

EUCERD JOINT ACTION DELIVERABLE

Work Package	WP5: Contribute to the Standardization of Rare Disease Nomenclatures at International Level
Deliverable	20112201_D06-00_OTH_EN_PS_pdf
Type of document	Report
Title	Relevant coding and classification of RD in International nomenclatures
Lead partner	INSERM (Institut National de la Santé et de la Recherche Médicale)
Date	September 2015

This work arises from the EUCERD Joint Action: Working for Rare Diseases N° 2011 22 01, co-funded through the European Union's 2nd Programme of Community Action in the Field of Health.

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Deliverable 20112201_D06-00_OTH_EN_PS_pdf

Relevant coding and classification of RD in International nomenclatures

Author(s): Ségolène Aymé (INSERM)	Approved by the:
Reviewer(s): Kate Bushby (UNEW)	<input checked="" type="checkbox"/> WP Leader
	<input checked="" type="checkbox"/> Project Coordinator

Keyword List:	Coding, classification, ICD-11, health information systems, Orphacodes
Abstract:	<p>The objective of this WP was to contribute to the 11th version of the International Classification of Diseases (ICD-11) to ensure an exhaustive coding of rare diseases (RD) and an appropriate classification in the framework of the revision process defined by the World Health Organization (WHO) in order to assure the traceability of RD in health information systems.</p> <p>All the objectives of this WP have been met in due time: thanks to this initiative, both ICD and SNOMED-CT will include most rare diseases in their nomenclature, and the EC Expert Group on Rare Diseases has recommended the use of Orphacodes in health information systems to improve the visibility of rare diseases. The only worry is linked to the capacity of WHO to publish on time a satisfactory version of ICD.</p>

Document Identifier: 20112201_D06-00_OTH_EN_PS_pdf	Date of Delivery to the EC M43
Status: Final	Contractual: M43
Dissemination Level: Public	Actual: M43

Document history

When	Who	Comments
21/08/ 2015	Ségolène Aymé	Draft of the text sent to Charlotte Rodwell
21/08/2015	Charlotte Rodwell	Review of text and English

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1. Introduction

Currently, only a small fraction of rare diseases have codes in international nomenclatures, making it impossible to trace patients with rare diseases in health information systems on a national and international level. Having codes for each and every rare disease would help European and national health authorities obtain a better knowledge of healthcare pathways and of their impact on specialised health care services (centres of expertise for instance) and on budget. Improved codification for rare diseases is cited as a priority in the *Council Recommendation on an action in the field of rare diseases* (2009).

The objective of this WP was to contribute to the 11th version of the International Classification of Diseases (ICD-11) to ensure an exhaustive coding of rare diseases (RD) and an appropriate classification in the framework of the revision process defined by the World Health Organization (WHO) in order to assure the traceability of RD in health information systems.

This work included:

- Cross-referencing the Orphanet nomenclature with other terminologies in Unified Medical Language System and with the Human Phenotype Ontology and free access to the resulting data;
- Identifying coding lacking in other nomenclatures and promoting an update of these nomenclatures;
- Preparing the alpha draft to be submitted to the WHO via a survey of literature at Orphanet;
- Reviewing of proposals for RD in ICD by expert groups at International level and negotiating with other Topic Advisory Groups;
- Annotating of diseases to comply with the content model of ICD11;
- Preparing the beta draft after the public consultation organised by WHO and organising the validation expert groups in the field of RD as well as contributing to field testing organised by WHO if requested;
- Promoting the use of Orphanet nomenclature which serves as a template for ICD11 in the field of RD, especially in health information systems and especially national repositories of data on patient with rare diseases.

2. Presentation of results

All the objectives of this WP have been met in due time. The results are presented in the order of the specific objectives listed in the introduction. The various reports referenced are included in the annexed list of references.

2.1. Cross-referencing the Orphanet nomenclature with other terminologies in Unified Medical Language System and with the Human Phenotype Ontology and free access to the resulting data

The Orphanet nomenclature is based on the inventory of RD which is managed by Orphanet and organised through a multi-hierarchical classification system. In the course of the JA, the nomenclature was cross-referenced with OMIM, SNOMED-CT, ICD-10, MeSH, MedDRA and HPO as planned. The data are made freely available to the community at large through a dedicated website at www.orphadata.org. The number of downloads of this file in 2014 was around 33'000 times.

