D2.2 Mid-term Report on ERN- Orphanet nomenclature and classification collaborations Report

June 2024

OD4RD
Orphanet Data For Rare Diseases

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Content summary

Introduction

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The main scope of OD4RD2 Work Package 2 (WP2) is to improve the Orphanet nomenclature and classification of rare diseases (RD) in collaboration with European Reference Networks, to reflect the evolution of scientific and clinical knowledge and provide the most up-to-date possible terminology to code RD patients.
This summary report will provide an overview of completed and ongoing collaborations with ERNs from April 2023 to June 2024. For every collaboration the following elements will be specified:

- The ERN involved and the composition of the working group;
- The group of diseases covered and the scope of the revision;
- A brief recapitulative of the advancement of the collaboration;
- For finalized and almost finalized collaborations: the list of entities that have been treated/revised up to now (as annex);
- For ongoing collaborations: an estimation of how many groups/entities will be revised and the expected timing to conclude the revision.

A final chapter will assess the lessons learned from the collaboration experiences, especially those that may benefit other ERN projects. Annex 1 includes the lists of entities revised by activity.

Moreover, a summary table showing the finalized and ongoing ERN-collaborations is released biannually in December and July via the OD4RD GitHub (link).

Methodology

A collaboration project is usually initiated when Orphanet receives a request from an ERN to update the nomenclature and classification of a certain group of disorders. A collaboration can also be initiated by Orphanet if, during internal quality control, the necessity for an update of the classification is identified. In this case Orphanet contacts the ERN(s) to ask experts' availability to begin a revision process.
Generally speaking, any collaboration project established for the revision of a group of disorders involves the following roles:

- **Experts**: medical doctors contributing their knowledge and validating the scientific accuracy of the information provided by the Orphanet nomenclature; when updates are proposed, they help determine if these will appropriately answer the needs of clinicians dealing with patients suspected/confirmed to have a RD.
- **Orphanet**: transposes the clinical knowledge provided by the experts and the scientific literature into a standardized terminological structure; prevents the introduction of inter- and intra-classification inconsistencies; anticipates any issue that may arise as a result of the proposed updates regarding disease coding/data sharing, and in such case, finds and suggests alternatives.

Collaborations usually follow these main steps:

- Assessment of the work necessary:

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(i) the type of revision needed: only at the diagnosis level (ORPHAcodes missing, outdated, wrongly named, or misclassified); only at the structural level (classification to reorganize, subgroups missing or outdated); or both;

(ii) a quantitative assessment: how many entities need to be analyzed, and the level of complexity of the issues at hand. A « weight » value is attributed to each project according to its scale and complexity among these values: 0.5 - 1 - 1.5 - 2 (from smallest size/lowest complexity to larger size/highest complexity).

- Prioritization between different ERNs, or between different thematic groups within the same ERN, guided by the above-mentioned assessment and the criticality of the revision for ERN activities (e.g. registries, publications, etc.).
- Definition of the methodology: experts to be involved, working group(s) to be created, tools for the revision, timeline.
- Training of the involved experts on the Orphanet nomenclature standards and update process.
- Review of the nomenclature by ERN experts.
- Review by Orphanet of the updates proposed by experts, to ensure compliance with the nomenclature standards and state-of-the-art publications.
- Discussion to clarify scientific issues, solve problems, find alternatives, and reach a consensus.
- Validation of actions to be implemented by Orphanet and implementation of all validated decisions in the Orphanet database.
- Finalization of the project: a project summary report and a master file listing all clinical entities discussed (with the associated validated actions) are sent to the ERN representatives.

This methodology has been progressively established since 2017 and draws directly from past and ongoing experiences with ERNs. While it outlines a general structure and requirements for the collaboration, it is flexible enough to adapt to the specific challenges and scale of each project. This methodology has been formalized and published on the Orphanet website in June 2022 (link).

