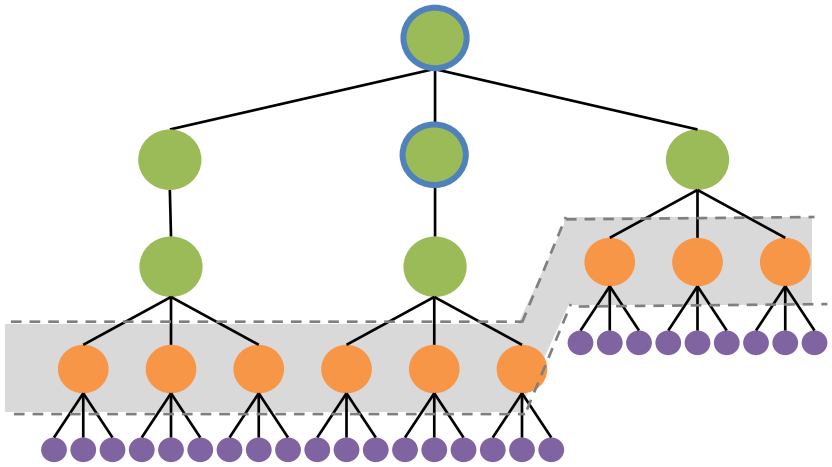
X-linked adrenoleukodystrophy

- Orphanet classification of rare inborn errors of metabolism
- Orphanet classification of rare genetic diseases
- Orphanet classification of rare neurological diseases
- Orphanet classification of rare endocrine diseases
- Orphanet classification of rare infertility disorders

Multi-hierarchical



Logical structure



Group

Category: clinically heterogeneous

Clinical group: clinically homogeneous

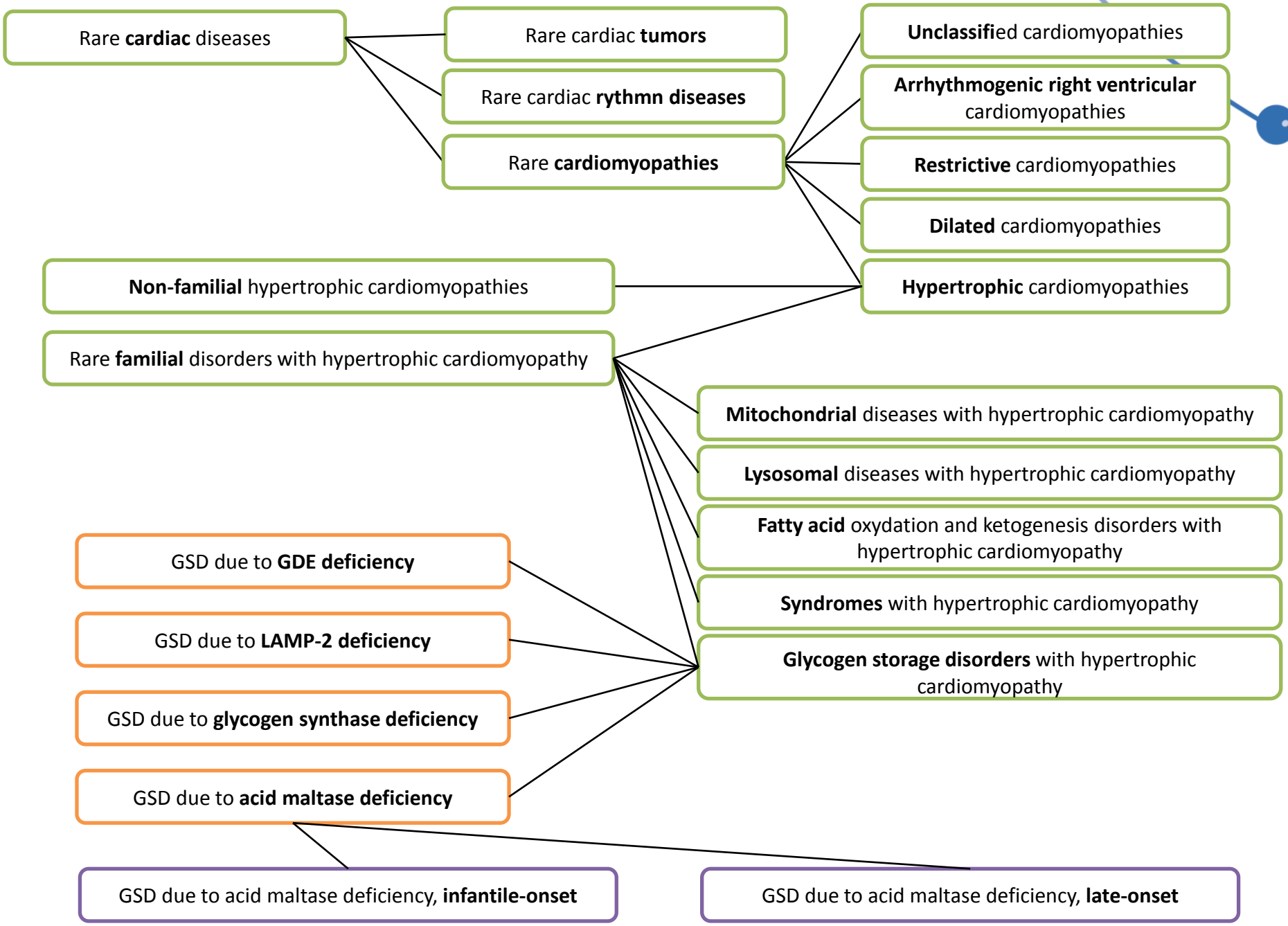
Disorder:

