# Deliverable 5.3

## *Implementing countries Report on ORPHAcodes adoption*

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**Disclaimer:**

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The RD-CODE project was launched in January 2019 for a 36 months period.
More information on the activities of the RD-CODE project can be found at www.rd-code.eu

## Reader notes:

This document contains country-specific insights on lessons learned, challenges and potential solutions emerging from different ORPHAcodes implementation experiences carried out in the framework of the RD-CODE project.

The reported contents derive from the analysis of the answers to a questionnaire administered to the teams in charge of implementing activities in the following RD-CODE participating countries (Czech Republic, Malta and Spain). The questionnaire constitutes Milestone 5.3 of the project.

The report includes also some contents presented during the country-specific sessions and the round table included in the Final meeting of the project.

The purpose of the document is to provide a starting point for other institutions and/or countries interested in using ORPHAcodes for the coding of RD patients.

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# Czech Republic

## 1. RD coding and ORPHAcodes implementation

The underrepresentation of RDs in codification systems used for morbidity and mortality recording and the absence of a minimal data set for the collection of RD-related data were identified as priority areas for action both in the first and second RD National Action Plan.

In the National Action Plan 2018-2020 this topic has been further addressed under action 8 “Unification and development of data collection and biological samples”, recognizing the Orphanet nomenclature as the leading system for RDs coding.

The expansion of a dedicated Czech portal (www.orphanet.cz, https://www.orpha.net/consor/cgi-bin/index.php?lng=CS) including the translation of the Orphanet database contents in the Czech language has been the basis for the further implementation of the Orphanet nomenclature, including the use of ORPHAcodes, into Czech health information systems.

The Institute of Health Information and Statistics of the Czech Republic (IHIS; UZIS) has been identified as the institution in charge of introducing ORPHAcodes, together with OMIM and the SSIEM (Society for the Study of Inborn Errors of Metabolism) classification system into the National Registry of Reproduction Health and into the Ministry of Health “Data Standard”.

The IHIS has established a minimum data set for the collection of RD data to be used in any new RD registries and incorporated in existing ones. Thus, so far the national strategy to produce data and statistics for RD in the Czech Republic has been based both on the re-use of existing data collections and on the development of new ones.

The use of ORPHAcodes for RD recording started in 2016 with the introduction of this option in the National Register of Congenital Malformations (NRVV; http://www.uzis.cz/registry-nzis/nrvv). Moving forward from this initiative, additional ways to enable further accurate identification of RD patients through ORPHAcodes in other data collections have been explored.

In the project framework, three clinics based in two University Hospitals (Motol University Hospital and Prague General Hospital) were involved in the ORPHAcodes implementation. Both these hospitals are health care providers (HCP) full members of ERNs.

During the project course, ORPHAcodes have been used mainly at the point of care. Professionals involved in the coding process differed according to the implementation setting (registry *vs* hospital level of implementation). They were namely clinicians, registry staff and coders, among which trained nurses.

In the Czech Republic ORPHAcodes have been implemented, but not the whole classification has been exploited.

All ORPHAcodes corresponding to the three classification levels (groups of disorder, disorder and subtype) have been made available for recording purposes. An analysis of the use of the aggregation level information will serve as the basis for possible future developments allowing the implementation of the entire classification.

During the project, it was not possible for coders to input information on the level of diagnostic assertion (suspected, confirmed, undetermined). This possibility will be taken into consideration for future developments as well, as it constitutes furthermore a guideline issued within the project framework. The idea is to add this information as a stand-alone part of the web-interface use for data input. In the web-interface developed, it is possible to further specify the diagnosis and more than one ORPHAcode can be entered, but recorded cases are *de facto* referred only to confirmed cases.

A patient ID at hospital level is available and allows carrying out record-linkages activities with other population-based registries, tracing RD patients' pathways.

In the Czech Republic, ORPHAcodes have been incorporated both in already developed IT systems intended for the collection of data on patients affected by congenital malformations and in IT systems used for the collection of data on both rare and non-rare patients.

