



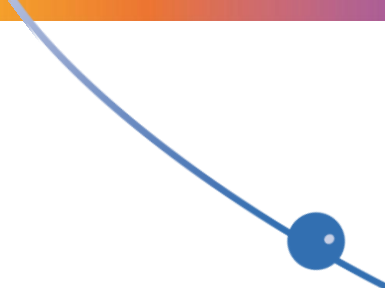
Rare diseases codification in health information systems:

current situation and evolutions forseen

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European Expert Group on Health Information
Luxembourg 26 November 2014



Improved codification for rare diseases is cited
as a priority in the Council Recommendation on
an action in the field of rare diseases (2009)

Need for coding RD

- **Make RD visible** in order to:
 - Have sound epidemiological data
 - Document the natural history of RD
 - Identify patients from health records for clinical research
 - Bring clinical data to 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

Steps so far

- **2009-2012 RDTF Joint Action:** support cross-referencing terminologies & ICD11 revision process for RD
- **2012 on: EUCERD Joint Action:** continuation of the RDTF work
 - Sept 2012: EUCERD JA workshop on cross-referencing terminologies
 - March 2014: EUCERD JA workshop on Orphacodes in HIS
- **July 2014: CEGRD:** draft recommendation on codification for rare diseases
- **October 2014 (JRC-ISPRA):** Workshop on the next steps to promote the implementation of Orphacodes in MS
- **November 2014:** Adoption of CEGRD recommendation

The current situation: EU MS

Country	Current coding systems used	Interest in/plans to use Orphacode	Plans to implement other system	Approach favoured
Austria	ICD 10	yes		Electronic link
Belgium	ICD 9	yes	Snomed, ICD 10	Parallel coding
Bulgaria	ICD	yes		Parallel coding
Croatia	ICD10	yes		Parallel coding
Cyprus	ICD10 CY			
Czech Republic				
Denmark	ICD10 DM, Nordic codes, OMIM	no		
Estonia				
Finland				
France	ICD10, Orphacode	yes		Parallel coding
Germany	ICD 10 GM	yes		Electronic link
Greece	ICD10	yes (registry)		
Hungary	ICD10	yes		Parallel coding
Ireland	ICD10	yes		

EGRD, July 2014

The current situation: EU MS

Country	Current coding systems used	Interest in/plans to use Orphacode	Plans to implement other system	Approach favoured
Italy	ICD9 CM (hospital) ICD10 (statistics) ICF, Orphacodes	yes		Electronic link
Latvia	ICD10	yes (registries)	OMIM	Parallel coding
Lithuania	ICD10	yes (CE)		Parallel coding
Luxembourg	ICD 10	yes		
Malta				
Netherlands	ICD10	yes (CE)		
Poland	ICD10	yes (CE)		Parallel coding
Portugal				
Romania	ICD10, some use of Orphacodes (CE)			
Slovakia	ICD10, OMIM	yes (registries)		Parallel coding
Slovenia	ICD10, OMIM, Orphacode (CE)	yes		
Spain	ICD9 ICD10	no	Snomed, ICD 10	
Sweden	ICD10	no	Snomed, ICD 10	
United Kingdom	ICD10, Snomed			



EGRD, July 2014

The current situation: terminologies

- Most health information systems use **ICD**
 - Some ICD-9
 - Most ICD-10
- WHO' ICD-11 revision is expected for 2017
- Some countries have adopted **SNOMED CT**
- Genetic databases use **OMIM**

- In Europe, countries having national plans/strategies for RD decided to integrate the Orphanet nomenclature of RD, and code patients with the **ORPHA** code

Terminologies currently used

- **SNOMED CT** (Systematized Nomenclature of Medicine – clinical terms, IHTSDO); 401,200 terms
 - comprehensive clinical terminology,
 - multihierarchical ontology
 - intended for use in EHR, and to semantic interpretation of EHR
 - translated in licensed countries
- **ICD-10** (International classification of diseases- WHO), 12,451 terms
 - Monohierarchical classification of diseases
 - Intended for statistical uses (morbidity, mortality)
 - Translated and adapted in different countries

Other terminologies/resources

- **OMIM** (Online Mendelian Inheritance in Man):
 - Genetic disorders and phenotypes (regardless their rarity)
 - Organised by genes
 - English only
 - Use in (genetic) databases

How many RD are included in these terminologies?

