RD-CODE

Co-funded by
the Health Programme
of the European Union

# RD-CODE FINAL WORKSHOP

## 29th and 30th November, 2021

# SUMMARY REPORT

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## Introduction

RD-CODE is a 36-month project (Jan 19-Dec 21) co-funded by the European Union's Third Health Programme whose objective was to support Member States in improving gathering information on rare diseases by implementation of ORPHAcodes (OC; rare diseases specific codification system). The implementation process was guided by Standard procedures and Guidelines for the coding with OC along with an implementation manual developed in the frame of the previous Joint Action on Rare Diseases RD-ACTION (2015-2018) and newly developed tools (Helpdesk, API, Dataviz).

The workshop was organized by CIBERER, with the support of the INSERM and the rest of partners in the project. Although it was originally planned to be celebrated in Valencia, Spain, due to the COVID pandemic it was decided to hold it online via Zoom on 29th and 30th November 2021. It was attended by 76 experts in the field of rare diseases, representing the various stakeholder groups (see Annex 1). Report and slides can be accessed here.

## Specific questions to be addressed

- Presenting the final results obtained by the four implementing countries (Czech Republic, Malta Romania and Spain).
- Presenting the results of additional studies carried out in the frame of the project, such as the transnational analysis performed by the Veneto Region RD Registry or the guidelines developed for the codification of undiagnosed patients in addition to the technical tools created to assist codification.
- To provide a forum for all stakeholders to discuss these results and how they might be used to foster and guide the use of the ORPHA codification systems in other countries/settings.
- To explore new alliances and collaboration with ERNs, Hospital Alliances, patient organizations and other projects, such as X-eHealth.
- To reflect on the project's legacy and discuss future action.

# AGENDA

## Day 1

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| **13:30-13:50** | **Welcome and introduction**<br>*Deputy Assistant Director of Promotion, Prevention and Quality - Spanish Ministry of Health, Social Rights and Consumer Affairs*<br>*Francesc Palau, CIBERER and Sant Joan de Déu Hospital, Spain* |
| **13:50-14:05** | **Project Overview**<br>***Speaker***<br>*Ana Rath, RD-CODE Coordinator (INSERM)* |

**Session 1: Presentation of results**

**Chair:** *Francesc Palau, CIBERER and Sant Joan de Déu Hospital*

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| **14:05-14:25** | **Implementation of ORPHAcodes in Czech Republic**<br>***Speaker***<br>*Miroslav Zvolský, Institute of Health Information and Statistics – IHIS, Czech Republic* |
| **14:25-14:45** | **Implementation of ORPHAcodes in Malta**<br>***Speaker***<br>*Francis Agius, Ministry for Health, Government of Malta- MFH* |
| **14:45-15:05** | **Implementation of ORPHAcodes in Romania**<br>***Speaker***<br>*Cristina Rusu, Department of Public Health Iasi- Directia de Sanatate Publica Iasi (DSP IASI), Romania* |

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| **15:05-15:25** | **Coffee break** |
| **15:25-15:45** | **Implementation of ORPHAcodes in Spain**<br>***Speakers***<br>*Clara Cavero/ Juan Rico, Fundación para el fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana – FISABIO, Spain* |
| **15:45-16:05** | **Transnational study results**<br>***Speaker***<br>*Monica Mazzucato, Regione del Veneto, Italy* |
| **16:05-16:50** | **Round Table / Q&A Session**<br>***Panelists***<br>*Miroslav Zvolský, Miriam Azzopardi, Cristina Rusu, Clara Cavero, Juan Rico*<br>***Moderator***<br>*Stefanie Weber, BfArM, Germany* |
| **16:50-17:20** | **Guidelines**<br>***Speakers***<br>*Monica Mazzucato(Regione del Veneto, Italy), Céline Angin (APHP, France) and Stefanie Weber (BfArM, Germany)* |
| **17:20-17:30** | **Day 1-Closing remarks**<br>*Ana Rath, INSERM* |

## Day 2

**Session 2: RD-CODE legacy**

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| **9:00-10:15** | **Collaborating projects: XeHealth**<br>**Presentation of a use case**<br>***Speaker:*** *Ana Rath, Orphanet*<br>**X-eHealth project: short presentation**<br>***Speaker:*** *HL7 Europe*<br>**Patient Summary general presentation**<br>***Speaker:*** *XeHealth*<br>**ePS: How it serves RD/ New content fields, data model**<br>***Speaker:*** *HL7 Europe*<br>**Orphanet nomenclature delivery services**<br>***Speaker:*** *Marc Hanauer, Orphanet*<br>**Possible future plans for a demonstrator**<br>***Speaker:*** *HL7 Europe*<br><br>***Roundtable*** |
| **10:15-10:30** | **Coffee break** |
| **10:30-11:30** | **Multistakeholder panel** Listening to the stakeholders: How can RD-Code meet your needs?<br>***Panelists***<br>*Celine Angin, APHP, France*<br>*Representative, Hospital Sant Joan de Déu, Spain, ECHO*<br>*Representative, University of Heidelberg, Germany – ERKNet*<br>*Coordinator IT tools for European Reference Networks for Rare Diseases. European Commission* |