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Finalized ERN collaborations

1. ERN-EuroBloodNet: Rare paediatric thrombosis

ERN involved: ERN-EuroBloodNet
Experts involved: the working group was composed of two ERN expert medical doctors, and a registry data manager.
Assessment of the collaboration: Low complexity (index 0.5); revision of 5 ORPHAcodes and no changes to the classification structure.

Based on coding needs in their clinical practice, the experts requested the inclusion of new codes for the following thromboses:

- Pediatric deep vein thrombosis (including deep vein thrombosis and pulmonary embolism)
- Pediatric arterial thrombosis
- Pediatric cardiac thrombosis
- Neonatal renal vein thrombosis
- May-Turner syndrome

The experts provided a Word document with a brief description of the entities and recommended several references for the documentation of the requests. After discussion in the Orphanet medical and scientific committee, some issues required the input of the epidemiology manager to evaluate the rarity. The final decision was to create 2 of the 5 requested ORPHAcodes:

- Neonatal renal vein thrombosis, ORPHA:664912
- May-Turner syndrome, ORPHA: 675404

The medical experts agreed to be contacted to participate in the writing of a short abstract for the two entities.

2. ERN-EYE: Optic neuritis

ERN involved: ERN-EYE
Experts involved: the working group was composed of one expert medical doctor.
Assessment of the collaboration: Low complexity (index 0.5); 9 creations evaluated and very small changes to the nomenclature and classification structure.

Based on coding needs in their clinical practice, the ERN expert requested the revision of Optic neuritis classification and asked for 9 creations. In July 2023 Orphanet was contacted by an ERN-EYE expert to revise the group of disorders ‘Isolated optic neuritis, ORPHA:499096’. The revision followed a consensus paper transmitted by the ERN medical expert (PMID: 36179757).
Some entities already existed in Orphanet and others required an update of the terminology. The final decision was modifying the classification of one entity, obsolete two entities, and create 2 ORPHAcodes:

- Single isolated optic neuritis, ORPHA:659626
- Relapsing isolated optic neuritis, OPRHA: 659634

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3. VASCERN: Rare vascular tumors

ERN involved: VASCERN, VASCA Working Group.
Experts involved: the working group was composed of the chair of the ERN working group, and two expert medical doctors.
Assessment of the collaboration: Medium-high complexity (index 1.5); revision of around 50 ORPHAcodes and changes to the classification structure. The complete list of revised codes is included in Annex 1.

In 2019 a first collaboration with VASCERN was carried out in order to revise the classification of the Primary lymphedema (PPL) group of diseases, in collaboration with the VASCERN-PPL working group.

This second collaboration project, started in March 2023, was instead aimed at revising the classification of the group 'Rare vascular tumors, ORPHA: 211237' in collaboration with the VASCA working group. This revision followed the International Society for the Study of Vascular Anomalies (ISSVA) classification from 2018 and the WHO Classification of Tumours. In the new classification, published in the Orphanet website in May 2024, all the rare vascular tumors entities have been reorganized in three newly created groups, according to their behavior as 'benign', 'borderline', or 'malignant', and 15 new codes that were missing in Orphanet have been created to complete the groups.

4. ERN-ITHACA + eUROGEN: Spina Bifida and other spinal Dysraphisms

ERN involved: ITHACA and eUROGEN, inter-ERN Working Group "Spina Bifida and other spinal Dysraphisms" (SBoD).
Experts involved: the working group was composed of three expert medical doctors, who were in parallel validating decisions with the entire working group.
Assessment of the collaboration: Medium-high complexity (index 1.5); revision of around 90 ORPHAcodes and changes to the classification structure. The complete list of revised codes is included in Annex 1.