- **ICD10**

- **466 specific codes** matching Orphanet rare disease entities (including groups of diseases) (= EXACT mappings)
- 431 inclusion terms matching Orphanet RD entities
- 82 index terms matching Orphanet RD entities
- → Total: only 979 Orphanet RD entities with an ICD-10 mention
- But >80% of ORPHA entries have been attributed an ICD10 code

- **SNOMED CT** (from UMLS AA2013)

- On 15,043 candidate mappings, 3,541 were EXACT (**2,883 ORPHA** entries)

- **OMIM**

- On 6,617 total mappings, 3,388 are EXACT (**3,380 ORPHA** entries)

The ICD - 11

ICD-11 Beta Draft (Foundation)

Search [Advanced Search] Foundation Linearizations Contributions Info

ICD-11 Beta Draft

- ▶ Infectious diseases
- ▶ Neoplasms
- ▶ Diseases of the blood and blood-forming organs
- ▶ Disorders of the immune system
- ▶ Endocrine, nutritional and metabolic diseases
- ▶ Conditions related to sexual health
- ▶ Mental and behavioural disorders
- ▶ Sleep-wake disorders
- ▶ Diseases of the nervous system
- ▶ Diseases of the eye and adnexa
- ▶ Diseases of the ear and mastoid process
- ▶ Diseases of the circulatory system
- ▶ Diseases of the respiratory system
- ▶ Diseases of the digestive system
- ▶ Diseases of the skin
- ▶ Diseases of the musculoskeletal system and connective tissue
- ▶ Diseases of the genitourinary system
- ▶ Pregnancy, childbirth and the puerperium
- ▶ Certain conditions originating in the perinatal and neonatal period
- ▶ Developmental anomalies
- ▶ Symptoms, signs, clinical forms, and abnormal clinical and laboratory findings, not elsewhere classified
- ▶ Injury, poisoning and certain other consequences of external causes
- ▶ External causes of morbidity and mortality
- ▶ Factors influencing health status and contact with health services
- ▶ Codes for special purposes
- ▶ Extension Codes
- ▶ Traditional Medicine conditions - Module I (Note: This is a provisional title for ICD-11 Beta Phase)

ICD-11 Beta Draft

Welcome to the ICD-11 Browser

You can browse the ICD-11 proposed content here

If you wish to participate in the Beta Phase please [register or sign-in here](#). Registering will, etc.

Caveats

ICD-11 Beta draft is:

- **NOT FINAL**
- updated on a daily basis
- It is **not approved** by WHO
- **NOT TO BE USED** for CODING except for agreed FIELD TRIALS

Related Information

[More information](#) on ICD-11 Beta Phase

[What to expect, when and how?](#)

[Known concerns about the ICD-11 Beta Phase](#)

For more information about how to use the ICD-11 Browser, please see the [User Guide](#)

