Deliverable N°: D3.1
Title: Central Repository of (validated) PCOMs for RDs

WP N° and Title: **WP3 – Patient-Centered Research**
Lead beneficiary: **INSERM**
Contributors: **VHIR, APHP, Mapi Research Trust, LUMC**

Introduction

ERICA WP3 aims to define Rare Diseases' priority areas for future Rare Patient Centered and Patient Reported Outcome Measures (PCOMs/PROMs) development, support ERNs in the implementation of PCOMs/PROMs and to create a central Repository of PCOMs/PROMs for ERNs.

In this deliverable, ERICA WP3 team describes the design process of the WP3 central Repository, the numerous website features and the associated methodology.

This deliverable also lays out the next steps in regards to WP3 objectives.

The aim of WP3 is to facilitate the Europe-wide implementation of standardized Patient-Centered Outcome Measures (PCOMs) and Patient Reported Outcome Measures (PROMs) for rare diseases. The WP3 Repository plays a central role in meeting this objective as it aims at containing an exhaustive list of PCOMs/PROMs, which will help medical experts and patient centered expert working groups to assess the quality of life/impact of rare disease on those affected.

PCOMs/PROMs Repository

The WP3 Repository is available at: https://erica-rd.eu/proms-Repository/.

The WP3 Repository's user-friendly interface allows for quick and refined searches for relevant PCOMs/PROMs with the following filters: PCOMs/PROMs Name, PCOMs/PROMs Type, Target Age, Domains, Disease (OrphaName), ORPHACode, related group of rare diseases, related ERNs and PROQOLID™ PCOMs/PROMs page link (Figure 1).

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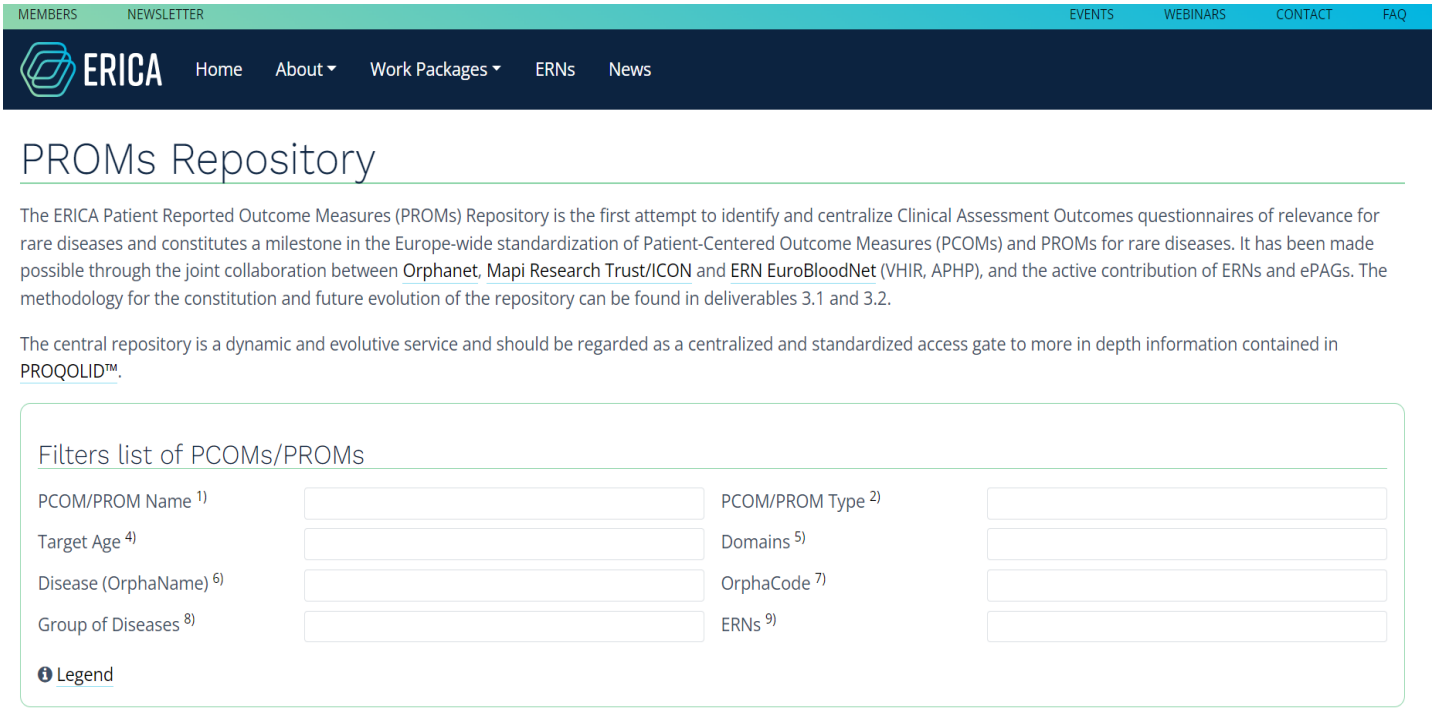

Figure 1 PROMs Repository Filters List

The Repository includes a legend at the bottom of the page, which describes all search filters and Repository column headers. Search fields were carefully selected based on the ERNs direct input and needs (Figure 2).