The classification of spina bifida and other dysraphisms was revised following the request from the inter-ERN Working Group SBoD, based on the observation that this classification was outdated in Orphanet. The revision of the spina bifida group was guided by the following elements:

- The group should include all the other dysraphisms described and not just restricted to the concept of spina bidifa.
- The new classification is based on the medical practice and the diagnostic process.
- The revision is based on dividing the disorders in 3 main classification groups of disorders: 'Closed spinal dysraphism', 'Open spinal dysraphisms', and 'Spinal dysraphism with a posterior meningocele'.

The revision was completed in May 2023 and presented during a trans-ERN meeting in June 2023 for final validation in presence of all experts. This revision was implemented for the Nomenclature pack 2023. Moreover, experts contribute to the validation of the medical texts in French and English. Definitions were published are the same time as the Nomenclature pack released in July 2023.

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Ongoing ERN collaborations

5. ERN CRANIO: Cleft palate

ERN involved: ERN CRANIO
Experts involved: the working group is composed of the ERN coordinator acting as the primary contact person and collaboration leader, and a group of four contributing expert medical doctors.
Assessment of the collaboration: Low complexity (index 0.5); revision of 5 ORPHAcodes from the group of disorders 'Cleft palate, ORPHA:2014'. The complete list of revised codes is included in Annex 1.

The revision was conducted following an expert's request for a missing ORPHAcode. Taking advantage of this interaction, all the entities included int the Group of disorders ORPHA:2014 'Cleft palate', were revised and validated. The experts are also revising Orphanet's definition of each entity. The estimated timeline for the end of this collaboration is August 2024.

6. ERNICA: Rare inflammatory bowel disease

ERN involved: ERNICA
Experts involved: the working group is composed of the ERN coordinator and four expert medical doctors.
Assessment of the collaboration: Medium-low complexity (index 1); revision of around 20 ORPHAcodes and changes to the classification structure. The complete list of revised codes is included in Annex 1.

In 2023 Orphanet received feedback from ERNICA experts claiming the current structure of the classification of rare Inflammatory Bowel Disease (IBD) was outdated.
After several email exchanges, the first contact meeting was performed in September 2023. It was decided to start an official collaboration in January 2024 to review the group of disorders 'Rare Inflammatory Bowel Disease, ORPHA:104012'.

In March 2024 an Orphanet Nomenclature manager introduced the experts to the Orphanet standards and rules. As a first step, the experts were asked to share proposals for the backbone of the IBD classification as the current one is not hierarchical.
To build the template for the new structure of the classification, the revision will follow recent literature (particularly the publication « An Integrated Taxonomy for Monogenic Inflammatory Bowel Disease », Bolton et al., 2022). A proposal will be discussed with the working group in a meeting planned for July 2024.

7. ERN EURO-NMD: Neuromuscular Junction disorders

ERN involved: EURO-NMD
Experts involved: the working group is composed of the ERN coordinator and expert medical doctors acting as the primary contact.

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Assessment of the collaboration: Medium-low complexity (index 1); revision of around 25 ORPHAcodes and changes to the classification structure.

The revision of the 'Neuromuscular Junction disorders, ORPHA:68381' follows a request from ERN EURO-NMD based on an Orphanet observation that this Orphanet classification is outdated.
In February 2024 Orphanet was invited to the EURO-NMD board meeting, to present the role of ORPHAcodes in the European health system and the current Orphanet classification of Neuromuscular diseases. Afterwards, the collaboration started with the creation of a small working group with experts in neuromuscular junction disorders to revise the classification and the nomenclature.
In March 2024 an Orphanet nomenclature manager introduced the experts to the Orphanet standards and rules. The experts are currently working on a proposal for the new classification structure, terminology and coding needs.

8. TransplantChild: Rare disorder potentially indicated for transplant

ERN involved: TransplantChild
Experts involved: the ERN coordinator, a project manager acting as the primary contact person, and a group of at least 3 medical experts by medical specialty.