For more questions, please contact icd@who.int

RD-TAG input since 2009

> 5,000 RD incorporated

> 3,000 definitions
Introduced by Orphanet

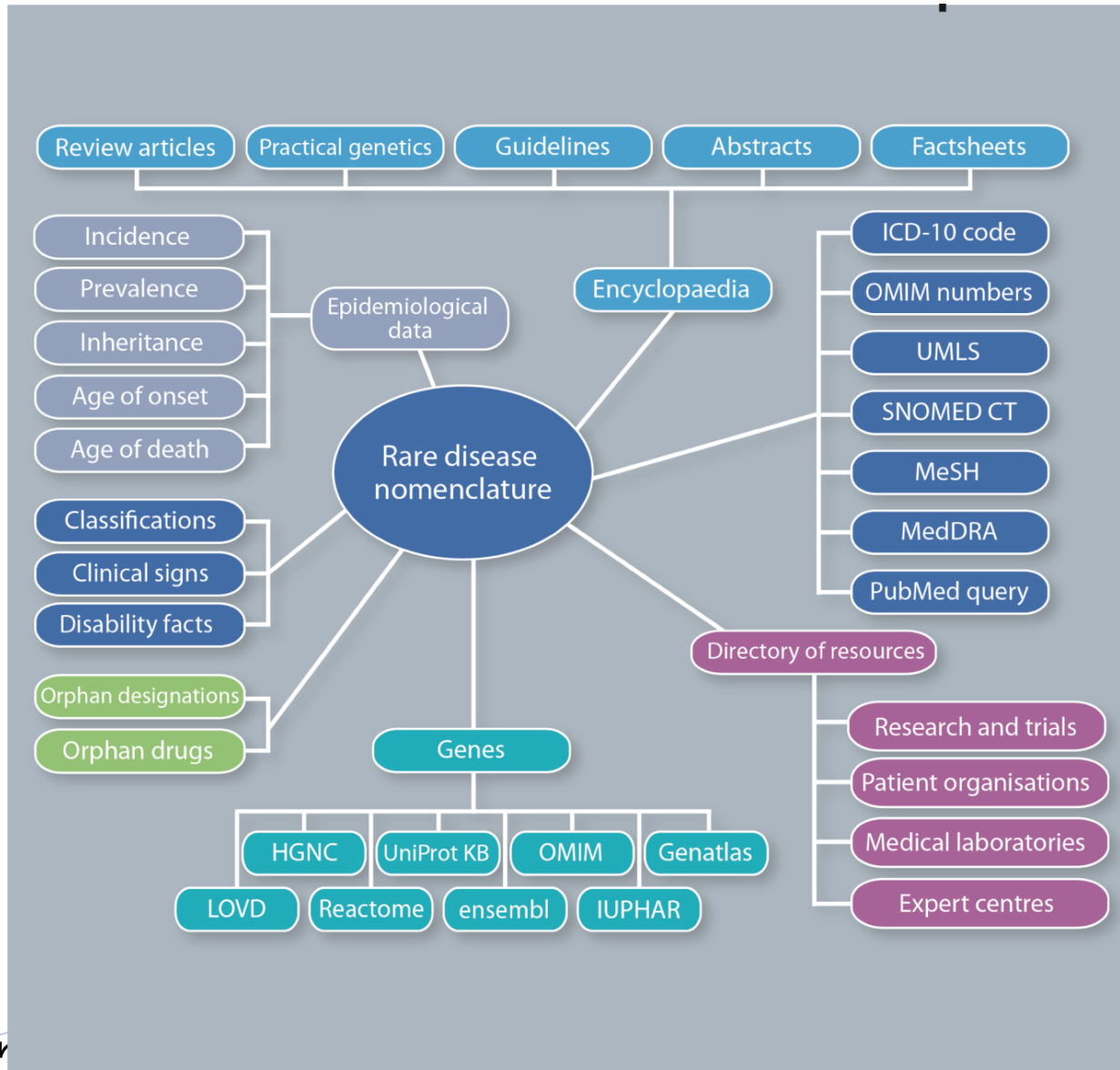
Currently, resolution of known problems, linearizations, tests

Still some conflicts to solve between TAGs

Release expected end 2017

Need for an update process (ORPHA – ICD11 alignments To be incorporated in ICD11)