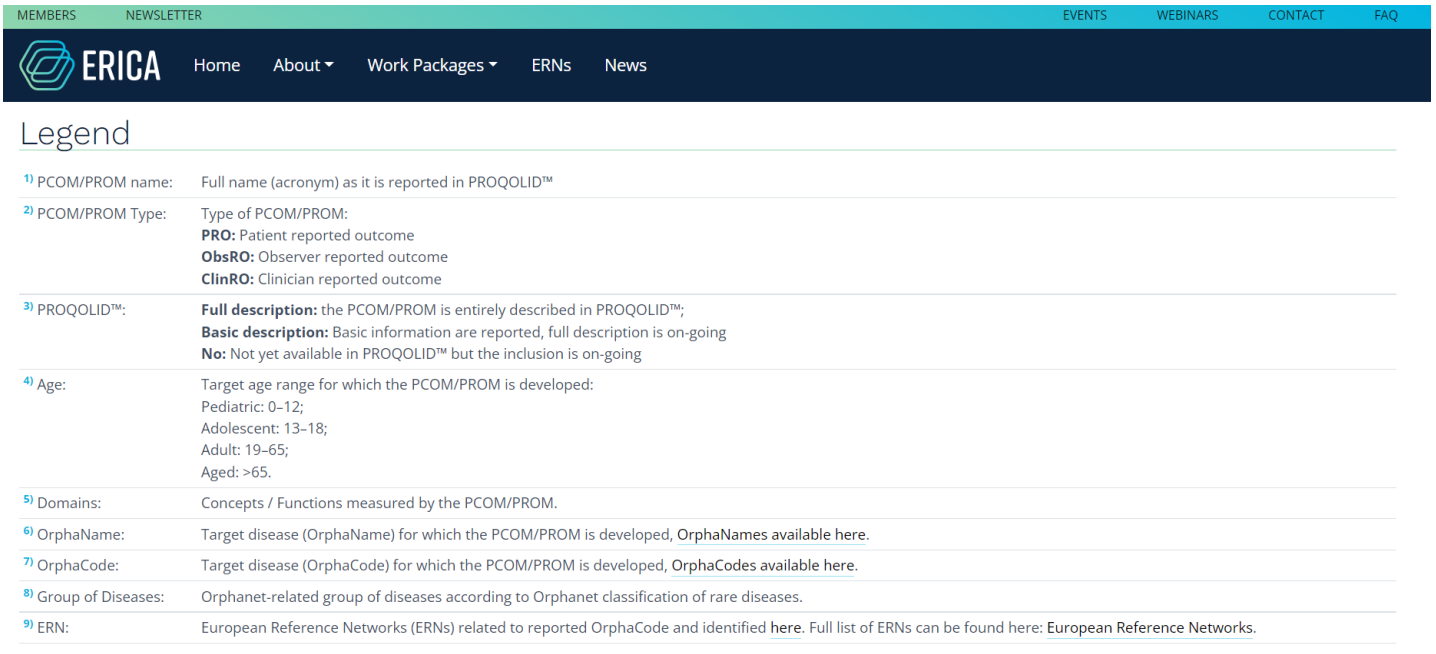

Figure 2 PROMs Repository Legend

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Results can be further sorted (from high to low or vice versa) using the arrows at the top of each vertical column. Once a search has been conducted, users can easily locate all pertinent summary information and, importantly, access the PCOM/PROM itself *via* the link to PROQOLID™, on the far-right hand side (Figure 3).

