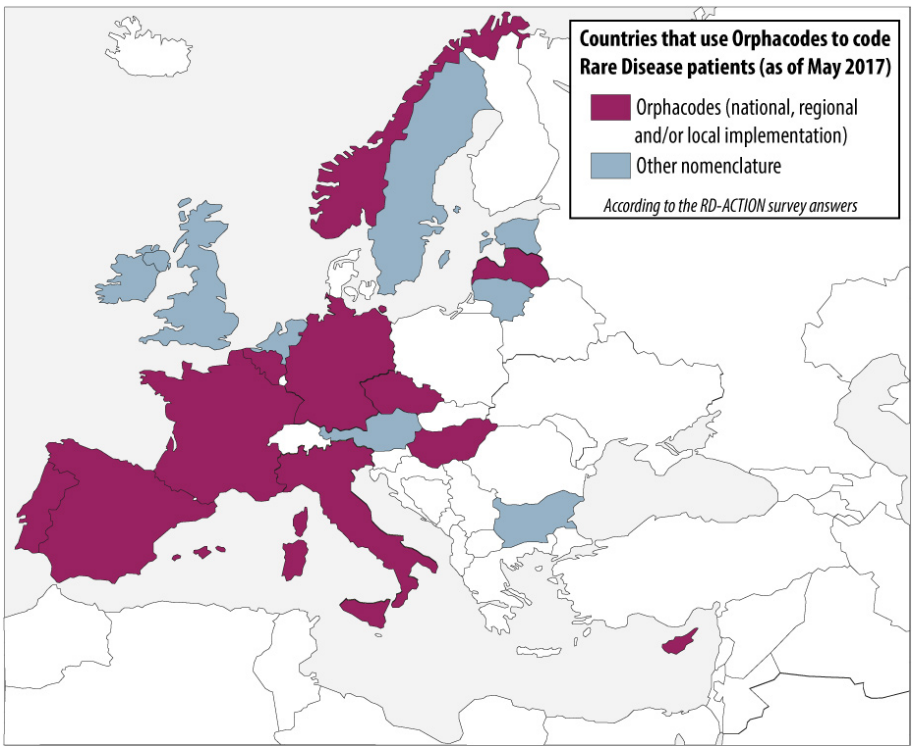
Orphan Drug Development Guidebook

Building Block I411

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	Coding of Rare Diseases: Orphanet nomenclature
References	Downloadable nomenclature and related resources here: http://www.orphadata.org/cgi-bin/rare_free.html SOPs for producing the nomenclature here: http://www.orpha.net/orphacom/cahiers/docs/GB/eproc_disease_inventory_PR_R1_Nom_04.pdf http://www.orpha.net/orphacom/cahiers/docs/GB/Orphanet_ICD10_coding_rules.pdf http://www.orpha.net/orphacom/cahiers/docs/GB/eproc_Disease_naming_rules_in_English_PR_R1_Nom_01.pdf http://www.orpha.net/orphacom/cahiers/docs/GB/eproc_Rare_disease_Nomenclature_Production__national-language.pdf Standard procedure and guide for coding with Orphacodes http://www.rd-action.eu/wp-content/uploads/2017/05/D5.2_Standard-procedure-and-guide_final.pdf Recommendation for routine maintenance http://www.rd-action.eu/wp-content/uploads/2018/09/677024_DEL5.5_Recommendation-routine-maintenance-codification.pdf State-of-Art of codification and Tool specifications here : http://www.rd-action.eu/leaflet-and-documents/
Description	The Orphanet nomenclature of RD comprises the list of rare clinical entities (<1/2000 in prevalence; <5/10000 according to Regulation 141/2000) defined by an ORPHA number (the Orphacode) unique and stable over time, a preferred term, exact synonyms, a typology (category, group of disorder, disorder (including: disease, malformation syndrome, clinical syndrome, morphological anomaly, biological anomaly, particular clinical situation), sub-type of disorder (including clinical, etiological and histopathological subtypes)), and a definition. Orphanet nomenclature is provided as a flat list and as a multi-hierarchical classification system. It is also provided with semantic alignments to