2.2. Identifying coding lacking in other nomenclatures and promoting an update of these nomenclatures.

In order to achieve this objective a workshop was organised in Paris on 27 September 2012 which gathered representatives of all current terminologies in use, including top level representatives of WHO-ICD and of SNOMED. A report of this workshop is annexed. The classification systems were compared. The draft of ICD11 which was currently available indicated that many RD were likely to be incorporated into ICD11 but probably not all, that the structure of the classification was not satisfactory, that the revision process was not sufficiently defined so as to ensure that experts' views are taken into account and that a permanent update process will be necessary to keep ICD11 up to date. The SNOMED CT disease terminology is intended for use in electronic health records to code the health status of patients. It is the most comprehensive terminology in the world. It does not focus on RD. The Orphanet poly-hierarchy classification system is entirely dedicated to RD and benefits from the contribution of many experts around the world. It is appropriately funded to ensure continuity. OMIM is the standard coding system for genetic phenotypes widely used for that purpose.

The expert group proposed to:

- Continue trying to influence ICD11 as much as possible but with limited hope that the new version will meet the needs of the RD community;
- Set up an active collaboration with SNOMED CT to ensure that missing codes are considered for incorporation, considering that SNOMED CT is on the track to become a *de facto* standard terminology for electronic health information;
- Recommend that Orphanet and OMIM codes are to be accepted as the standards of the rare disease community which means that any database for RDs should have either Orphanet codes or MIM numbers or both. The scientific community has been using MIM codes for a very long time and will continue to need the "splitter" perspective OMIM offers. But using the Orphanet nosology for the structure, which OMIM does not offer in this form, is really useful for clinicians and ontologists. To work with a combination of both is ideal.
- Continue cross-referencing OMIM and Orphacodes with the standard terminologies (ICD and SNOMED CT), as it is a quality-control exercise for all parties and as it is necessary for navigation from one classification to another.

Following this workshop, a formal agreement was signed between SNOMED-CT and Orphanet (2015), and the collaboration between Orphanet and WHO was strengthened so as to ensure that a maximum of RD are included in the ICD11 in preparation.

During the same workshop, a review of the relevant terminologies in use to describe phenotypic traits was made. They were all presented and their strengths and weaknesses discussed. The terminologies which were considered were PhenoDB (2846 terms), London Dysmorphology Database (LDDDB; 1318 terms), Orphanet (1243 terms), Human Phenotype Ontology (9895 terms, 22/08/2012), Elements of Morphology (AJMG; 423 terms), ICD10 (1230 terms), as well as medical terminologies in use: Unified Medical Language System Metathesaurus (UMLS; 7,957,179 distinct concept terms), Systematised Nomenclature of Medicine - Clinical Terms (SNOMED CT ; >311,000 concepts), Medical Subject Headings (MeSH ; 26,853 concepts) and Medical Dictionary for Regulatory Activities (MedDRA, 69,389 concepts). The Orphanet team established a strategy to compare them to find commonalities and differences, using ONAGUI as a tool to pick up exact matches. The non-exact matches were verified manually by an expert. After discussion it was agreed that, given the multitude of needs and applications in the field of rare diseases, it is not currently realistic or even desirable to have one terminology for all applications. Prominent terminologies have different focuses and user bases. The expert group decided to identify a core set of about 2 000 terms that represent the major phenotypic abnormalities encountered in persons with rare diseases which will be cross-matched with the available terminologies. This core set of terms will be recommended for use in any new information system intended to collect phenotypic data, either for research or clinical purposes.

The core set of phenotypic terms was set up by comparing the different terminologies, considering that terms used by the majority of them are likely to constitute the candidates for standard terms. The Orphanet team carried out the preparatory work and the expert group acted as reviewers and decision makers to ensure that there is a good coverage of all body systems for which descriptors are needed. This set of terms will be proposed for inclusion in SNOMED CT and ICD-11. As there is a need to continuously revise the proposal, the

expert group proposes to set up an International Consortium of Human Phenotype Terminologies. Therefore, the core set of terms is now named ICHPT codes and are now available from the IRDiRC website (www.irdirc.org) (<http://www.irdirc.org/ichpt/>).

2.3. Preparing the alpha draft to be submitted to the WHO via a survey of literature at Orphanet; Reviewing of proposals for RD in ICD by expert groups at International level and negotiating with other Topic Advisory Groups; Annotating of diseases to comply with the content model of ICD11; Preparing the beta draft after the public consultation organised by WHO and organising the validation expert groups in the field of RD as well as contributing to field testing organised by WHO if requested