This collaboration is intended to revise the classification of the group of disorders in relation to kidney, liver, lung, heart, intestine and hematopoietic stem cell transplantation. The project was initiated by Orphanet following an internal quality control that revealed several diseases classified as "Rare disorder potentially indicated for transplantation, ORPHA:506207, even if their risk of transplantation is very low or inexistent. The final aim of the collaboration is to exclude entities that do not have an indication for transplantation from the transplant classification, and to include entities present in Orphanet but that are potentially missing in the transplant classification, following the expert's guidance. No creation of codes is foreseen in this project.

Due to the complexity of the collaboration (in terms of size) and the independence of each working group, the original collaboration was split up into 6 parallel revision processes by medical specialty. The collaboration began with the assemblage of the working groups made up of experts from the 6 domains. The Orphanet manager prepared and shared to each working group a file containing the clinical entities related to each organ. The entities of this list must be evaluated by the doctors, to decide whether they should be included in the classification based on their risk of transplantation. Finally, the restructuring of the classification will be proposed according to the experts' recommendations.

Rare disorder potentially indicated for liver transplant, ORPHA:506210
Assessment of the collaboration: Medium-low complexity (index 1); revision of around 160 ORPHAcodes to determine inclusion/exclusion and minimal changes to the classification structure. The complete list of revised codes is included in Annex 1.
Rare disorder potentially indicated for lung transplant, ORPHA:506222
Assessment of the collaboration: Medium-low complexity (index 1); revision of around 150 ORPHAcodes to determine inclusion/exclusion and minimal changes to the classification structure. The complete list of revised codes is included in Annex 1.
Rare disorder potentially indicated for heart transplant, ORPHA:506225

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Assessment of the collaboration: Medium-low complexity (index 1); revision of around 170 ORPHAcodes to determine inclusion/exclusion and minimal changes to the classification structure. The complete list of revised codes is included in Annex 1.

Rare disorder potentially indicated for bowel transplant, ORPHA:506216

Assessment of the collaboration: Medium-low complexity (index 1); revision of around 160 ORPHAcodes to determine inclusion/exclusion and minimal changes to the classification structure. The complete list of revised codes is included in Annex 1.

Rare disorder potentially indicated for HSC transplant, ORPHA:506219

Assessment of the collaboration: Medium-high complexity (index 1.5); revision of around 600 ORPHAcodes to determine inclusion/exclusion and minimal changes to the classification structure. The complete list of revised codes is included in Annex 1.

Rare disorder potentially indicated for kidney transplant, ORPHA:506213

Assessment of the collaboration: Medium-high complexity (index 1.5); revision of >450 ORPHAcodes to determine inclusion/exclusion and changes to the classification structure.

The project is currently being validated by experts. The end of this collaboration is scheduled for the end of 2024. The complete list of revised codes is included in Annex 1.

9. VASCA: Rare vascular malformation

ERN involved: VASCERN

Experts involved: the working group is composed of the chair of the ERN working group, and two expert medical doctors.

Assessment of the collaboration: Medium-high complexity (index 1.5); revision of around 40 ORPHAcodes and major changes to the classification structure adding granularity. The complete list of revised codes is included in Annex 1.

This collaboration was initiated in May 2024 and aimed to revise the classification of the group of diseases 'Simple vascular malformation, ORPHA:211243'. According to experts, the existing representation did not appropriately answer diagnosis coding needs, and the necessary level of granularity needed to be reassessed at each level of classification. This third collaboration with ERN VASCERN will follow the methodology of the revision of Rare vascular tumors: monthly follow-up videocalls in which the progress of the revision, the eventual issues while documenting the requests, and the feedback from the working group meetings are discussed.

10. ERN EYE: Rare disorder of the posterior segment of the eye

ERN involved: ERN EYE

Experts involved: the working group is composed of one ERN expert medical doctor acting as the primary contact person, and a registry data manager.

Assessment of the collaboration: High complexity (index 2); revision of around 260 ORPHAcodes and changes to the classification structure. The complete list of revised codes is included in Annex 1.