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| | *Representative EUHA, Karolinska Institutet, Sweden*<br><br>***Moderators***<br>*Inés Hernando, EURORDIS*<br>*Debby Lambert, Genetic Counselor, Ireland* |
| **11:30-12.30** | **Open discussion: *Project's legacy and future.***<br>***Moderator***<br>*Ana Rath, INSERM* |
| **12:30-13:00** | **Final closing remarks**<br>*Ana Rath, INSERM* |

# Day 1

## *Opening* (Francesc Palau)

The workshop was opened by Francesc Palau (CIBERER and Sant Joan de Déu Hospital, Spain), who introduced the Deputy Assistant Director of Promotion, Prevention and Quality of the Spanish Ministry of Health, Social Rights and Consumer Affairs. The Ministry representative recognized the importance of RD codification and paid mention to the Spanish RD Registry and to the imminent evaluation and update of the Rare Diseases Strategy of the Spanish National Health System.

## *Project Overview* (Ana Rath)

In this presentation, Ana Rath, RD-CODE Coordinator (INSERM) provided an overview of the RD-CODE project, covering the following aspects: framework, objectives, expected outcomes (implementation in 4 countries, services and tools, guidelines, enhancements), and main achievements:

- Implementation in Czech Republic, Romania, Malta and Spain;
- Helpdesk, nomenclature pack, API-Dataviz;
- Guidance documents for codification and exploitation; Standard procedures and guide for Orphacoding; Consensus recommendations on codification of undiagnosed patients;
- Dissemination material: Website, Leaflet and Video, in addition to e-learning training material.

Ana concluded by stressing the importance of OC implementation as a means to approach a range of public health and research questions, thus supporting evidence-based decision-making regarding RD and undiagnosed patients.

# Session 1: Presentation of results

## ***Implementation of ORPHAcodes in the Czech Republic*** (Miroslav Zvolský)

In this presentation, Miroslav Zvolský, Institute of Health Information and Statistics – IHIS, Czech Republic, provided a detailed description of the background and approach followed by the team and presented the work concluded to date.

In 2020, pilot data collection on rare diseases was started with >1100 patients from 8 reporting hospitals registered to date using OC. This represented a 16-fold increase in the number of cases reported as compared to the 2016-2017 period. Since Jan 2021, the Health Insurance Funds' data reporting interface also allows for OC to be used.

Another fundamental pillar of the implementation was training, which rendered great results, with more than 44 clinicians trained at the 3 courses offered at the Motol University Hospital, the General University Hospital in Prague and the University Hospital Brno. In addition, an OC e-learning course was launched through the Moodle platform.

The project has also fostered other activities already initiated, such as the translation of the Orphanet nomenclature and webpage into Czech, and it has also driven some debate such as the introduction of OC in the neonatal screening databases or in Hospital Information Systems (following the change of the Health Insurance Funds' data interface). Starting in 2022, the National Registry of Healthcare Services will also start to accept OC.

The main challenges encountered / lessons learned were discussed at the subsequent roundtable.

### ***Implementation of ORPHAcodes in Malta*** (Francis Agius)

In this presentation, Francis Agius, Ministry for Health, Government of Malta- MFH, provided an overview of Rare Disease Registration in Malta from three main sources (Treatment Abroad registry; Congenital Anomalies registry, and Cancer Registry) approached through this project by means of 2 main objectives:

- to educate users around the use of OC, and
- to develop an electronic health records (EHR) solution for generating OC allowing for the accurate reporting of RD cases.

Main results include the celebration of a training event and the development of an electronic platform for RD registration with a total of 5,600 patients registered corresponding to 1,007 different ORPHAcode diagnoses (please note that case registration in Malta started manually in 2016 (ca.800 cases registered/year, it was then automatized with the RD-CODE project starting 2019 to reach approx. 1,400 Cases registered per year).

The main challenges encountered/ lessons learned were discussed at the subsequent roundtable.