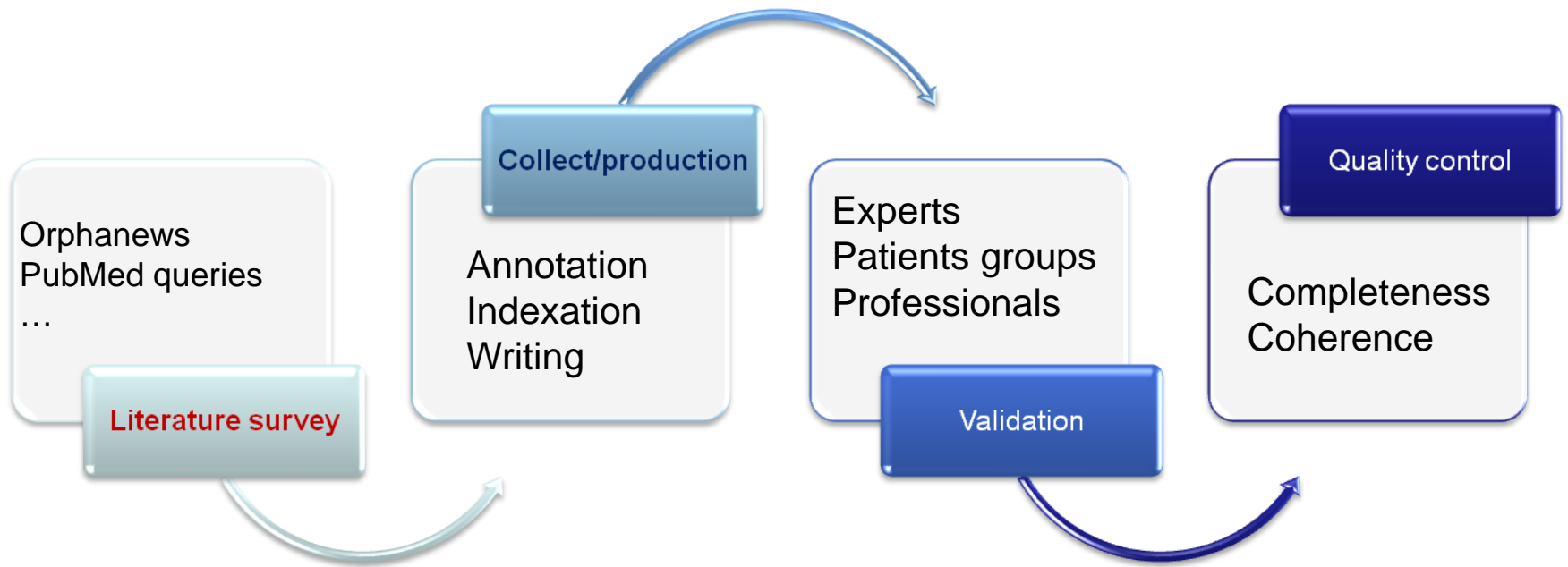
Orphanet , the European database for RD



Rare disorders in Orphanet

- Since 1997: **Inventory** of rare disorders (prev<1/2 000)
 - Mapped to OMIM
- 2005: Mapping to ICD-10
- 2007: **Classification** of rare disorders
- 2011: Mappings to UMLS, SNOMED CT, MeSH, MedDRA
- 2014: ORDO (Orphanet **ontology** of rare diseases) in collaboration with the EBI.

Edition process



Orphanet nomenclature

- Each entry (group, disorder, subtype) is given a unique, stable **ORPHA number**
 - The Orphacode
- Each entry is given a preferred term and as many synonyms as necessary
- Nomenclature is translated (FR – ES – IT – PT – DE – NL)
- Nomenclature and classifications are updated monthly.


Orphanet nomenclature

- Produced by the INSERM (France), hosting Orphanet, the EU RD database
 - Institutional support
- Under Creative Commons
 - Free for re-use
- Strong position in international terminologies
 - Ongoing process to be a WHO collaborating center
 - Population and updates of ICD11
 - Ongoing MoU with IHTSDO (SNOMED CT)
 - Population of SNOMED CT and mappings

A multidimensional classification

- Orphanet classifications by medical specialty based on international literature and experts advice

View classifications by disease or by group of diseases



The screenshot shows the Orphanet website interface. The 'Classification' menu item is highlighted in red. Below the search bar, the search results for 'adrenoleukodystrophy' are displayed, with several categories listed: 'Orphanet classification of inborn errors of metabolism', 'Orphanet classification of genetic diseases', 'Classification of rare forms of diabetes', 'Orphanet classification of rare neurological diseases', 'Orphanet classification of rare infectious diseases', and 'Orphanet classification of rare fertility diseases'. Three orange arrows point from these categories to the corresponding text boxes on the right.

Rare metabolic disease
Metabolic disease involving complex molecules
Peroxisomal disease
Adrenoleukodystrophy, X-linked
Adrenoleukodystrophy, X-linked, cerebral form
Adrenomyeloneuropathy

Rare neurologic disease
Neurometabolic disease
Adrenoleukodystrophy, X-linked
Adrenoleukodystrophy, X-linked, cerebral form
Adrenomyeloneuropathy

Rare neurologic disease
Rare epilepsy
Metabolic diseases with epilepsy
Peroxisomal disease
Adrenoleukodystrophy, X-linked
Adrenoleukodystrophy, X-linked, cerebral form
Adrenomyeloneuropathy

Rare neurologic disease
Leukodystrophy
Adrenoleukodystrophy, X-linked
Adrenoleukodystrophy, X-linked, cerebral form
Adrenomyeloneuropathy

Rare endocrine disease
Rare adrenal disease
Primary adrenal insufficiency
Chronic primary adrenal insufficiency
Genetic chronic primary adrenal insufficiency
Adrenoleukodystrophy, X-linked
Adrenoleukodystrophy, X-linked, cerebral form