In July 2023 the ERN data manager contacted Orphanet for revising the group of diseases 'Rare disorder of the posterior segment of the eye, ORPHA: 519311'. The revision was mainly motivated by the project to establish a coding registry system for gene therapies, which made it a priority.

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In Mach 2024, an Orphanet nomenclature manager started the cycles of discussion with the ERN to train the experts involved and plan the timeline of the collaboration.
The first expert's proposals of the new classification did not follow some of the Orphanet rules. These issues were addressed following a dynamic revision process in which the Orphanet manager shared an Excel file every week with the experts to solve doubts and communicate intermediate decisions. After three cycles of exchanges, most of the modifications were implemented in May 2024, and are included in the Nomenclature Pack 2024. The complete implementation of the classification is expected for September 2024.

11. EpiCARE: Rare epilepsies

ERN involved: EpiCARE
Experts involved: the working group is composed of one ERN expert medical doctor acting as the primary contact person, a registry and data manager, and a research project manager.
Assessment of the collaboration: High complexity (index 2); revision of around 500 ORPHAcodes and major changes to the classification structure. The complete list of revised codes is included in Annex 1.

The collaboration is being carried out in three stages, the first targeting the revision of the group of epileptic syndromes, the second targeting the revision of the other epilepsy phenotypes, and finally the restructuring of the classification according to the recommendations of the *International League Against Epilepsy (ILAE).*
The first stage is currently under documentation and active revision. The first set of actions involves nomenclature changes and inactivations (obsolescence and deprecation) and follows the recently published new guidelines. Their implementation is planned for the coming months. The second phase of the collaboration will be launched in early 2025.

12. ERN BOND: Primary bone dysplasia and Dyostoses

ERN involved: ERN BOND, in collaboration with the International Skeletal Dysplasia Society (ISDS).
Experts involved: the working group is composed of the ERN coordinator, an expert medical doctor acting as the primary contact person and collaboration leader, and a group of thirty-eight contributing expert medical doctors.
Assessment of the collaboration: High complexity (index 2); revision of around 250 ORPHAcodes and the classification structure.

The collaboration, aimed at revising the classification of Rare bone disease, and in particular the 'Primary bone dysplasia, ORPHA: 364526' and 'Dysostosis, OPRHA:364559' groups, was initiated in 2020. The state of play of the collaboration together with the work accomplished and future planning has been presented to the ERN BOND plenary meeting in September 2022.
The file containing the entire classification to be revised (276 clinical entities) has been initially distributed between 11 groups of experts for a total of 38 experts from ERN BOND/ISDS involved. It has been challenging to validate the proposed actions and to lead consensual decisions between the experts, Orphanet, and the recent literature. Due to the complexity and the scale of the project, the collaboration has been initially divided in two steps:

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- Step 1: focused on comparing the Orphanet disorder level with the Nosology and classification of genetic skeletal disorders (2019 edition and 2023 edition) published by the *International Skeletal Dysplasia Society*. This comparison revealed many entities present in Orphanet that are not listed in the Nosology. As of June 2024, 220 entities have been revised, leaving 56 entities/phenotypes to be revised. It mostly concerned historical entities (no new patients described in the literature in the last 25 years) that are not present in the published Nosology. The estimated timeline for the end of this step is July 2024.
- Step 2: focused on revising the group's structure and the reclassifications of the phenotypes. A few specific clinical groups where experts required classification update were detected. They consisted in withdrawing entities from the primary bone dysplasia classification or in the creation of missing clinical groups. The complete list of the codes revised and implemented until May 2024 (+ 56 pending) is included in Annex 1. The estimated timeline for the end of this step of the revision is August 2024.

Any other specific group classification revision for bone diseases will be treated individually (by group of disorder's code) further on and upon request of specific clinical group of experts.