Starting from January 2021 the reporting data interface to health insurance funds allowed the use of ORPHAcodes and this option will be extended to the National Registry of Healthcare Services in 2022.

The implementing team reported that a quality control process is not yet in place, but it is planned, especially focusing on data submitted to health insurance funds, as they have reimbursement implications.

The ORPHAcodes' implementation in health information systems required the involvement of IT professionals in the process. In the Czech experience, this exchange has been challenging especially at the hospital implementation level. The main hurdle encountered was the clear identification of contact person/s in charge of the IT implementation tasks, to be of reference also for the necessary updates, depending on the annual release cycle of release of the nomenclature. The identified problem is that the process to manage the changes in the classification should be aligned to the IT developments plan and this requires a strict interaction with IT staff, which is not at the same level of definition in each implementation setting. No suggestion of changes regarding the timing of the coding resources release cycle emerged during the project.

According to the implementation experience carried out, the changes that are perceived as more difficult to manage are changes in disease names and in synonyms. As insurance companies are interested in mapping ORPHAcodes to ICD-10 codes, changes in cross-referenced codes are considered critical to manage as well.

The Czech team considers that in terms of usefulness in supporting a successful implementation process the following Orphanet resources were very helpful: Orphadata, cross-referencing of terminologies and API. The reported limited knowledge of other resources as ORDO, DataViz and Github is probably because these resources were developed in the second half of the project course and thus their knowledge was less familiar for the team.

The Czech team pointed out how the Orphanet website is considered by users the easiest way to support their coding process. The difference in contents between the website and the Orphanet nomenclature pack was explained in detail during the training sessions organized for coders.

These meetings, during which the coding resources were presented, were considered very helpful to guide users in the implementation process. Training sessions took place both in presence and online due to the pandemic evolution. In-presence events were considered more appropriate to achieve training goals as they included practical sessions and Q&A time to solve coding issues starting from real use-cases. New training material in Czech language was specifically developed for these meetings. Already existing resources have been used as well and made available for attendees.

In case of questions emerging when using ORPHAcodes during the project course, users have contacted the Czech implementing team directly. As the number of users involved was limited, the implementing team has considered this activity manageable during the project. As ORPHAcodes will become more widely used and considering also that other HCPs will enter additional ERNs hopefully in the near future as a result of the second call and thus will start using ORPHAcodes, it is planned to organize a local helpdesk managing requests from users.

## 2. Lessons learned and proposals

According to the Czech team the main barriers potentially affecting ORPHAcodes implementation depend on the motivation of their use perceived by IT staff involved in their incorporation in the systems at the basis of the data collection process. For coders, and clinicians in particular, it is important to input information which can be retrieved from other systems used to collect health information, and which can be referred to the same patient across different care settings in an easy way.

According to the Czech team, for countries not using ORPHAcodes yet, e-health initiatives constitute a good opportunity in the next years to build a common infrastructure able to support the data collection process. Nevertheless, in the opinion of the Czech implementing team it has to be discussed which is the level of detail needed for RD patients compared to patients affected by more common diseases.

Moving from the Czech experience, the team considered the implementation of ORPHAcodes in hospital information systems of the utmost priority with respect to other settings (i.e. registries).

At the same time, the Czech team defined the implementation at this level as the most challenging. On the contrary, the implementation of ORPHAcodes in registries, whether population-based or developed by ERN, was considered relatively easy.

According to the experience gained during the project, they considered health authorities representatives and hospital managers as key stakeholders that need to be involved from the beginning for a successful ORPHAcodes implementation. They reported a higher level of knowledge of ORPHAcodes strategic value in tracing RD patients by clinicians working in ERNs or in other RD Centers and by patients' association and EPAGs.

Finally, the creation of a community of practice sharing achievements, problems encountered and solutions for an effective ORPHAcodes' implementation was considered as a strong priority for the future. Furthermore, webinars like the ones promoted by WHO to spread knowledge on the ICD-11 implementation process were suggested by the Czech team as appropriate tools to raise interest and motivation in users and in other stakeholders interested in increasing RD patients' visibility in health information systems.