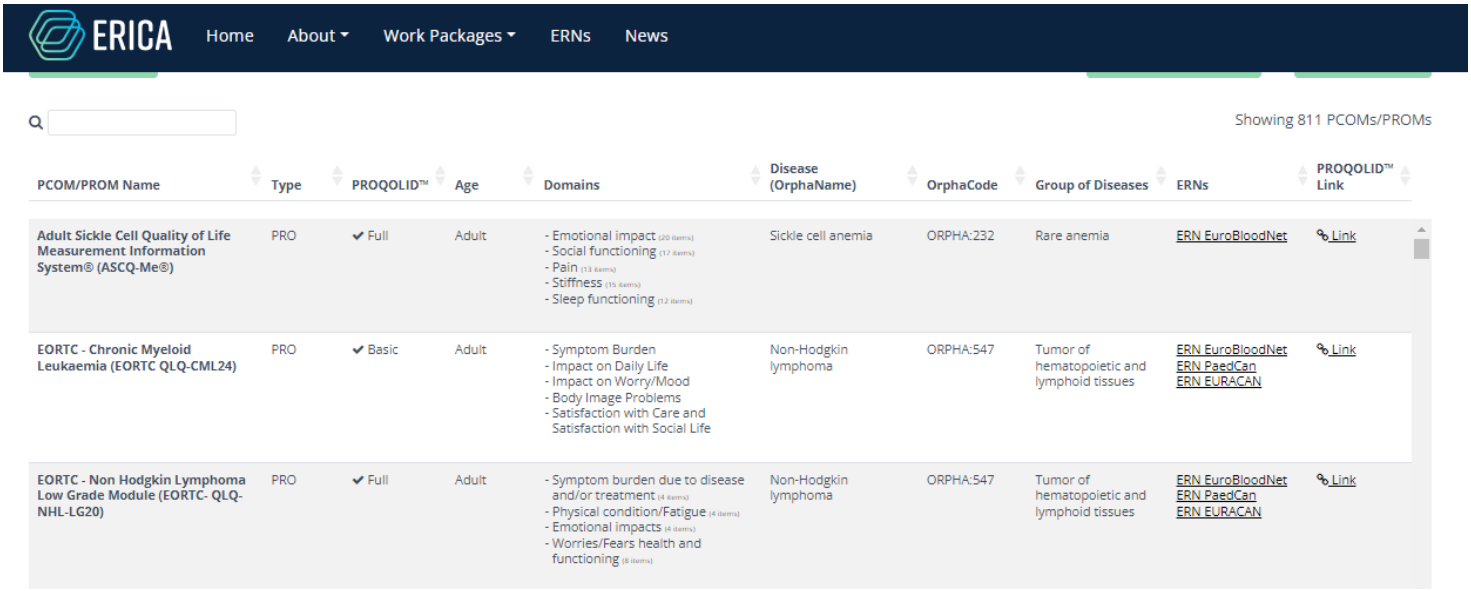

Figure 3 PROMs Repository sample search results

Within PROQOLID™, there is additional PCOMs/PROMs information, which can help ERNs decide if the selected PCOM/PROM is well suited to their needs (Figure 4).