In order to contribute to the revision of ICD, a process was defined at Orphanet to align the classification system with the most recent scientific literature and to prepare draft version of ICD 11 by chapter of ICD to be submitted to experts in the field for review. Orphanet collected series of rare diseases classifications mainly based on scientific grounds (etiology and mechanism). To complement these classifications, a clinical in-house classification was developed to meet the needs of the clinicians. For chapters where rare diseases feature prominently, or were dealt with early in the revision process, we proposed a whole revision of the structure together with the addition of rare diseases. These are the chapters for the blood and immune systems (ICD-10 chapter III), endocrine system, nutritional and metabolism (ch. IV), nervous system (ch. VI), respiratory system (ch. X), and developmental anomalies (ch. XVII). For the other chapters, the new structure revision has been set up by the specific Topic Advisory Group for the body system and rare diseases were added into it. These are the chapters for infectious and parasitic diseases (ch. I), neoplasms (ch. II), eye (ICD-10 ch. VII), ear (ICD-10 ch. VIII), circulatory system (ch. IX), digestive system (ch. XI), skin (ch. XII), musculoskeletal and connective tissue (ch. XIII), genitourinary system (ch. XIV), pregnancy, childbirth and the puerperium(ch. XV), perinatal conditions (ch. XVI). No proposal was made in the chapter on mental and behavioural disorders (ch. V). The reason is that the mental and behavioural disorders chapter is set up to allow the coding of levels of disabilities independently from their cause. Therefore it was not possible to establish new levels of coding to include rare diseases impacting on mental status and behaviour, but conditions with disorders of intellectual development as a relevant clinical feature were listed in a dedicated grouping in the chapter for developmental anomalies. The inclusion of a new chapter for multi-systemic diseases was considered for a time and advocated for by us. Nevertheless, the WHO decided against its creation and struck out the in-work draft chapter. The diseases that it would have contained were later redistributed into chapters for the individual body systems. The WHO introduced during the writing of the alpha-draft a division of labour between TAGs when their areas of interest overlapped. The Rare Disease TAGs frequently experienced it, since rare diseases are found in every area of medicine.

So far 5,400 rare diseases listed in the Orphanet database have an endorsed representation in the foundation layer of the ICD-11, and are thus provided with a unique identifier in ICD-11, which is 10 times more than in ICD10. A mapping of those identifiers with ORPHA numbers has been established to allow data exchange and to ensure compatibility between the two information systems; it will need to be regularly updated as new frozen releases of the ICD-11 beta version are issued.

The content model is far from complete for most ICD-11 entities, and in all likelihood will never be completed. The amount of data to be gathered is simply too great for the limited means available to the editors, both in terms of time and funding. Besides, keeping such a large repository of data up-to-date is bound to become quickly overwhelming, especially regarding genetic data which are rapidly evolving. The only realistic way to achieve the initial purpose of annotating ICD-11 entities with the planned set of properties at a professional level of quality would be for the WHO to establish long-time partnerships with stable institutions dedicated to gathering and managing the relevant biomedical data.

In the meantime, the focus on filling the whole of the content model has been scaled down: emphasis is chiefly put on writing definitions for every disease in ICD-11. At least, this will allow the codes to be used without ambiguity. Around 4,000 rare diseases represented in ICD-11 have an associated definition so far: 2,600 were expressly created by the Rare Diseases TAG, the remaining 1,400 were imported or created by other groups and need yet to be reviewed by us. 1,400 definitions remain to be written by these other groups.

The current state of the ICD-11 beta version is open to the public for consultation and comment on an online platform: <http://apps.who.int/classifications/icd11/browse/f/en#/>. Everybody is entitled to create an account with a profile and to post comments, which are filtered by the WHO and dispatched among the relevant TAGs. The TAGs advise on what is to be done and the corresponding corrections are then carried out by the WHO.

The beta version is now frozen, so that it may be stable enough to be used for practical tests in the field. Corrections are nonetheless still possible, but are implemented globally as packages: the beta version now evolves through successive releases rather than being in a state of continuous flux. The last frozen releases of the beta version occurred on 14 August 2014 and 1 October 2014.

A detailed description of the process which was followed and of the results can be found in the following publication: “Ségolène Aymé, Bertrand Bellet and Ana Rath, “Rare diseases in ICD11: making rare diseases visible in health information systems through appropriate coding”, Orphanet Journal of Rare Diseases 2015, 10:35”.

2.4. Promoting the use of Orphanet nomenclature which serves as a template for ICD11 in the field of RD, especially in health information systems and especially national repositories of data on patient with rare diseases;

The revision of the International Classification of Diseases, which is the main instrument at world level, to code health events and draw statistics for International comparisons, is in its final stage. The current beta version is open for public consultation and comments, and for field testing use. The adoption by the World Health Assembly is planned for 2018. In the context of uncertainty around the outcome of the field testing and the potential willingness of countries to adopt this new version, it was decided by the EUCERD to promote the use of Orphacodes as it is not fair to the large community of patients with rare diseases, not to make their case visible in health information systems. A solution should be adopted at least until the ICD11 is fully implemented in countries. An intermediate solution for the codification of rare diseases could be to add the Orphacode to the current ICD version in use.

To discuss the desirability and feasibility of the objective, two workshops were organised. The first workshop on Orphacodes in health information systems was held on 18 March 2014 in Paris (France). The Expert Group prepared a draft recommendation on how to use Orpha codes (with the publication of a leaflet by WP5) and laid down key points for action, including the organisation of a working group of stakeholders and countries wishing to implement Orphacodes in their health information systems in order to seek solutions and possibilities at EU level to support the implementation of these solutions. The recommendations were presented to the Expert Group on Rare Diseases in July 2014 and modified according to the discussions.