### ***Implementation of ORPHAcodes in Romania*** (Cristina Rusu)

In this presentation, Cristina Rusu, Department of Public Health Iasi- Directia de Sanatate Publica Iasi (DSP IASI), Romania, shared her experience of implementation of OC at Iasi Regional Medical Genetics Centre (pilot center), later on extended to other major centers dealing with rare diseases diagnosis. For such purpose, an IT system was developed and sessions aimed at training clinicians linked to ERNs in the use of OC were organized. Thanks to this initiative, close to 600 RD patients were registered using OC and Health Authorities are planning to create a RD national registry based on the IT tool developed in the frame of RD-CODE.

The main challenges encountered/ lessons learned were discussed at the subsequent roundtable.

### ***Implementation of ORPHAcodes in Spain*** (Clara Cavero – Juan Rico)

In this presentation, the team from the Fundación para el fomento de la Investigación Sanitaria y Biomédica de la Comunitat Valenciana – FISABIO, Spain, provided a description of the approach and methodology followed by the team and presented the work concluded to date, which included a first pilot phase in the six regions (Basque Country, Castile-Leon, Catalonia, Murcia, Navarre and Valencia) joining the project from the beginning and a second phase in which another region (Madrid) and a pediatric hospital (HSJD, Barcelona) were incorporated. Some of their main achievements are:

- Having managed to establish an ICD-10-ES / ORPHAcode correspondence for 95% of the entities in the Master File.
- Having made the necessary changes to their registries' IT systems to allow for ORPHA codification.
- Establishing cross-references with Congenital Anomalies ICD-10-BPA codes
- Presenting the results at several conferences and scientific publications.

The main challenges encountered/ lessons learned were discussed at the subsequent roundtable.

### ***Transnational study results*** (Monica Mazzucato)

In this presentation, Monica Mazzucato, Rare Diseases Coordinating Centre- Rare Diseases Registry, Veneto Region - Italy, provided details regarding the analysis performed on the data collected from the four implementing countries plus the Veneto Region. The study was centered in the active OC used in the Jan 2019 - Sept 2021 period, along with the confirmed level of diagnostic assertion and ICD cross-references, if available. The study has allowed obtaining preliminary results related to:

- the aggregation level (distribution of OC used per classification level and country/region; why and when OC corresponding to the aggregation level «group of disorders» have been used in each country; OC overlap among countries/regions; OC used in all countries/regions.).
- the disease prevalence class (distribution of OC per country/region and disease prevalence class).
- the preferential parent, indicating the main medical domain (distribution of OC used per country/region and preferential parent).
- ICD mapping (distribution of OC used (active entities) per country/region and Orphanet alignment concept).

## **Round table / Q&A session** (*Moderator:* Stefanie Weber, BfArM, Germany)

Following the implementing countries and the transnational analysis presentations, a space for discussion was opened focused on:

- Issues or problems identified with the coding guidelines when implementing OC in the four implementing countries.
- Recommendation for changes to the coding guidelines for the final release at the end of the RD-CODE project.
- Common implementation barriers/ lessons learned by the implementing countries.

Czech Republic - Miroslav Zvolský

Miroslav explained the difficulties faced by the integration of OC into software products in hospital information systems. At present, it requires entering the information twice, so it would be desirable to have information systems updated to allow the input of OC.

Software developers differ throughout the country, so there isn't a unique nationwide health information system. Some developments have value sets that have the same content as the Orphanet web and API, but not all. In fact, the two hospitals participating in the project have two different health information systems. In the past there was an attempt to adapt the methodology but it failed. The reason for it is that data reporting has two targets: the National Registry and the Health Insurance Funds. Each one has its specific value sets and it can´t be updated frequently. This means two different approaches, two different results, etc.

In addition, the data set of the National Registry is very large; in consequence, it is very time consuming for the clinicians to fill out the information, and sometimes they don´t have all the information required. Thus, the recommendation is to define a simple template and software.

Regarding the training activities, one of the lessons learnt is that they should start once the system is ready to initiate OC implementation and focus both on Orphanet and coding, avoiding some tools which are not meant for clinicians (Orphadata and API).

Malta - Miriam Azzopardi

Miriam pointed out that due to the discrepancy between ICD-10 and OC, they recommend starting with an OC text so that it generates the details according to the Orpha system and not according to the ICD-10, and then use the nomenclature pack provided.

Regarding the training for physicians, the Maltese team recommended to provide extensive, detailed information regarding OC. Also, ways to overcome resistance to enter data due to the fact that it is a time-consuming process need to be found.

The opportunity offered by the European Reference Networks (ERN) to promote the use of OC was also highlighted.

Miriam also mentioned the importance of defining a wider dataset which includes variables of interest for research and to facilitate the near future application of personalized medicine. For such reason, databases should be able to cross talk with each other. Thus, problems should be anticipated from the beginning by trying to share common classifications.