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

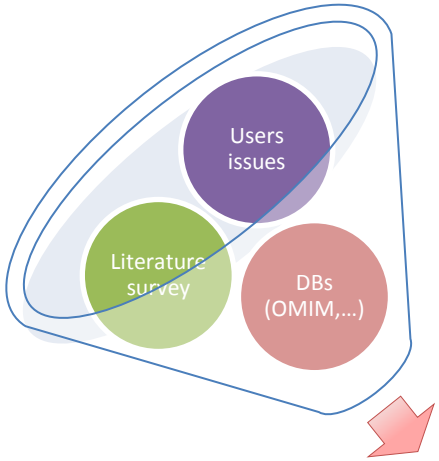
Subtype:

- Clinical, etiological, histopathological

- Every entity is **meaningful**
- Entities are **disjointed**
- **Parts** are added to form the **wholes**
- **Transitivity** applies at every level


Rare **cardiac** diseases
Rare cardiac **tumors**
Rare cardiac **rythmn diseases**
Rare **cardiomyopathies**
Unclassified cardiomyopathies
Arrhythmogenic right ventricular cardiomyopathies
Restrictive cardiomyopathies
Dilated cardiomyopathies
Hypertrophic cardiomyopathies
Non-familial hypertrophic cardiomyopathies
Rare **familial** disorders with hypertrophic cardiomyopathy
Mitochondrial diseases with hypertrophic cardiomyopathy
Lysosomal diseases with hypertrophic cardiomyopathy
Fatty acid oxydation and ketogenesis disorders with hypertrophic cardiomyopathy
Syndromes with hypertrophic cardiomyopathy
Glycogen storage disorders with hypertrophic cardiomyopathy
GSD due to **GDE deficiency**
GSD due to **LAMP-2 deficiency**
GSD due to **glycogen synthase deficiency**
GSD due to **acid maltase deficiency**
GSD due to acid maltase deficiency, **infantile-onset**
GSD due to acid maltase deficiency, **late-onset**