13. ERN MetabERN: Rare inborn errors of Metabolism

ERN involved: MetabERN
Experts involved: the working group is composed of the two ERN expert medical doctors acting as the primary contact persons.
Assessment of the collaboration: High complexity (index 2); revision of around 500 ORPHAcodes and major changes to the classification structure. The complete list of revised codes is included in Annex 1.

The collaboration, aimed at revising the Metabolic Disorders classification, and in particular the Rare inborn errors of Metabolism, has been initially divided in two steps due to the complexity and the scale of the project:

- Step 1: to complete the missing ORPHAcodes of the classification according to Metabolic Disorders following the *International Classification of Inherited Metabolic Disorders (ICIMD)*. To do so, a recent publication will be used as guide (An international classification of inherited metabolic disorders (ICIMD), PMID 33340416).

- Step 2: to revise the classification structure and nomenclature of 'Rare inborn errors of Metabolism, ORPHA:68367'. Following the first exchanges with the experts, it has been decided to start with the classification and nomenclature revision of groups 'Organic acidurias, ORPHA:289899', and 'Mitochondrial diseases, ORPHA:68380'. The revision of the latter will be tackled with the inter ERN Mito-Working Group (see future collaborations). The next group to be revised will be 'Lysosomal Diseases, ORPHA:68366'. The timeline and priorities will be assessed in a future meeting. The complete list of revised codes is included in Annex 1.

The collaboration was officially initiated in November 2023, when Orphanet was invited to the MetabERN Board meeting held in Barcelona.

In January 2024 an Orphanet Nomenclature manager introduced the experts to the Orphanet standards and rules.

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An Excel spreadsheet containing the ORPHAcodes for the group Organic acidurias and associated information (synonyms and classification level) was sent in a format that enabled the experts to indicate their suggestions and comments. Several emails and documents were shared between experts and Orphanet toke place and are planned for the next months. The new revised classification is expected for November 2024 to be presented during the annual MetabERN Board meeting.

The communication was continued with email exchanges and the need of an update of the group 'Coenzyme Q10 deficiency, ORPHA:35656' raised (small revision, including 7 entities). This revision along with the completion and re-structuration of the classification following the genetic axis will be addressed in the context of the collaboration.

As part of an ongoing collaboration with MetabERN, Orphanet will participate in a project dedicated to a metabolic disease specific database called the "Online Inherited Metabolic Disorders" (OIMD) website. This website dedicated to metabolic diseases gathers a large amount of data on metabolic diseases, including metabolic pathways and alignment with different terminologies. In this context, Orphanet will contribute by providing the best match between the entities in OIMD and Orphanet, including a link with the ORPHAcodes that will give access to the Orphanet website.

14. ERNICA: Digestive duplications

ERN involved: ERN ERNICA.
Experts involved: the working group will be composed of the ERN coordinator acting as the primary contact person and collaboration leader, a group of six contributing expert medical doctors, and a project manager.
Assessment of the collaboration: Low complexity (index 0.5); revision of less than 20 ORPHAcodes from the group of disorders 'Digestive tract malformation, ORPHA:98039'. The complete list of revised codes is included in Annex 1.

Orphanet's medical and scientific committee has recently validated the creation of several ORPHAcodes related to digestive tract duplications and the inactivation of some related entities belonging to the group 'Rare abdominal surgical disease, ORPHA:165711'. To confirm the consistency of the classification and the appropriateness of its structure and terminology, Orphanet contacted ERNICA for its revision. The ERN ERNICA has been very proactive in this exchange and created a working group to revise the representation of the classification and homogenize the nomenclature.

The first meeting to discuss the steps of this collaboration is scheduled for 1 July 2024.

Planned collaborations

15. Inter ERN Mito-WG: Mitochondrial diseases

ERN involved: Inter-ERN working group on mitochondrial diseases composed of five ERNs: Euro NMD, MetabERN, ERN RND, ERN EpiCARE, ERN Eye.
Experts involved: In June 2024 the experts forming the working group will be decided, a call to action has been sent out in May 2024.