## Malta

### 1. RD coding and ORPHAcodes' implementation

The Maltese strategy on RD coding is still based on the RD Registry initiative, which was launched in 2016, collecting data from 2008 onwards, and which is based at the Department of Health Information. This initiative relies on an *a posteriori* data collection and can be defined as a secondary registry. Existing data collections used to identify within them RD cases are the national cancer registry for rare cancers, the congenital anomalies registry, other specific diseases registries and the database of patients sent to other countries for tertiary care not available in Malta (the so-called Treatment abroad registry). In all these data sources, coding of RD cases was manually done.

In the Maltese setting the coding activities within the project involved mainly registry staff. The registration of ORPHAcodes take place directly in an IT system developed *ad hoc* within the project framework. Professionals involved in the coding process were namely registry staff personnel.

In Malta ORPHAcodes have been implemented, but not the whole classification. All the three levels of diagnostic assertion (suspected, confirmed, undetermined) can be recorded in the codification process. Furthermore, all the classification levels could be used in the coding process (group, disorder and subtype). In case of ongoing diagnoses, it is possible for coders to further specify the patient diagnosis and thus trace the patient's history, thanks to the availability of a unique patient ID in use across different health information sources in Malta.

In the project framework, ORPHAcodes have been used together with other terminologies, namely ICD-O for rare neoplastic diseases and OMIM for genetic diseases. SNOMED CT and HPO have not been used. In the Maltese setting, the parts of the classification that have been mostly used for codification purposes are the classification of neoplastic diseases and the one of developmental defects. Additional disease entities derive from the Treatment Abroad List.

The implementing team reported that a quality control process of data collected is not yet in place, but it is planned, as it requires the availability of dedicated professional resources. For the same reason the process to manage the changes in the classification is planned, but not in place yet. According to the experience carried out, the Maltese team considers the changes in the disease status the most difficult to manage, followed by the changes involving the levels of the classification. Regarding the annual release cycle the Maltese team suggested to plan a dedicated communication to be sent to potential users of the coding resources, to alert them in case of their updating.

A training session was organized within the project course in a mixed modality (in presence and online). The training activities were based on already existing resources, developed by the Orphanet team and by the WP5 team. All the material presented was made available for attendees. The Maltese team considered that an important objective of the training was to explain in detail the Orphanet nomenclature and the differences in aims and contents between the website and Orphadata. The Maltese team considered Orphadata as the most useful resource to navigate the classification, followed by the Orphanet website.

The reported limited knowledge of other resources as ORDO, DataViz and Github is probably because these resources were developed in the second half of the project course and thus their use is less familiar for the team.

Due to the limited number of persons involved in the use of ORPHAcodes, emerging issues were asked directly to Orphanet. A local helpdesk managing requests from users is considered a valuable resource that could be helpful for future implementation activities.

In the Maltese experience, the necessary involvement of IT professionals is considered a challenging aspect of the ORPHAcodes' implementation process. The IT staff was already familiar with a multidisciplinary work modality, so it was not a problem to work jointly for the development of the system at the basis of the data collection. The challenge relies namely on funding issues potentially affecting the necessary updating of what has been developed during the project

## 2. Lessons learned and proposals

According to the Maltese team, ORPHAcodes' implementation is very much conditioned by the level of engagement of health authority representatives and existing motivation to support ORPHAcodes use for counting RD patients and tracing their care pathways. The Maltese team thinks that this is particularly important in a small setting as the Maltese one, where political commitment could allow achieving concrete results in a relatively short time period.
They suggested that also the pharmaceutical industries representatives could be key figures in promoting ORPHAcoding as they are interested in numbers of patients potentially eligible to new treatments. A good level of knowledge of ORPHAcodes strategic value in tracing RD patients was reported among patients' association representatives and ePAGs.