Update process



Orphanet DB verification, literature search, expert advice

Verification of prevalence, database and classification consistency

Decision
Disease committee

Qualify the demand

Creation

Modification

New entry

Reject

+ info

Nomenclature

Obsolescence

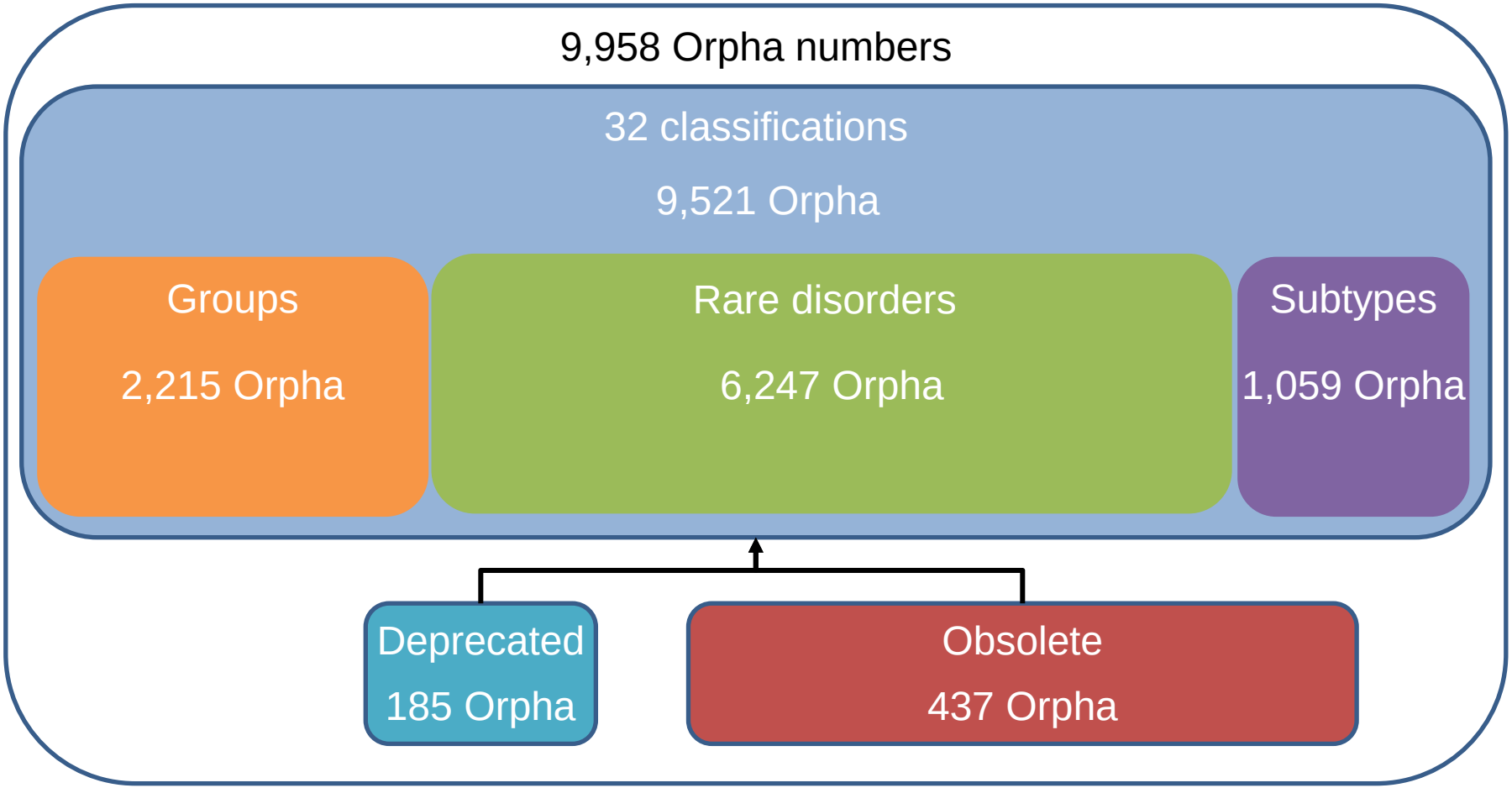
Deprecation

Expert advice

Impact on the inventory → New Orpha numbers, Status modification

Impact on the classification → New hierarchy including new orpha numbers consitency inter- and intra-classification

Some figures



Mappings with other terminologies

Terminology	mapped	RD
ICD-10	Manually	All
OMIM	Manually	4,390
Snomed-CT	Manually	3,800
GARD	Semi-automatically	2,998
UMLS	Semi-automatically	2,885
MeSH	Semi-automatically	1,763
MedDRA	Semi-automatically	1,224

Qualifier	
E	exact mapping (the terms and the concepts are equivalent)
NTBT	narrower term maps to a broader term
BTNT	broader term maps to a narrower term
W	incorrect mapping (two different concepts)
ND	not yet decided/unable to decide

ICD10 codes only :	
Specific code	The term has its own code in the ICD10
Inclusion term	The term is included under a ICD10 category and has not its own code
Index term	The term is oncluded in ICD10 index and refers to one more general code
Attributed code	The term does not exist in ICD10 and a code was attributed by Orphanet