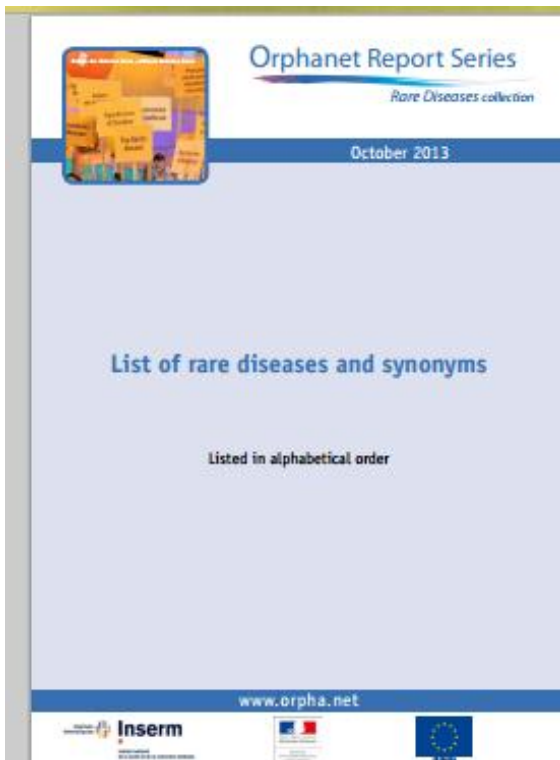
Mappings to other terminologies

- Disorders mapped to OMIM (manually)
- Disorders mapped to ICD-10 (manually)
- Disorders mapped to UMLS, MeSH, SNOMED CT, MedDRA (semi-automatically)
- Mappings are qualified (exact ; narrow-to-broad ; broad-to-narrow)
- Information on the validation status is noted
- Updates depending on the target terminology
 - Monthly (ICD10, OMIM)
 - Twice a year (UMLS, SNOMED CT, MeSH, MedDRA)

Qualifying mappings

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)
NTBT/E	narrower term maps to a broader term because of an exact mapping with a synonym in the target terminology
BTNT/E	broader term maps to a narrower term because of an exact mapping with a synonym in the target terminology
W/E	incorrect mapping (two different concepts) but syntactically exact mapping to a synonym or a preferred term in the target terminology
ND	not yet decided/unable to decide
The following are attributed to 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

To find the Orphanet nomenclature



Alphabetical list of names and synonyms
with ORPHA code
Updated every 6 months
Translated.
PDF (download, print)

ORPHA nomenclature
Cross-references
Monthly updated
6 languages (7 soon)
For download
XML

Free access data from Orphanet
orphanet

February-2014

Rare Diseases And Cross-Referencing

Files available in XML format.

Rare diseases and cross-referencing

Language	links	size
English	http://www.orphadata.org/data/xml/en_product1.xml	6.14 MB
French	http://www.orphadata.org/data/xml/fr_product1.xml	6.15 MB
Spanish	http://www.orphadata.org/data/xml/es_product1.xml	6.10 MB
Italian	http://www.orphadata.org/data/xml/it_product1.xml	6.05 MB
Portuguese	http://www.orphadata.org/data/xml/pt_product1.xml	5.81 MB
German	http://www.orphadata.org/data/xml/de_product1.xml	5.99 MB

Home

- About Orphadata
- About Orphanet
- Access Orphanet[→]
- Contact

Freely accessible datasets

Diseases, cross referenced with other nomenclatures

www.orpha.net

ORDO

Orphanet Rare Disease Ontology

Summary Classes Notes Mappings Widgets

Details

ACRONYM	ORDO
VISIBILITY	Public
BIOPORTAL PURL	http://purl.bioontology.org/ontology/ORDO
DESCRIPTION	<p>The Orphanet Rare Disease ontology (ORDO) is 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), r epidemiological data and connect SNOMED CT, UMLS, MedDRA), dat: Reactome, IUPHAR, Geantlas) or Free access data from Orphanet maintained by Orphanet and furt classifications can be browsed in Ontology is updated monthly and deprecation of terms. It constitu produced and maintained by Orp</p>
STATUS	Production

BioPortal

Ontology Lookup Service

OLS

- OLS Home
- Documentation
- Project
- Publications
- Developer Resources
- Download
- Implementation
- Overview
- Updates
- Vocabulary
- Documentation
- Contact Us
- Acknowledgements

Orphanet Ontology Browser

Tree view of Orphanet classes:

- isolate_class
- gene
- type of connect
- phenoma
- biological anomaly
- clinical antibody
- clinical syndrome
- disease
- biological subtype
- group of phenoma
- Rare obstetrical surgical disease
- Rare allergic disease
- Rare bone disease
- Congenital vascular bone syndrome
- Cysticosis
- Congenital pseudofriosis of clavicle
- Ornithinemia
- Isolated ornithinemia
- Familial lamboid syndrome
- Isolated brachycephaly
- Isolated acrocephaly
- Isolated plagiocephaly
- Isolated asplachycephaly
- Isolated trigonocephaly
- Syndromic craniofacial

Term Information:

10: Orphanet:2243

Name: Isolated divergent skull syndrome

Associated information:

Alternative term	Cleidocranial syndrome
Orphanet	Orphanet:2243
Orphanet	Orphanet:4500
Orphanet	Orphanet:1510

Term Hierarchy:

orphadata

Orphanet Rare Disease Ontology (ORDO)

The Orphanet Rare Disease ontology (ORDO) is 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.