Based on the experience carried out, the Maltese team considered the implementation of ORPHAcodes in hospital information systems of the utmost importance. They considered important, but to a lesser extent, ORPHAcodes' implementation within ERN registries. Mater Dei hospital participates as full member in a limited number of ERNs. As all RD patients are usually referred to this hospital, ORPHAcodes implementation at this level could greatly increase the number of ORPHAcoded patients.

The implementation of ORPHAcodes in hospital information systems was considered achievable with appropriate resources and a close follow-up with clinicians in charge of the coding process.

According to the experience gained during the project, the implementation team reported as main difficulties the lack of human resources, as they were redistributed to other duties during the pandemic emergency.

Regarding sustainability issues, the team reported a general need to reallocate resources in a post-pandemic setting as especially human resources are lacking, not only with clinician expertise but also with a health planning background.

The creation of a community of practice sharing achievements, problems encountered and solutions for a successful ORPHAcodes implementation was considered a great opportunity to further promote ORPHAcodes' implementation, not only at European, but also at international level.

# Spain

## 1. RD coding and ORPHAcodes' implementation

The Spanish strategy to produce data on RD was first defined at national level in 2009. The Strategy was based on seven lines of action; for each area objectives and recommendations were clearly defined. The issue of RD codification was addressed within the strategy line "Information on RD".

The updated Rare Diseases Strategy of the Spanish National Health System, approved in 2014, further addressed the issue of RD coding and classification under the "Registries" chapter.

The *Real Decreto* 191/2015 established the national RD Registry. Its aims are to provide epidemiological data to inform health planning and the evaluation of interventions addressing RD patients' needs. Another important aim is to provide indicators that could support interregional and international comparison. The National RD Registry gathers information from the regional registries. Currently, a subset of RDs is of compulsory notification to the national registry (n=22), while the rest are registered either at hospital or regional level.

As Spain has a decentralized healthcare system, the funding of the RD Strategy is transferred from the national level to the Autonomous Communities in the framework of a more general funding process. It is up to each region to establish which percentage of those funds is specifically dedicated to rare diseases-related activities. RD coding related activities were not specifically funded within the National Strategy, but regions could decide to allocate part of the funds received to coding activities.

Now, each region has a population-based registry collecting metadata from the following primary information sources: the hospital discharges database (CMBD); direct notification by clinicians; other registries collecting data on renal diseases and transplantations, primary care, drugs, disabled patients, congenital anomalies and genetics. Therefore, the strategy to produce data on RD in Spain is developed at national and regional level and is based both on the development of new data collections and on the re-use of existing ones.

In particular, the use of ORPHAcodes started in 2015. Initially ORPHAcodes were used in regional RD population-based registries, established in some Autonomous Communities. Despite difficulties in achieving a global coverage of the population in some regions, progressively the coverage of the Spanish population steadily increased. The last published national report presented data from 12 regions out of 17.

In the framework of the WP5 activities, a questionnaire was sent to all implementing regions with the help of the Spanish project coordination team. Answers were received by two implementing regional teams, Valencia and Murcia ones, and they have been included in the present Report.

In Spain, ORPHAcodes are recorded in regional registries using the different primary data sources cited above. Therefore, during the project course, they have been used mainly *a posteriori*. Only in the primary care setting physicians retrieve ORPHAcodes for consultation purposes, but they do not record diagnoses directly using ORPHAcodes. Professionals involved in the coding process were namely registry staff and coders. In Valencia region, an IT system was developed within the RD-CODE activities allowing cases recording. In Murcia, ORPHAcodes have been incorporated in an already developed IT system specifically intended for the recording of RD patients' data, the RD Information System of Murcia region (SIERrm). In SIERrm ORPHAcodes are added to the patient file once a RD diagnosis is confirmed.