Coding perspective

Orpha number	Preferred label	Synonyms	Typology	Status	ICD-10	Definition/relationship
ORPHA:93545	Renal or urinary tract malformation	CAKUT Congenital anomalies of kidney and urinary tract	Category	_	_	_
ORPHA:216	Neuronal ceroid lipofuscinosis	NCL	Clinical group	_	E75.4	Yes
ORPHA:586	Cystic fibrosis	CF Mucoviscidosis	Disease	_	E84.0 E84.1 E84.8 E84.9	Yes
ORPHA:355	Gaucher disease	Acid beta-glucosidase deficiency Glucocerebrosidase deficiency	Disease	_	E75.2	Yes
ORPHA:1245	BIDS syndrome	Amish brittle hair syndrome Trichothiodystrophy type D	Disease	Deprecated	_	moved to Trichothiodystrophy
ORPHA:77259	Gaucher disease type 1	Non-cerebral juvenile Gaucher disease	Subtype	_	E75.2	yes
ORPHA:101042	Taussig-Bing syndrome		Subtype	Obsolete	_	Refered to Double outlet right ventricle with subpulmonary ventricular septal defect

Orpha Code

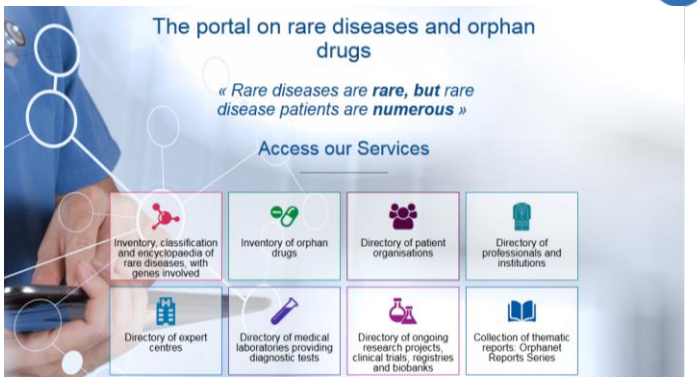
=

Orpha numbers used to be assigned to a patient within an information system

Users and information media

Health professionals
Patients
Public health stakeholders

→ Information on a specific disorder



R&D
Public health stakeholders
HIS

→ Computational use subset of disorders/data

R&D

→ Computational analysis logical inference

ordo
Orphanet Rare Disease Ontology

Similarities and differences

orphanet

Updated daily

- Orpha numbers in use
- **deprecated** disorders

orphadata

xml format

Updated monthly

- Orpha numbers in use
- **deprecated** disorders

ordo

Orphanet Rare Disease Ontology

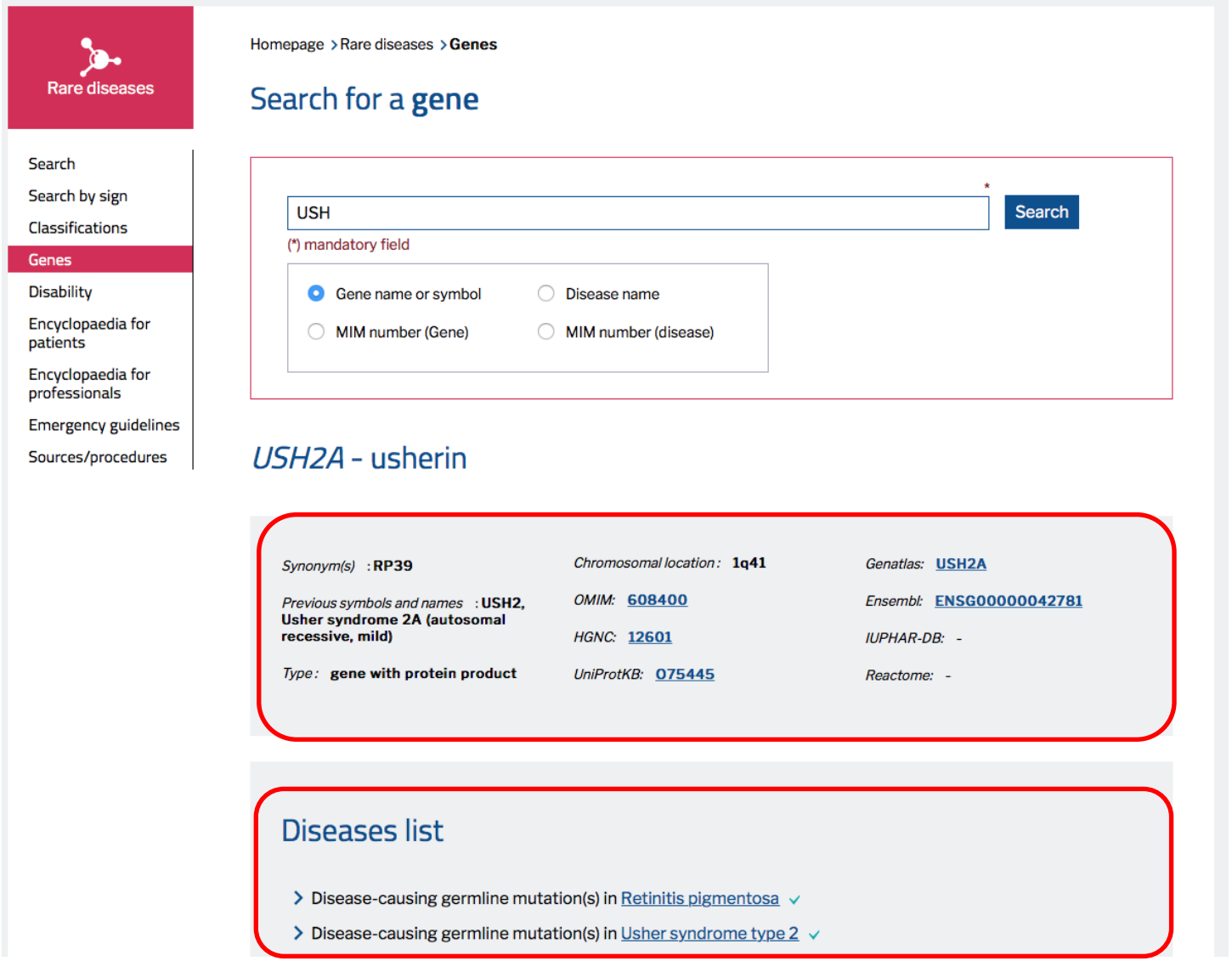
owl format

Updated bi-annually

- Orpha numbers in use
- **deprecate**d disorders