	OMIM, ICD10, MedDRA, MeSH, UMLS, GARD, and mapping files with ICD11 and SNOMED CT are under development. The European Commission Expert Group on Rare Diseases has also promoted the inclusion of ORPHA codes in health information systems ("Recommendation on Ways to Improve Codification for Rare Diseases in Health Information Systems" 2014). The Orphanet nomenclature is annotated with genes (gene-disease relationships) (with genes being aligned to HGNC, OMIM, and other resources), as well as with phenotypes (HPO terms), and disability-related terms (controlled vocabulary derived from WHO's ICF). These annotations are semantic (qualified) and computable as xml and JSON formats and as OWL and obo formats: the Orphanet Rare Diseases Ontology (ORDO) and the HPO-ORDO ontological module (HOOM) from Orphadata.org Orphanet nomenclature is released monthly as xml and JSON files in 9 languages, together with obsolete and deprecated entities and their corresponding active codes. Differentials between monthly versions can be retrieved and computed in the Orphanet GitHub https://github.com/Orphanet/Orphadata.org Finally, documentation is provided (User's guides, procedures) both in Orphanet and in Orphadata.
Category	Regulatory Building Block
Geographical scope	International
Availability	Applicants developing medicines for rare diseases.
Scope of use	Being able to identify RD patients in healthcare systems should speed recruitment, and a specific RD codification is therefore a key step toward this aim. RD are poorly represented in any other medical terminology for use in hospitals. Orphacodes have been recognized a best practice by the SGPP (Steering Group for Promotion of health and Prevention of non-communicable diseases) and EU funding is dedicated to fasten the implementation in EU MS. Orphacodes are increasingly adopted in EU countries, as well as in Australia, Japan and Argentina. China will also adopt it and translations will start soon. Orphacodes are adopted in ERNs CPMS and in RD registries and biobanks progressively. The use of Orphacodes is also recommended in the Common Data Elements defined by the Joint Research Center (JRC) when building a registry for RD. It also constitutes the core of RD representation in aggregated ontologies like MONDO (Monarch initiative). In use in healthcare and in research the adoption of Orphacodes as

	a standard codification system for RD increases semantic interoperability between resources and therefore improves data sharing and exchange.  Countries that use ORPHA codes to code rare disease patients (as of May 2017) - Source: http://www.rd-action.eu/wp-content/uploads/2017/09/2017-09_RD-ACTION-implementation-coding-survey2.pdf

Stakeholders	• Funders:
	  ○ Public: Inserm, French Ministry of Health, European Commission, Agence de la Biomédecine, Ministries of health, universities and hospitals in the countries of the Orphanet network;
	  ○ Private: AFM-Téléthon, Fondation Groupama pour la Santé
	• Users:
	  ○ Health information systems (ex DIMDI in Germany, BNDMR in France) and registries (ex: Veneto registry)
	  ○ Pharma companies and bio-techs
	  ○ Academic researchers, public administrations and Patient organisations

	○ Health professionals, patients, researchers, students, decision makers (Orphanet website users) ○ European Reference Networks: both using and contributing to Orphanet data.
Enablers / Requirements	Any particular requirement for open access datasets (see above) that are available in: • XML • JSON • Sparql EndPoint • Ontology: OWL, txt, obo (and for ORDO : http://bioportal.bioontology.org/ontologies/ORDO (OWL, CSV, RDF/XML) **Tutorials were developed to support the use of Orphanet nomenclature:** Orphanet Tutorials channel – What is the Orpha nomenclature
Output	A nomenclature and classifications of RD accessible at the Orphanet website (www.orpha.net), as a flat list in PDF format updated twice/year (https://www.orpha.net/consor/cgi-bin/Education_Home.php?lng=EN), and as dowloadable formats (XML, JSON) in Orphadata (www.orphadata.org), updated the 1st day of each month. An ontology of RD: Orphanet rare diseases ontology (ORDO) updated twice/year (OWL, txt, obo) available at orphadata.org and on http://bioportal.bioontology.org/ontologies/ORDO (OWL, CSV, RDF/XML)
Best time to apply and time window	N/A
Expert tips	PROs: – Computable structured data, manually curated, organized hierarchically (thus allowing for clustering and aggregation of data) and described with unique identifiers. Numerous cross-references with other relevant resources (gene function, pathways, compounds and targets,…). – Versioning and differentials for open access data. Documentation provided. – A number channels are available to help users wishing to access and re-use Orphanet data. Firstly, there is a contact form on the Orphadata website (http://www.orphadata.org/cgi-bin/contact.php) as well as a dedicated alias data.orphanet@inserm.fr, with a 24 hour first response time during office days.

	A FAQ and user guide is also available. In addition, there is an ORDO user mailing list (ordo-users.orphanet) to deliver updates concerning the ontology. CONs: – APIs in development, not yet available. – Hands-on assistance can be necessary to make the best use of the resource (as proven by the Orphanet participation to the training courses organized by ISS for RD registries: BYOD (RD-Connect/Excelerate). Not already available as a service, but in discussion.