The classification systems through which the diagnoses are received from the different primary information sources are diverse. Since 2016, the ICD-10-ES has been implemented in Spain as the reference classification for clinical coding and for the collection of morbidity in-patient data, in accordance with the Royal Decree 69/2015. Within the project framework, a work to interrelate the ICD-10-ES and ORPHAcodes at the disorder level of the classification was performed by a consortium including 6 Regional RD Registries (Basque Country, Castile and Leon, Navarre, Catalonia, Murcia and Valencia Region), the RD Joint Research Unit FISABIO-UVEG and CIBERER (Biomedical Research Networking Centre on RD). An article published in the OJRD describes in detail the results of this activity (Rico J et al. *Orphanet J Rare Dis.* 2021).
The work carried out helped a lot increasing homogeneity as common criteria for mapping between ORPHAcodes and ICD-10-ES were discussed and adopted, based on the Orphanet Procedural document "Orphanet ICD-10 Coding Rules for RD".
The mapping process included not only ICD-10 ES, but furthermore SNOMED-CT, used in Spain for morbidity recording, ERA-EDTA (used in registries collecting data on patent affected by renal diseases) and ICD-BPA, used in congenital anomalies registries.
In addition to this work, a quality control process is in place at registry level, as the registry staff for each newly recorded case performs a validation process.
In the Spanish experience, only ORPHAcodes have been implemented and not the whole classification. This is in line with the fact that ORPHAcodes have not been used in the Spanish contexts at the point of care, as the data input process relied on previously recorded information. Regarding the level of diagnostic assertion, it was possible to record information on suspected and confirmed cases. The availability of a patient ID can allow the tracing of the patients' diagnostic journey and the estimation of time needed to reach a RD diagnosis.

Information on undetermined diagnoses is not available in the considered primary data sources feeding the registries.
As the mapping exercise started from the Master-file developed in the framework of the RD-Action, only the disorder level has been considered in establishing equivalences at the basis of ORPHAcodes implementation. Probably this explains why the Orphanet website is still considered the most useful tool to navigate the classification by users.
A process to manage changes in the classification contents is not in place yet. Following the work carried out to establish equivalences, the consortium team focused on the importance of the annual analysis of the Orphanet nomenclature pack contents when released. Not only to track the relevant changes (e.g. inactive or newly added ORPHAcodes), but also to manage potential discrepancies on ICD-10-ES already established correspondences. The consortium discussed possible strategies to manage these changes. Their availability as a new added information in the nomenclature pack is considered very helpful.
Respondents suggested setting up a dedicated communication which alerts when the coding resources are updated, according to the established annual release cycle.
According to the Spanish teams, the most useful resources supporting the coding process are Orphadata, the cross-referencing of terminologies and the ICD-10 coding rules document. The following resources were not very familiar to the implementing teams: DataViz, API and GitHub.
The guidance documents were considered of limited usefulness in the implementation process.

During the project, some training sessions were organized for users. They were focused on very specific issues and organized mainly for the training of the coding staff.

The major knowledge gap perceived by the interviewed implementing teams was referred to the nomenclature structure, its rules and contents.

**Recent developments**

During the project course, in addition to regional registries, the Sant Joan de Déu (SJD) Hospital in Barcelona joined the implementation consortium. This hospital has accreditations as a regional and national reference Center for a wide range of RD. Furthermore, is full-member of 9 ERNs, and has applied for 12 more receiving positive preliminary reports in the ongoing evaluation process.

A RD Tranversal Task Force was established within the Hospital. Its main objectives were the following: quantify the number of RD patients attended at SJD by implementing ORPHAcoding into the local hospital information system; facilitate the completion of mandatory notification registries; define common data elements allowing the identification of transversal monitoring indicators.

The ORPHAcodes considered for implementation were referred only to pediatric disease diagnosed and treated at SJD. Clinicians of each Unit/Service involved in RD patients care reviewed the list compiling a “SJD RD Catalog”. Equivalences between ORPHAcodes and ICD-10 CM codes have been made available developing an *ad hoc* interface for data input in the electronic health record in use in the hospital. The pilot phase has begun in November 2021 allowing so far the recording of cases corresponding to 680 different RD entities.

This experience highlights ORPHAcodes versatility, and their potential parallel implementation both at registries level and within hospital information systems, with a clear benefit especially in hospitals of reference for RD and participating in ERNs.