- **obsolete** disorders

- Versioning with change log

Where to find a gene ?



Genes-RD relationships

- Qualified
  - Disease **causing germline** mutation(s) in (+/- loss of function/gain of function)
  - Disease **causing somatic** mutation(s) in
  - **Modifying germline** mutation in
  - Major **susceptibility factor** in (multifactorial diseases)
  - Part of a **fusion gene** in (cancers)
  - **Role in** the phenotype of (chromosomal anomalies)
  - Biomarker tested in
  - Candidate gene tested in

- **Standardized** decision process

- **Manually curated**: 6,500 PMID

- **7030 Gene-RD** relationships (4449 genes – 3624 RD)

Homepage > Rare diseases > **Search**

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- Genes
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- Encyclopaedia for patients
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usher

Search

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- (•) Disease name
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Usher syndrome

Suggest an update

Disease definition

Usher syndrome (US) is characterized by the association of sensorineural deafness (usually congenital) with retinitis pigmentosa and progressive vision loss.

Additional information

Further information on this disease

- Classification(s) (5)
- Gene(s) (16)
- Publications in PubMed
- Other website(s) (15)

Health care resources for this disease

- Expert centres (258)
- Diagnostic tests (59)
- Patient organisations (73)
- Orphan drug(s) (2)

Research activities on this disease

- Research projects (34)
- Clinical trials (0)
- Registries/biobanks (38)
- Networks (20)