Regarding undiagnosed cases, she suggested that the development of a registry could be explored.

Finally, it was suggested to carry out the mapping with other ontologies; for instance with ICD-O-3, which is the gold standard of classification for oncology. In rare cancer cases, this classification (ICD-O-3) captures behaviors but also histology /morphology code. Without this coding system, important details are missed. The National cancer registry uses the ICD-O-3, and this should be linked in a standardized way to the rare disease registries. Another classification they consider important to be aware of is the Rare Cancer Classification and use the appropriate filters to extract information from Cancer Registries.

One additional challenge is keeping up with updates. And having an inventory of obsolete codes is recommended.

Romania - Cristina Rusu:

Cristina explained the difficulties regarding the involvement of professionals in the pilot due to the extra effort and time required, specially taking into account the COVID pandemics, and the difficulty to organize face-to-face meetings and training activities. Their recommendation regarding the tools used for implementing OC is that they should be kept as simple as possible. In their experience, this made a big difference and it has managed to involve some clinicians.

Spain - Juan Rico

The team has found some difficulties and advantages to the establishment of cross references between OC and ICD-10ES, but in conclusion they find it to be highly recommended, almost mandatory to avoid the difficulty of establishing direct codification with OC at every health service level. The cross-referencing work carried out has allowed homogenizing the selection of OC to a particular disorder at the different regional RD registries of special relevance in Spain given that each registry has its own characteristics, features, classifications, IT developments, etc. Thus, it has allowed the interoperability between RD information systems from the different registries, although with some limitations; for instance, when there isn't an ICD 10-ES code for a specific OC.

Some of the cons pointed out were that there are few true exact mappings, that criteria to establish cross-refs must be agreed upfront but it might not fit all coding purposes and that cross-refs need to be regularly quality-checked and updated. Updating of the classification (new diseases, obsolete or deprecated RD, new criteria, etc.) requires regularly checking and updating the nomenclature, this being time-consuming. He also advised that each country, especially those with many regional health systems, should maintain the figure of a coordinating team and a core working group.

Also, it is advisable to have the Masterfile translated to each country's language.

Questions from the audience

Miroslav Zvolský (Czech Republic) asked if any other countries are working towards reaching interoperability among health information systems in the way ERNs are doing, for instance.

Céline Angin (France) indicated that there is an ongoing proof of concept between the ERN ITHACA and the French National Registry.

E.S. (Germany) exposed the problems encountered when trying to register syndromic forms of congenital malformation cases using OC because of the loss of information. Thus this will represent a big problem once coding with OC becomes mandatory in all clinical setting in Germany and it is already a problem at ERNs already coding with OC.

The Orphanet French team explains that this specific problem obeys to the fact that approximately 70% of RD are multisystemic, so they propose to code the main diagnosis using OC and complete the information with HPO terms. A working group to deal with HPOs used by ERN is being set up.

Stefanie Weber (Germany) mentioned that this last topic will be reflected in the upcoming version of the Guidelines by saying that OC may not be a solution for all situations, advising using additional codifications in specific settings (eg. Rare cancer, congenital malformations).

Ana Rath underlined that maintenance of ICD-10 extension over time is problematic because it needs specific funding and dedicated teams. Therefore, should it be mandatory to keep OC linked to ICD-10 or could OC be considered as a code aside from ICD-10 coding than may be chosen for other purposes? Thus, the proposal would be to use OC even if the correspondence with ICD-10 code has not been updated in order to at least have OC as an accurate and specific epidemiological indicator.

Juan Rico (Spain) agreed with this approach in those cases that are already diagnosed and identified with an OC at source, because this avoids making a correlation with ICD-10 or other classification system. However, in Spain there is not a mandatory regulation to code with OC at clinical level and that is why it is necessary to use the cross-refs provided by the OC tools. Nonetheless, there are some initiatives like the one at the San Joan de Déu Hospital (HSJD), where it is intended to include OC directly in the health records.

Related to the latter point, Francesc Palau (Spain) clarifies that, at the SJD Hospital, every diagnosis includes ICD-10 and that designated team within the hospital assigns an OC to each patient. In this sense, the plan is to automate the linkage process to go from ICD-10 to OC at the health record level for all the hospital services in the next months.

## ***Guidelines*** (Céline Angin)

Céline Angin, French National Registry for Rare Diseases (BNDMR), presented the work done in the frame of the project in relation to existing experiences and guidelines about the coding of undiagnosed rare diseases patients which concluded with the workshop celebrated on September 28th and the deliverable published on the RD-CODE website (http://www.rd-code.eu/wp-content/uploads/2021/01/Existing-experiences-and-guidelines-about-coding-of-undiagnosed-RD-patients.pdf ) summarizing a series of recommendations for coding undiagnosed patients.