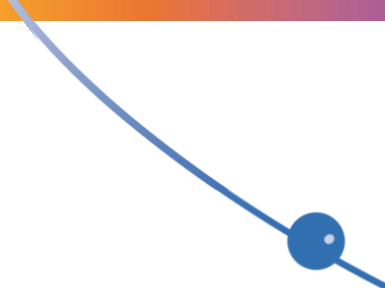
It integrates a nosology (classification of rare diseases), relationships (gene-disease relations, epidemiological data) and connections with other terminologies (MeSH, SNOMED CT, UMLS, MedDRA), databases (OMIM, UniProtKB, HGNC, Ensembl, Reactome, IUPHAR, Geantlas) or classifications (ICD10).

The ontology will be maintained by Orphanet and further populated with new data. Orphanet classifications can be browsed in the OLS view. The Orphanet Rare Disease Ontology is updated monthly and follows the OBO guidelines on deprecation of terms. It constitutes the official ontology of rare diseases produced and maintained by Orphanet (INSERM, USA).

Site	URL	Type
Bioportal	OrDO	OWL format
EBI Ontologies Lookup Service	OrDO	OBO view
Orphadata	OrDO	OWL direct download (RDF)

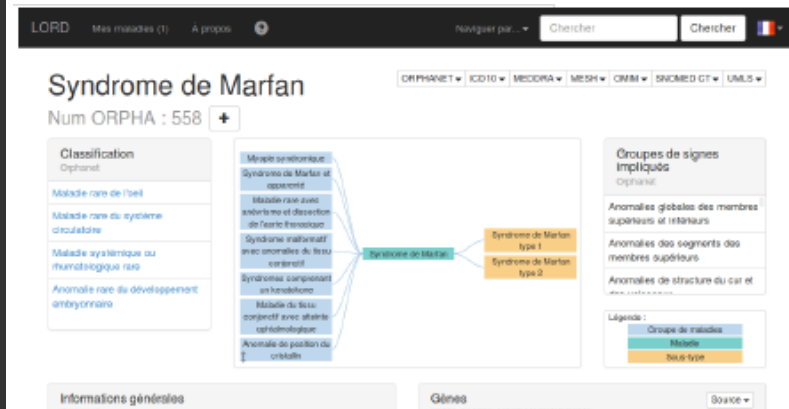
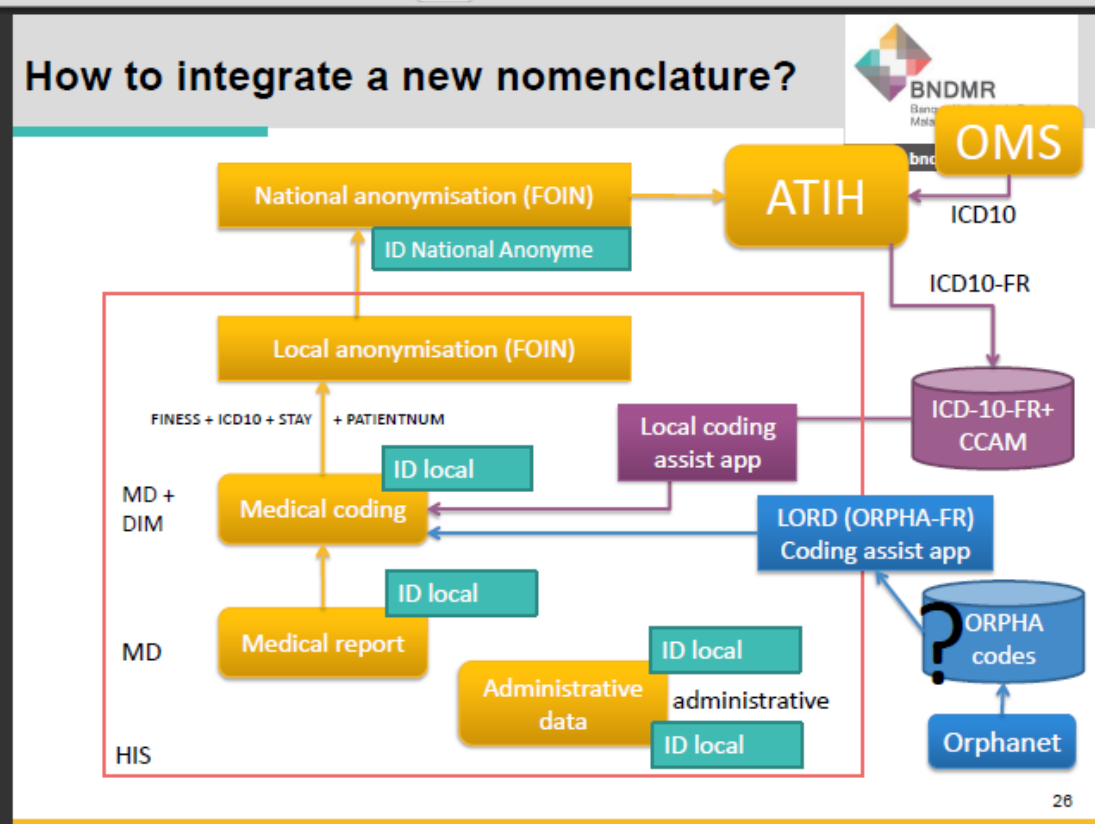
[User guide](#)
For any type of products please contact us through the tab "contact"