Specialised Social Services

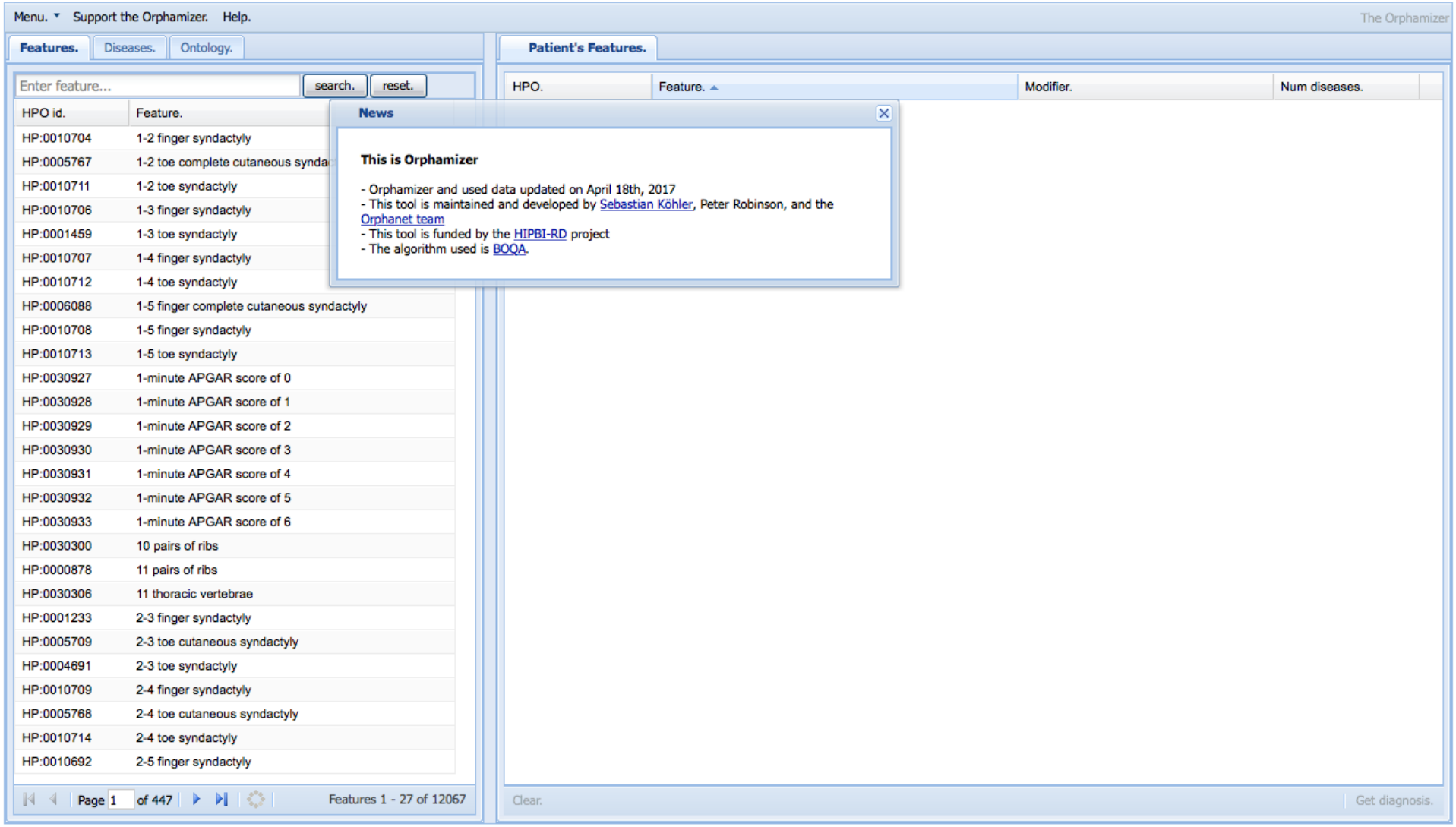
- Eurordis directory

Phenotype annotations

- 2,583 annotated RD with **HPO** phenotypes
- **Manually curated**: 2,000 PMID
- Feed **Orphamizer**

Frequencies	Diagnostic criteria
Obligate (100%)	Pathognomonic sign
Very frequent (99-80%)	Diagnostic criterion
Frequent (79-30%)	
Occasional (29–5%)	
Very rare (1-4%)	
Absent 0%	