# Day 2

## Session 2: RD-CODE legacy

### *Collaborating projects: X-eHealth*

***Presentation of a use case*** (Ana Rath)

In this short presentation, a brief case report served to introduce the following presentations related to the X-eHealth project by exemplifying the need of collaboration between the RD community and X-eHealth related initiatives, in particular, to improve RD patients' unplanned healthcare.

Ana concluded by launching a series of questions to the audience to foster reflection and discussion:

- *What's the utility of the PS in your setting? (as a clinician, patient, hospital information manager..)*
- *How ready is your system/ organization to support such implementation?*
- *Which are the challenges and bottlenecks? What can we do to overcome them?*

***X-eHealth project: short presentation*** (HL7 Europe)

In this presentation, the HL7 Europe representative , provided an overview of the EC funded project, which aim is to lay the foundations to advance the integration process of the eHealth services features into the already in place European Cross Border Patient Summary, also developing a common framework for RD patients' information exchange, and creating a Electronic Health Records Exchange Format (EEHRxF) Community of Practice, one of which next steps is to carry out a proof of concept of EEHRxF in rare diseases working in an RD-Code / X-eHealth Demonstrator.

Following this presentation, a poll was launched to get to know the audience and to assess their degree of knowledge / awareness regarding the Patient Summary (PS) and the EEHRxF. The group of participants was mainly constituted by clinicians and researchers, followed by registry managers, others, and patient advocates. Most participants answering the poll (31) were familiar with the PS and a smaller percentage of them knew the EEHRxF.

***Patient Summary*** (XeHealth representative)

In this presentation, the XeHealth representative provided some details related to the work being done towards the Patient Summary (PS) as an identifiable "essential and understandable" core dataset in the context of the X-eHealth project and its connection with the EHR as the source for producing the PS.

The collaboration with Orphanet ensures the inclusion of OC in the dataset as an essential element of the EHR/PS when dealing with patients affected by a RD.

***ePS: How it serves RD/ New content fields, data model*** (HL7 Europe)

This presentation by HL7 Europe representative, was centered on the International Patient Summary (IPS) dataset for RD patients focused both on unplanned and planned healthcare. The different items include information related to care pathways, treatments and diagnosis, the latter being based on OC.

***Orphanet nomenclature delivery services*** (Marc Hanauer)

In this presentation, Marc Hanauer, INSERM, provided a summary of the contents of the Orphanet nomenclature pack and all the files that comprise it: set of XML files, ICD mappings, classifications, linearization file, master file (Excel file - minimal set of OC, aligned with ICD-10 codes), ORPHA nomenclature differential file and description of the Orphanet nomenclature file for coding.

In addition, Marc presented the Orphanet Nomenclature application programming interface (API) and the Data visualization tool (Dataviz) developed in the frame of the project. The API is embedded in Orphanet's information system and it exploits data from the main knowledge base. Other delivery services include the website itself, the Orphadata platform or the HPO-ORDO Ontological module.

***Questions & Answers***

Main issues revolved around:

- The need to revise the child health data set to include growth and development related information
- The possibility of retrieving information from RD Registries to be used in the PS
- Assessment by physicians of the relevance of the information included in the PS
- The need of standards and a coding system for reporting treatments
- The importance of having Orphacode registered in the PS' diagnostic text field.

***Possible future plans for a demonstrator*** (HL7)

In this presentation, HL7 Europe representative, launched a proposal for a demonstrator focused on the utility of X-eHealth specifications for rare disease patients, including medical images, labs, prescriptions, patient summaries and hospital discharge reports, among others, in addition to education/capacity building on how RD-CODE tools can be used with X-eHealth

specifications in different contexts, e.g. telemedicine, tumor boards, emergency department, exchange/sharing of patient summaries.

With this presentation, HL7 intended to encourage discussion around exploring ways to accelerate adoption of RD-CODE tools, assessing its costs and benefits and conducting use case driven X-eHealth debates.