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Assessment of the collaboration: High complexity (index 2); revision of around 200 ORPHAcodes and changes to the classification structure. The complete list of revised codes is included in Annex 1.

The revision of the classification of the group of 'Mitochondrial diseases, ORPHA:68380' is complex and involves several disciplines. For this reason, Orphanet asked the Inter-ERN Working Group of Mitochondrial Diseases made up of five ERNs, to bring together the efforts of different medical fields for multi-classify and update the nomenclature.

A first meeting was held on May 2024 with the coordinator of Inter-ERN work group of mitochondrial diseases and several experts from Inter-ERN work. The creation of the working group dedicated to the revision of the classification of Mitochondrial Diseases with Orphanet was discussed and a call to action was sent out to the experts. In June 2024 the ERNs involved will announce the experts that would like to participate in this project.

Lessons learned

Drawing from past and ongoing collaboration projects, Orphanet has been able to improve its collaboration methodology and gain experience and knowledge, both positive and negative, that will help continuously improve the collaboration process. The following points are the most relevant lessons learned.

Importance of regular interactions with ERN experts

The dynamic of the revision process effectively relies on the reactivity of the two sides of the collaboration: the projects that Orphanet can absorb (given by the availability of Nomenclature project managers) and the ERN reactivity to Orphanet requests for expertise.

It is sometimes difficult to efficiently communicate and interact with ERN experts. Experts are usually medical doctors that are extremely busy between their clinical and research practice and ERN activities. Consequently, sometimes they might not be reactive when contacted by email. Moreover, organizing meetings with several experts at the same time might be difficult due to time constraints. This can also generate a delay in the starting of the collaboration, or a bottleneck during the revision process.

This need for improved communication has highlighted the importance of having a reactive ERN contact point, that could either be an ERN project manager in charge of soliciting experts' responses and organizing meetings with several participants, or an ERN medical doctor that acts as spokesman for all expert participants of the revision and is fully implicated in the revision process.

A revision process should not therefore be initiated if a full commitment of the ERN has not been obtained, together with an indication of the contact person that will follow the project on the ERN side.

If Orphanet is not able to obtain a timely follow-up on the ERN side, the collaboration might be paused and left on hold until the ERN has the adequate resources to dedicate to the project.

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Importance of providing an adapted training to ERN experts

Training experts on the general Orphanet concepts (definition of the nomenclature and structure of the classification) and on the nomenclature update process facilitates the collaborative work.

Adapted training, along with frequent discussions provide experts with a full understanding of the different types of actions applicable in the Orphanet database. Experts are shown to how to compile their suggestions in the provided supports in a standardized and easy format. Globally, this makes the ERN-Orphanet communication clearer and more efficient.

The training needs are generally assessed by the Orphanet nomenclature project manager, taking into consideration the eventual previous collaborations of the experts with Orphanet and the proportions of the revision. They usually take place at the beginning of the collaborative process; however, further trainings can be proposed even at later stages of the collaboration, especially for complex projects (implicating several expert fields or ERNs, or the ones that were hold on for a while).

Importance of defining the priorities and a precise methodology

To achieve the objectives of the revision and meet the planned deadlines, it is necessary to establish the priorities of the project at a very early stage of the collaboration. This is especially relevant for high complexity revisions, that usually rely on the contribution of large groups of experts, that complicate the process and the timeline.

In order to reduce the delivery time of the nomenclature updates as much as possible there are some solutions that seem to work to speed up the process and render it more efficient:

1. Subdividing the workload by identifying smaller clinical blocs of entities/groups to be revised in a subsequent way during the collaboration;
2. Subdividing the workload by separating the ORPHAcodes revision process from the restructuring of the classification process in two consecutive phases;
3. Avoiding working with large groups of clinical experts at the same time. A better approach is to work with a restricted group of 2/3 experts and submit the final proposition for commentary and approval at the end to the entire ERN working group.

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