Orphamizer


Menu.
Support the Orphamizer.
Help.
The Orphamizer
Features.
Diseases.
Ontology.
Patient's Features.
Enter feature...
search.
reset.
HPO id.
Feature.
HPO.
Feature.
Modifier.
Num diseases.
News
This is Orphamizer
- Orphamizer and used data updated on April 18th, 2017
- This tool is maintained and developed by Sebastian Köhler, Peter Robinson, and the Orphanet team
- This tool is funded by the HIPBI-RD project
- The algorithm used is BOQA.
HP:0010704 1-2 finger syndactyly
HP:0005767 1-2 toe complete cutaneous syndac
HP:0010711 1-2 toe syndactyly
HP:0010706 1-3 finger syndactyly
HP:0001459 1-3 toe syndactyly
HP:0010707 1-4 finger syndactyly
HP:0010712 1-4 toe syndactyly
HP:0006088 1-5 finger complete cutaneous syndactyly
HP:0010708 1-5 finger syndactyly
HP:0010713 1-5 toe syndactyly
HP:0030927 1-minute APGAR score of 0
HP:0030928 1-minute APGAR score of 1
HP:0030929 1-minute APGAR score of 2
HP:0030930 1-minute APGAR score of 3
HP:0030931 1-minute APGAR score of 4
HP:0030932 1-minute APGAR score of 5
HP:0030933 1-minute APGAR score of 6
HP:0030300 10 pairs of ribs
HP:0000878 11 pairs of ribs
HP:0030306 11 thoracic vertebrae
HP:0001233 2-3 finger syndactyly
HP:0005709 2-3 toe cutaneous syndactyly
HP:0004691 2-3 toe syndactyly
HP:0010709 2-4 finger syndactyly
HP:0005768 2-4 toe cutaneous syndactyly
HP:0010714 2-4 toe syndactyly
HP:0010692 2-5 finger syndactyly
Page 1 of 447
Features 1 - 27 of 12067
Clear.
Get diagnosis.

To know more about…

Orphanet process

Rare diseases

Homepage > Rare diseases > **Search**

Search for a **rare disease**

Sources / Procedures

ICD-10 coding rules for rare diseases

Creation and Update of Disease Summary Texts for the Ophanet Encyclopaedia for Professionals

Orphanet Standard Operating Procedures

International Advisory Board rules of procedure

Orphanet Advisory Board on Genetics Rules of procedures

Glossary and representation of terms related to diagnostic tests

Synonym(s):