## *Listening to the stakeholders: How can RD-CODE meet your needs?*

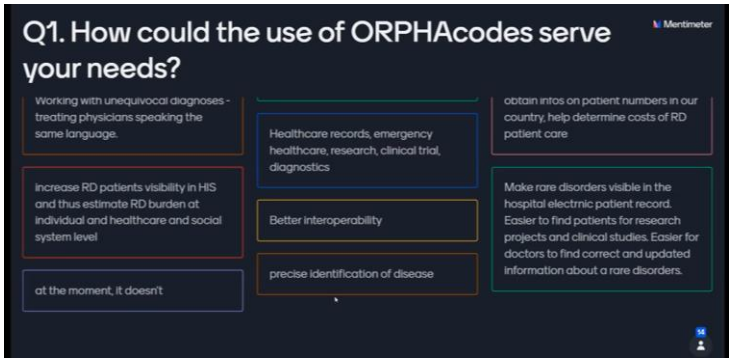
### *Moderators*

Inés Hernando, EURORDIS

Debby Lambert, Genetic Counselor, Ireland

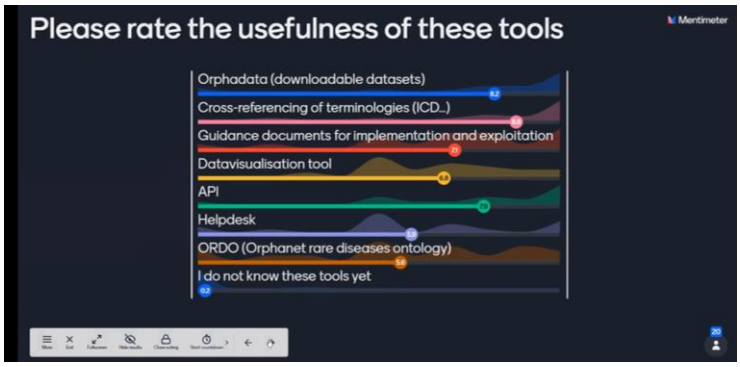
The aim of this multi-stakeholder panel was to present some RD-CODE unrelated OC implementation initiatives. The session began with a poll launched to the audience with the following questions:

*Q1. How could the use of OC serve your needs?*

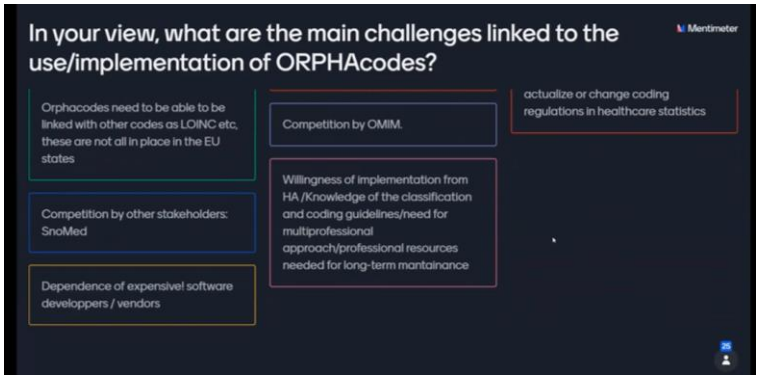



*Q2. What would you prioritize? Having OC implemented in ...EHR / RD Registries / National and/or Regional HIS / Hospital IS.*


*Q3. Please rate the usefulness of these tools: Orphadata / Cross-referencing of terminologies / guidance documents for implementations / Dataviz / API / Helpdesk / ORDO.*




*Q4. In your view, what are the main challenges linked to the use/implementation of OC?*




*Q5. What kind of help would you require to implement OC in your organization?*


## Multistakeholder Panel Presentations

Céline Angin, APHP, France

In this presentation, Céline described the implementation of the Orphanet nomenclature in the BNDMR Registry, where a minimum data set was defined in order to collect information from hospitals' HER and from the BaMaRa hub, where Expert Centers report directly. Implementation of the Orphanet nomenclature was done by means of the OC lists (no classification), using the disorder and subtype levels for coding and the group level for clinical description coding (along with ICD-10 and HPO). In addition to the OC, the description of patients includes the diagnostic assertion and the phenotype and genotype.

The possibilities of data exploitation are numerous and include counting the number of patients affected by a RD or a group of RD in a geographic area for epidemiological studies, clinical trials feasibility studies, comparison studies, etc..

In total, >140 projects (concluded/ongoing) have been developed by exploiting this database.

Collaboration with the BNDMR is also crucial for the Health Data National System (SNDS), since this system, working with ICD-10, is unable to identify RD patients. Linkage of the SNDS to the BNDMR will allow performing health economic analyses, mortality studies, treatment compliance or care pathways referred to the RD population.

Céline concluded her presentation by providing useful suggestions for improvement of the Orphanet nomenclature use.

ECHO represnetative, Hospital Sant Joan de Déu, Barcelona

ECHO representative presented the strategy adopted by the hospital to address the RD codification in order to approach their contribution to more than 20 registries in a standardized manner.