## 2. Lessons learned and proposals

According to the Spanish teams interviewed, the main barriers potentially affecting ORPHAcodes implementation are the need of dedicated human resources and time for their routine use. A suggestion for a successful implementation is to embed ORPHAcodes in the care activities. This is interesting as in most cases, in the Spanish experience the ORPHAcodes’ use derives from the care dimension, but takes place mainly *a posteriori*, following care activities performed by clinicians.

Of course, such an extended approach will involve a wider range of users, highlighting the need for training initiatives, helpdesk services and appropriate funding to tackle emerging sustainability issues.

According to the Spanish respondents, ORPHAcodes implementation is considered easiest within registries’ framework, whether population-based or disease-specific ones. It is considered more challenging in ERN registries, at hospital level and in electronic health records.

An interesting comment was that at the specialized health-care level no common standardized electronic resource listing which RD can be added in the patient electronic record exists. According to respondents this resource could act as an alert mechanism of possible help for clinicians in the identification of RD patients and thus in the codification process. The participation and guidance of “local” experienced teams is considered crucial for a successful ORPHAcodes implementation process.

As in other countries, the involvement of health authorities is perceived as crucial for ORPHAcodes implementation on a vast scale. Important, but to a lesser extent, is considered the engagement of hospital managers, registry staff and clinicians dealing with RD.

Finally, the creation of a community of practice sharing achievements, problems encountered and solutions for a successful ORPHAcodes implementation is viewed as a fruitful and viable option not to lose the project achievements and to evolve in the process of RD coding to increase patients’ visibility across diverse health-care settings.

## Final considerations

The ways in which ORPHAcodes have been implemented thanks to the project activities and the work carried out by the implementing teams, differ under many aspects. Inter-country and intra-country variability characterized the described implementing experiences.
The snapshot provided by this report highlights a huge diversity of the implementing countries/regions in terms of health-care organization, coding system used to record morbidity data, settings in which ORPHAcodes have been used, personnel involved, IT systems used for data collection, languages used to record RD diagnoses. Despite these diversities, ORPHAcodes have demonstrated to be a versatile coding resource, which can be effectively introduced in different settings preserving consistency.
The guidelines and recommendations developed and refined within the project according to the ORPHAcodes' real-world use are indispensable tools to guarantee the appropriate use of the coding resources allowing comparability across countries and settings.
The ongoing transnational OC analysis (in progress) based on data coming from implementing countries will allow to further explore this issue.

In all the countries, the training of coders has been reported as a key-intervention for achieving a successful implementation. Several new tools and documents supporting the codification process have been developed in the project framework. This report highlights the need for promoting and disseminate appropriate knowledge of these resources beyond the project activities, also using new communication means (i.e. videos). As the new developed tools developed by Orphanet serve different purposes, the training should be organized according to the different users' needs, and should involve not only medical staff, but also IT personnel, strategic for a successful implementation and maintenance of the coding resources according to all the feedback provided by implementing teams.

Together with registries, all the respondents identified the hospital as a key-setting in which the ORPHAcodes' use should be promoted. This is in line with the development of the European Reference Networks, based on the involvement of hospitals highly specialized in RD patients' care. Pilot experiences involving hospitals of reference for many RD and participating in different ERNs appear to be very promising in demonstrating the added-value of using ORPHAcodes at this level. The involvement of hospital managers is strategic to understand how ORPHAcodes can be effectively introduced in this setting and to quantify actions and resources needed.

Finally, all respondents consider the creation of a Community of Practice sharing achievements, problems encountered and solutions for a successful ORPHAcodes implementation a valuable opportunity not to disperse the project legacy. Starting from the project participants, the community ideally should involve a growing critical mass of people interested in ORPHAcoding, including health authorities' representatives, hospital managers, IT people, patients' representatives. This community of practice could serve as a collaborative environment to move forward in the process of RD coding to increase patients' visibility across diverse health-care settings.

# ABOUT

This report is based on information, which is accurate to the best of the Authors' knowledge. However, contents of this report should be considered illustrative and not exhaustive.

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