EBI - OLS



Ongoing initiatives implementing Orphacodes

France: ORPHA besides ICD10



Lord.bndmr.fr

Rémy Choquet, BNDMR project leader, ISpra, 2014

Germany: Orpha aligned to ICD10

ICD10-GM / alpha-ID

ORPHA code assigned to
ICD10-GM / alpha-ID

Interdisziplinäre Anämie

ICD-10	ICD-10	Termin
D64.9	D64.9	Anämie
D64.9	D64.9	Anämie
D64.9	D64.9	Anämie bei Infekt
D64.9	D64.9	Anämie bei Infektion
D64.9	D64.9	Anämie durch Hämoglobinmangel
D64.9	D64.9	Anämie in der Kindheit
D64.9	D64.9	Atypische primäre Anämie
D64.9	D64.9	Blutarmut
D64.9	D64.9	Eitrige Anämie
D64.9	D64.9	Erythrocytopenie
D64.9	D64.9	Essentielle Anämie
D64.9	D64.9	Hämoglobinmangel
D64.9	D64.9	Hb [Hämoglobin]-Mangel
D64.9	D64.9	Hypochromie
D64.9	D64.9	Hypoglobulinie
D64.9	D64.9	Idiopathische Anämie
D64.9	D64.9	Infantile Anämie
D64.9	D64.9	Latente Anämie
D64.9	D64.9	Niedriges Hämoglobin s.u.L.
D64.9	D64.9	Normochrome Anämie
D64.9	D64.9	Normozytäre Anämie
D64.9	D64.9	Oligämie
D64.9	D64.9	Oligoglobulinie
D64.9	D64.9	Oligozythämie
D64.9	D64.9	Pernäre Anämie
D64.9	D64.9	Progressive Anämie
D64.9	D64.9	Schwere Anämie
D64.9	D64.9	Sekundäre Anämie

Alpha-ID	ICD-10-GM code	Asterisk code	Orpha number	Term
I15988	Q77.0		932	Achondrogenesis
I17761	Q79.3		2368	Gastroschisis
I83662	Q87.2		2614	Nail-patella syndrome
I82099	Q87.2		2614	Turner-Kieser syndrome
I24937	K90.8+	M14.8*	3452	Whipple disease
I75193	H35.0		40923	Eales disease
I9770	H53.5		49382	Achromatopsia

Stephanie Weber, DIMDI, ISPRA 2014

Italy: alignments + multi-hierarchies

Automatic tool

Based on oRPHA – ICD10 alignments

Retrieving information on the health care utilisation

Registro Malattie Rare

- Rare developmental defect during embryogenesis
 - Syndromic genetic deafness
 - Alport syndrome
 - Autosomal dominant Alport syndrome
 - Autosomal recessive Alport syndrome
 - X-linked Alport syndrome
- Rare eye disease
 - Rare genetic eye disease
 - Lens and zonula anomaly
 - Lens chape anomaly
 - Alport syndrome
 - Autosomal dominant Alport syndrome
 - Autosomal recessive Alport syndrome
 - X-linked Alport syndrome
 - Rare cataract
 - Syndromic cataract
 - Systemic disease with cataract
 - Renal disease with cataract
 - Alport syndrome
 - Autosomal dominant Alport syndrome
 - Autosomal recessive Alport syndrome
 - X-linked Alport syndrome

Registro Malattie Rare

Malattie Rare

Nuovo Paziente
Ricerca Pazienti
Albero Malattie
Cambio Password
Manuale

Salva
Esci

Sintomi e Sospetto diagnostico

Sintomi:
Sospetto diagnostico:
Medico segnalante: Data segnalazione:

Diagnosi Definitiva

Malattia: [Vedi scheda sul sito](#)
Malattia di riferim.:
Codice esenzione: Codice ICD-10:
Orpha number:
Medico che inserisce:

	A	B	C	D
1	idpaz	icd-10	ORPHAcod	percorsoORPHAcod
2	12524	Q87.8	ORPHA88819	ORPHA98053;ORPHA101435;ORPHA183607;ORPHA98640;ORPHA98641;ORPHA98643;ORPHA98646;ORPHA63;ORPHA

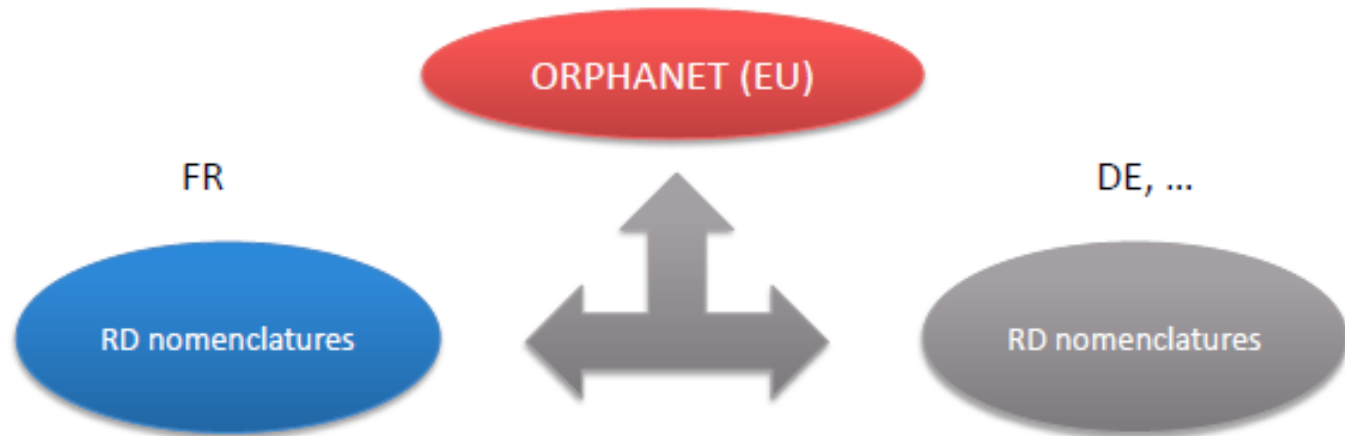
Paola Facchin, Veneto registry, ISPRA 2014

Needs at MS and EU level



- 195 Orphanet classification of rare immunological diseases (Pat)
 - 13022 Rare immune disease
 - 14933 Primary immunodeficiency
 - 18068 Primary immunodeficiency due to a defect in adaptive immunity
 - 14908 Combined T and B cell immunodeficiency
 - 18303 Severe combined immunodeficiency**
 - 21578 T-B+ severe combined immunodeficiency
 - 170 T-B+ severe combined immunodeficiency due to gamma chain deficiency
 - 10366 T-B+ severe combined immunodeficiency due to JAK3 deficiency
 - 17829 T-B+ severe combined immunodeficiency due to IL-7Ralpha deficiency
 - 17830 T-B+ severe combined immunodeficiency due to CD45 deficiency
 - 17831 T-B+ severe combined immunodeficiency due to CD3delta/CD3epsilon/CD3zeta
 - 19062 Severe combined immunodeficiency due to CORO1A deficiency
 - 21579 T-B- severe combined immunodeficiency
 - 993 Severe combined immunodeficiency due to DCLRE1C deficiency
 - 1258 Short-limb skeletal dysplasia with severe combined immunodeficiency
 - 8023 Severe combined immunodeficiency due to adenosine deaminase deficiency
 - 10318 Reticular dysgenesis
 - 20431 Severe combined immunodeficiency due to LCK deficiency
 - 21580 Severe combined immunodeficiency due to DNA-PKcs deficiency
 - 21997 Severe combined immunodeficiency due to complete RAG1/2 deficiency
 - 22703 T+ B+ severe combined immunodeficiency
 - 22219 Severe combined immunodeficiency due to CARD11 deficiency
 - Genes
 - 22042 CARD11 (Disease-causing germline mutation(s) in)
 - 22702 Severe combined immunodeficiency due to IKK2 deficiency
 - Genes
 - 22826 IKKB (Disease-causing germline mutation(s) in)

Needs at EU level



**Definition of a common level of interoperability
&
Codification standards**

Next steps

- WP in the Rare diseases joint action 2015-2017
- Steering group
 - Common denominator at EU level
 - Guidelines and coding instructions
 - Definition of a common resource
 - To ensure consistency in quality of data
 - To allow interoperability between MS

Thank you !