In 2019, a Hospital RD Task Force integrated by the coordinators of the hospital's reference units was created with the objective of: 1. Implementing OC in the Hospital Information System; 2. Facilitate the complementarities with other mandatory notification registries; 3. Identifying undiagnosed RD patients and; 4. Defining Common Data Elements. In addition, a RD catalogue including rare pediatric diseases previously seen in the hospital was produced including the following elements: Descriptive/literal, internal code, OC and ICD-10-CM code. The number of entities included in the catalogue is 5.000 (before duplicate depuration), grouped in 27 categories.

The catalogue was then integrated in the EHR and a first pilot was initiated with the participation of 4 Hospital Units (primary immunodeficiencies, kidney, urology and neurocutaneous) in November 2021.

It is expected that the catalogue is concluded by February 2022, along with a user manual and a dissemination plan. Next steps also include a helpdesk for case consultation.

ERN representative, University of Heidelberg, Germany – ERKNet

ERN representative informed about the use of OC within ERKNet, where an ERN wide registry for rare kidney diseases was set in 2019.

At the design phase, this ERN collaborated very closely with Orphanet in order to classify the diseases, starting by reviewing all OC assigned to a rare kidney disease. Out of the 335 OC, 79 were revised/ updated. This work also turned out to be very useful to get experts acquainted with OC. Subsequently, 350 diagnoses with their OC were preselected to be included in the registry, which allows introducing cases by diagnosis, gene, OC of by doing a search of the

diagnosis name. The registry in not yet linked to the hospitals' EHR; thus, cases are entered manually.

At present, the registry's data annotated with OC is being exploited to do epidemiological research and work is being done to enable interoperability with other ERNs, most of which have already adopted OC as well.

EUHA representative, Karolinska Institutet, Sweden - European Hospital Alliance

In this presentation, EUHA representative provided an overview of the European University Hospital Alliance (EUHA), constituted in 2017, integrated by 9 hospitals and created to be complementary to the work developed by ERNs providing support at three levels: healthcare, education and research. It is structured in networks on different topics, one of them being the RD & ERN Network coordinated by Rula. One of this network's strategic goals was to produce an inventory of coding systems in use at the different hospitals, identifying the challenges and analyzing the use of OC.

In Sweden, RD coding at a national level is being discussed and there is an ongoing pilot, while the Karolinska Institute and centers linked to ERNs are already advancing towards OC implementation.

Coordinator IT tools for European Reference Networks for Rare Diseases. European Commission

This intervention concerned the Clinical Patient Management System (CPMS) in use by ERN to facilitate medical discussion across countries. The tool, created in 2017, is now in its second version, and its data entry structure could serve as a use case for OC.

In January 2022, a call for tender to develop this new tool will be launched and its release is planned for mid-2023. Collaboration with the OC community would be very much appreciated to make of this a successful use case of RD codification in an IT system of the European Commission.

**Multistakeholder Panel - Round Table**

The session was opened by sharing a reflection about the accelerating power of ERNs and Hospital Alliances and the need to count with documents and guidelines based on the evidence and the examples shown here to engage institutions and governments.

Panelists agreed that sharing experiences regarding the investment needed in terms of time, human and economic resources is necessary and it would be of great benefit to other hospitals, regions and countries. An example of this is the work being done by the Sant Joan de Déu Hospital, which is sharing its expertise with the European Children's Hospitals Organization (ECHO).

This issue raised a question regarding the best possible approach when tackling the adoption of ORPHAcoding and whether it would be more efficient and successful to address it at the hospital or at the national level. As pointed out by the ERKNet representative, in Germany this required a national legislation approach. It was a lengthy process that should involve IT developers and must be accompanied by training activities. In this country, the Research Ministry financed a Medical Informatics Unit's project with RD as a use case to connect hospitals to each other using OC. In the near future, it will be compulsory to use OC for coding and it will be linked to reimbursement.

From the point of view of the BNDMR and INSERM representatives, national decisions to make it mandatory are required and this should also be financially supported as it was done in the 3rd French National Plan. Thus, advocacy at both levels is important: it should be included in national plans but for practicality reasons it should be implemented at the hospital level. In this sense, one of the lessons learnt from the project is that local support is very important.

Other ongoing initiatives include the promotion of the use of OC in Spain (the RD Strategy of the NHS is currently under evaluation).

To conclude, a comment was made on how the work done in the preceding project (RD-ACTION, which WP5 generated the Master File and Guidelines that constituted the starting point for RD-CODE) didn't manage to achieve OC adoption. It hasn't been until real cases of implementation have proven their utility that interest and the launching of pilots have increased. There is far more evidence now about the costs, benefits, time, technology and training needed to accomplish it. Therefore, at this point, it is crucial to publish the results presenting valuable enough evidence to allow institutions and governments to adopt the necessary measures to achieve it.