Retinitis pigmentosa-deafness syndrome

USH

Prevalence: **1-9 / 100 000**

Inheritance: **Autosomal recessive**

Age of onset: **Infancy, Neonatal**

ICD-10: **H35.5**

OMIM: 276900 276901 276902 276904 500004 601067 602083 602097 614990

UMLS: **C0271097**

MeSH: **D052245**

GARD: 7843

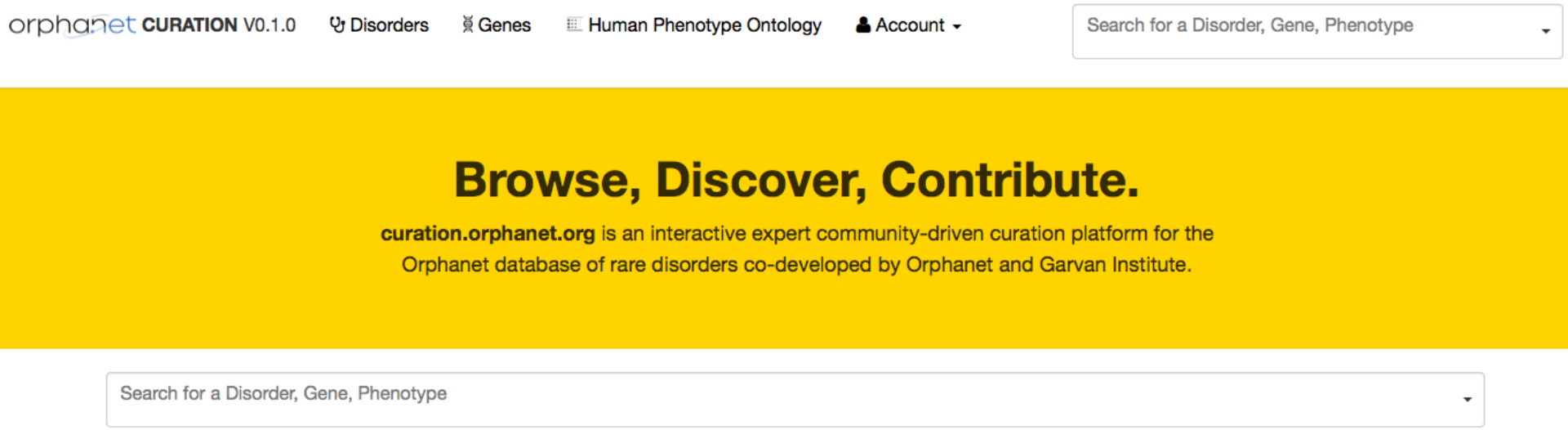
MedDRA: **10063396**

orphanet

www.orpha.net

How to contribute

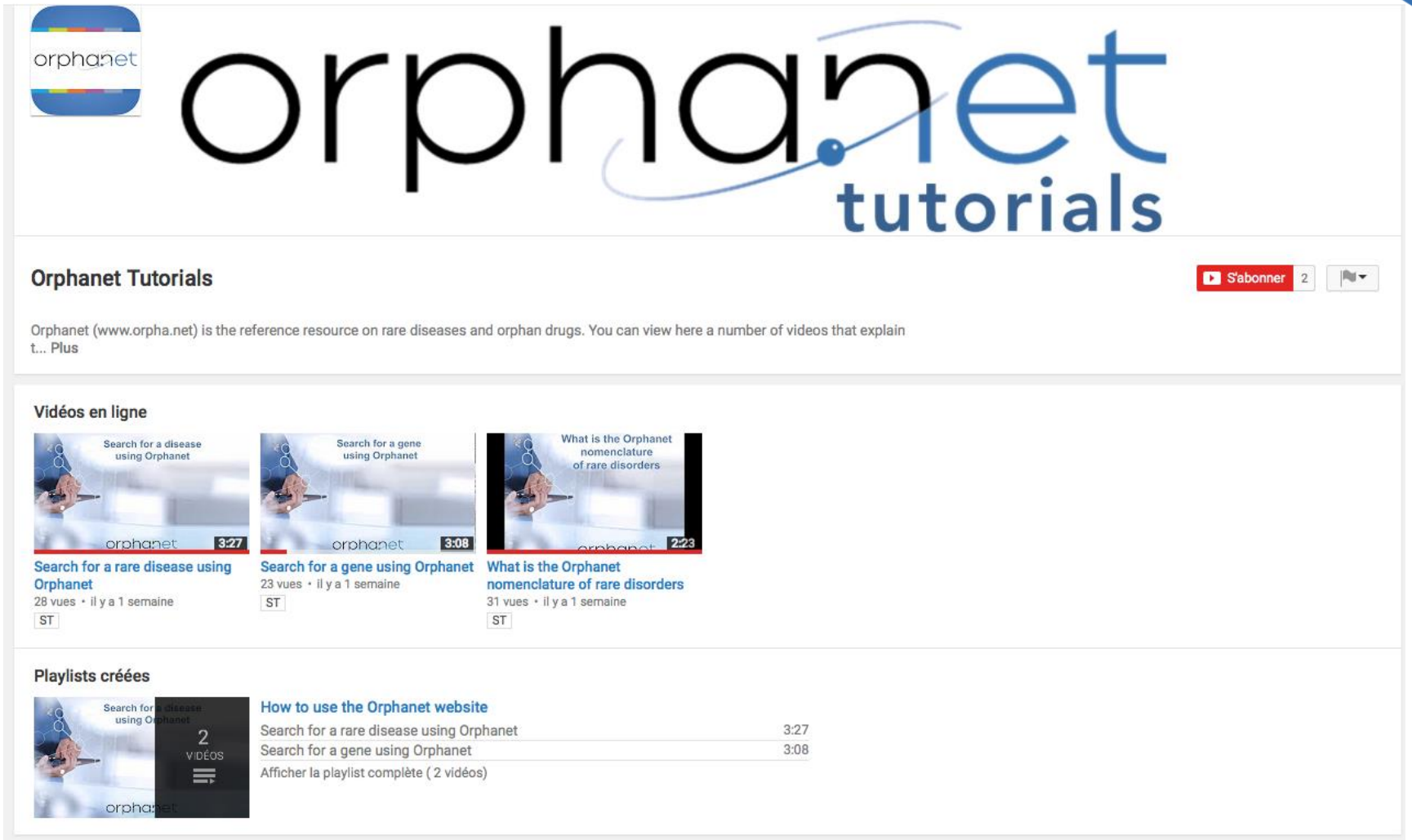
to Orpha terminology, definitions, …



to classifications…

- Publish consensus on restricted domain or medical speciality

To know more about…



Thank you for your attention!