A workshop on the next steps concerning the implementation of Orphacodes in health information systems, co-organised by the EC's Joint Research Centre (JRC) and the EUCERD Joint Action was also held on 1-2 October 2014 in Ispra to bring together MS representatives and specialists from coding agencies. The second workshop was organised in Ispra with the support of the JRC to review the past experience concerning the use of Orphacodes in Member States, and to discuss technical options. A preliminary discussion concerning the road map to help countries interested in Orphacodes with the implementation of appropriate measures was also a focus. Representatives from competent authorities from many EU MS were present, as well as experts in the field of coding, EC and JRC representatives and a patient representative. All countries, apart from Denmark, Finland, Spain, Sweden and UK are considering the use of Orphacodes in their health information systems and are at different stages in their reflection with Italy, France and Germany in or entering pilot phases.

The workshop concluded that the situation at MS level is highly diverse in terms of coding tools, systems and practices, therefore a sole solution responding to all countries' needs is impossible to identify. An agreement was reached that coding systems for management and reimbursement purposes will remain based on ICD10, but that Orphacodes are the best instrument to complement ICD10 for diseases with no specific code. Countries willing to implement Orphacodes are recommended to start coding in centres of expertise in order to demonstrate their added value. Interested MS wishing to exchange experiences will be able to do so through a dedicated working party supported by the next Joint Action on rare diseases. A number of topics were identified for further discussion, including: versioning of Orphacodes/tracked changes, production of a masterfile (alignment of Orphacodes and versions of ICD used in MS), and production of guidelines for coders so they can effectively navigate the granularity of the Orpha nomenclature. The sustainability of Orphanet and a need to implement an improved system for data release was also highlighted. It was agreed that all efforts to implement Orphacodes in addition to ICD10 should be carried out at national level due to national specificities. However, a common approach at European level for data exploitation will be needed and this activity will need additional funding: a strategy in this area was to be defined by the working party to be established in this area, and as a result a dedicated WP in the future RD-Action will be dedicated to tackling these issues.

The European Commission Expert Group on Rare Diseases adopted in November 2014 the previously discussed recommendation for national health care coding systems to consider using Orphacodes in addition to ICD10 codes when a rare disease has no specific ICD10 code. As Orphacodes will be linked with ICD11 the switch from ICD10 to ICD11 will be made easier if decided.

This recommendation served as a basis to shape the Joint Action on Rare Diseases (RD-Action) 2015-2018.

3. Critical analysis of results

This WP has delivered as planned and the outcomes have, and will have in the future, a decisive impact.

Thanks to this initiative, both ICD and SNOMED-CT will include most rare diseases in their nomenclature. The only worry is linked to the capacity of WHO to publish on time a satisfactory version of ICD. Even if published, it may not be adopted by the World Assembly. Even if adopted, it may not be implemented by many countries, if they are not sufficiently convinced of the added-value of this new version compared to ICD-10, knowing the cost of a transition from one version to another. This is the limit of the potential impact of this work on ICD, but this, however, is out of our control.

4. Conclusion

This WP directly served the goals of the EUCERD, then of the EC Expert Groups on RD. The Member State Representatives were involved in all the political discussions on the potential adoption of Orphacodes at national level and most of them are willing to implement this coding system in their health information system. This will provide quickly the data which are so urgently needed to trace patients with RD in the health care system, to assess the impact of RD and adapt services to the real needs.

This WP was not very much related to the other ones, but the importance of adequate codification for rare diseases and the utility of Orphacodes was highlighted in the programme of WP4's national conferences. Dissemination concerning the activities of WP5 was ensured via OrphaNews and the State of the Art on RD Activities report.

5. Annex: References

5.1. **WP5 Workshop reports**

- [Summary report of the workshop on cross-referencing of terminologies \(27-28 September 2012\)](#)
- [Summary report of the workshop on Orphacodes in health information systems \(18 March 2014\)](#)
- [Summary report of the workshop on Orphacodes in health information systems, \(1-2 October 2014\)](#) (financed by JRC in Ispra)

5.2. **WP5 Outcomes**

- [Rare diseases in the ICD-11 Beta Draft](#)
- [Information leaflet on how to use the OrphaCode: Making rare diseases visible in your health information system](#)
- [Rare diseases cross-referenced with other terminologies \(via Orphadata\)](#)
- [Orphanet Report Series: List of rare diseases in alphabetical order \(with corresponding Orphacode\) \(via Orphanet\)](#)
- [Commission Expert Group on Rare Diseases – Recommendation on Ways to Improve Codification of Rare Diseases \(November 2014\)](#)
- [List of ICHPT terms](#) (via IRDiRC website)