### *Open discussion: Project's legacy and future*

Ana Rath opened up the session by summarizing the next steps after RD-CODE concludes at the end of December 2021. From then on, Orphanet will continue delivering the nomenclature pack and it will maintain the different tools developed in the frame of the project: API, Dataviz, Helpdesk. Guidelines are being updated by BfArM taking into account the feedback received throughout the project and will also be available, along with the new Guidelines produced for the use of OC in undiagnosed patients.

In addition, most activities, developments and achievements of RD-CODE will find continuity in the New Direct Grant, Orphanet Data for Rare Diseases (OD4RD), starting next January, which main objectives are:

- Provide support to the CPMS
- Collaborate with ERNs and the European Health Data Space (EHDS)
- Reinforce national support hubs to add European value: taking the lessons learnt from RD-CODE, create a network of national hubs starting with 13 Orphanet national teams that will provide local support (helpdesk for technical support), training and

assistance to make possible that hospitals linked to ERNs implement OC. This will allow generating additional evidence from hospitals to the EHDS.

Ana concluded by saying that RD-CODE has come to an end and that we are in a critical moment to leverage the project's results. Thus, she launched a proposal to create an RD-CODE Community of Practice (CP) to keep this initiative alive in order to build capacity, promote implementation, share experiences and mutualize guidelines, training materials and tools. This CP could be formalized by constituting a Stakeholders group in the EC Health Policy Platform (HPP).

At this point, RD-CODE partners and collaborators expressed their interest and support to the creation of a Community of Practice. Also, it was mentioned that the invitation to participate should be extended to Patients Organizations, Hospitals Alliances and ERNs, as well as to IT developers/ implementers.

To close the workshop, Catherine Chronaki's proposal for a RD-CODE/ X-eHealth Demonstrator was brought up for discussion. Its main objective is to demonstrate the utility of X-eHealth specifications in RD patients, showcase its use in different cases (e.g. telemedicine, tumor boards, emergency department, exchange/sharing of patient summaries), and discuss and explore ways to accelerate adoption assessing costs and benefits. Some RD-CODE partners showed interest in participating (Veneto Region, BNDMR, Czech Republic). Expression of interest is open and a first meeting with X-eHealth will be held in January to explore this collaboration.

## Annex 1 _Workshop Participating Institutions

| Institution (# participants) |
|---|
| Acibadem University - Turkey [1] |
| APHP - France [1] |
| Association AHC18+ e.V. - Germany [1] |
| BfArM - Germany [1] |
| Catalan Health Service - Spain [3] |
| CEDEM - Spain [2] |
| CIBERER - Spain [5] |
| Consejería de Sanidad, Junta de Castilla y León - Spain [1] |
| Department of Health of the Basque Government - Spain [2] |
| DSP Iasi - Romania [1] |
| European Commission [1] |
| EURORDIS [1] |
| FISABIO - Spain [3] |
| Freelance - Spain [1] |
| Fundación Pública Gallega de Medicina Genómica - Spain [1] |
| General Directorate of Public Health, Madrid Regional Health Authority - Spain [1] |
| Genetic Counselor - Ireland [1] |
| HaDEA [1] |
| Health Service Executive (HSE) - Ireland [1] |
| HL7 Europe - Belgium [1] |
| Hospital Sant Joan de Deu - Spain [3] |
| Hospital Universitario Virgen del Rocío - Spain [1] |
| INSERM - France [7] |
| Institute of Health Information and Statistics - Czech Republic [3] |
| Instituto de Salud Pública y Laboral de Navarra - Spain [1] |
| IRCCS Istituto Ortopedico Rizzoli - Italy [2] |
| Karolinska University Hospital, Center for Rare Diseases - Sweden [1] |
| Medical University of Vienna - Austria [2] |
| Ministry for Health - Malta [2] |
| Ministry of Health -Turkey [1] |
| Murcia Region Rare Diseases Information System - Spain [2] |
| National Advisory Board on Rare Disorders, Oslo University Hospital - Norway [2] |
| Orphanet Switzerland - University Hospitals of Geneva [1] |
| Patient Association for Atypical Parkinsonian Syndromes - Czech Republic [1] |
| Rare Care World Foundation - Netherlands [1] |
| RD Coordinating Centre Veneto Region, Padua University Hospital - Italy [3] |
| SoMA patient organisation - Germany [1] |
| Spanish Ministry of Health, Social Rights and Consumer Affairs - Spain [2] |
| Telethon Kids Institute - Australia [1] |

The Health Institutes of Turkey [1]
The National Rare Diseases Office - Ireland [2]
University Hospital Motol - Czech Republic [1]
University of Heidelberg - Germany [1]
Western Australian Register of Developmental Anomalies [1]
X-eHealth - United Kingdom [1]