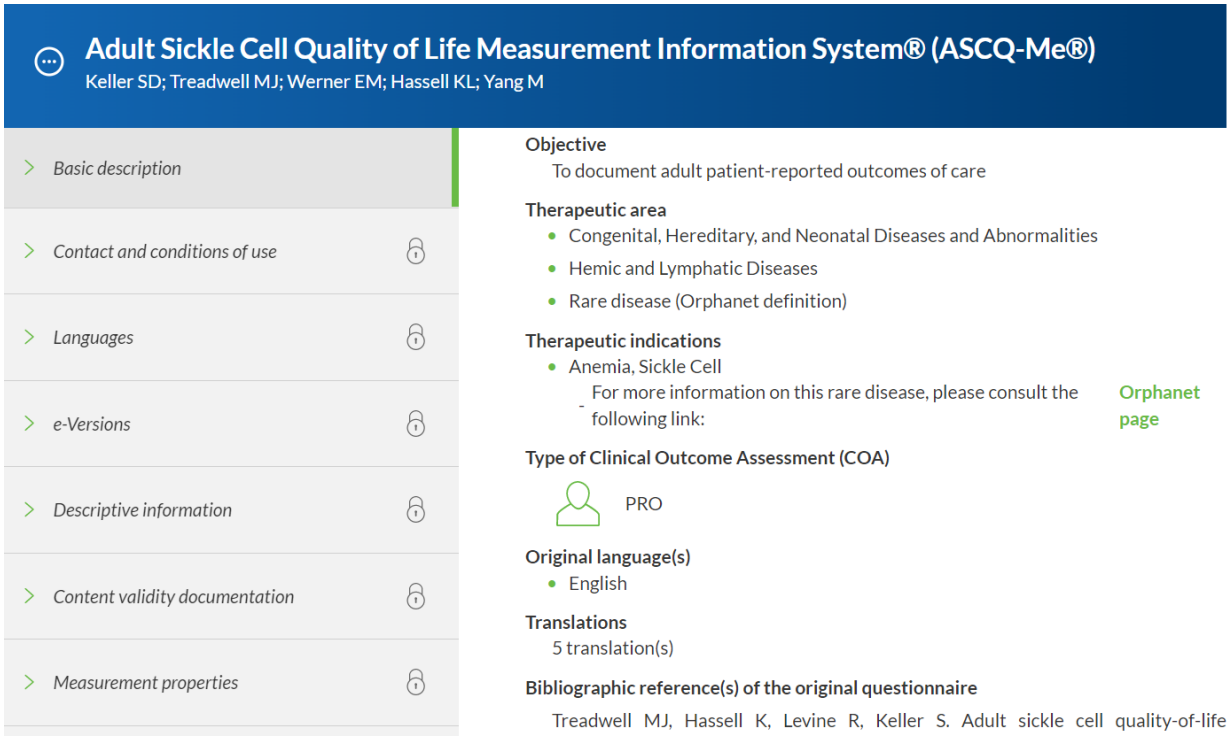

Figure 4 example of PCOM/PROM PROQOLID page developed for a rare disease

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Users can also link back to the Orphanet disease page if additional information is needed regarding the disease itself or the different subtypes (Figure 5).

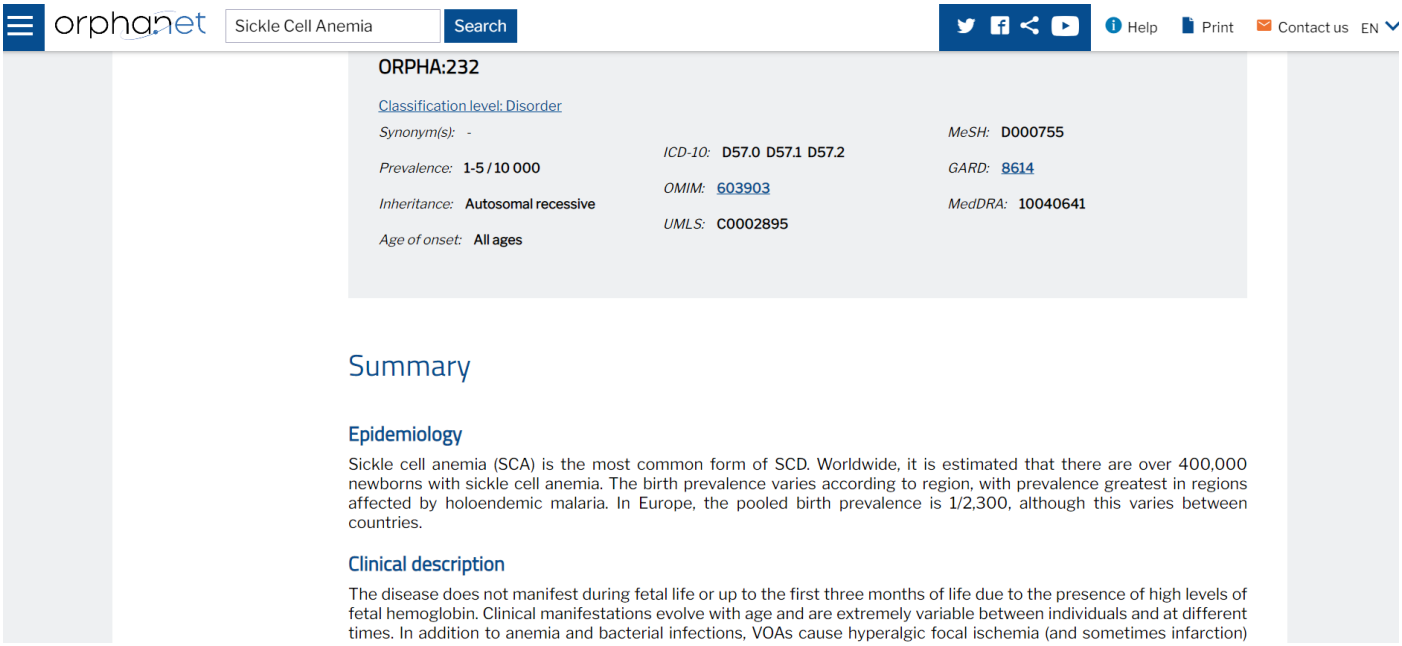

Figure 5 example of Orphanet disease page

Note : The preliminary Repository is subject to change based on internal and external feedback from medical experts. These changes may include content as well as data presentation based on future user feedback.

Methodology

The WP3 Repository is the direct result of numerous collaborations that have allowed our team to collect and verify **781 unique PCOMs/PROMs** relevant to RD. This work has been largely made possible through the joint collaboration between Orphanet, MRT/ICON and ERN EuroBloodNet.

The three following steps were taken to create the WP3 Repository:

1. MRT – Orphanet – Mesh

Orphanet and MRT connected their databases (Orphadata and PROQOLID™), which were then crossed using Orphanet's curated mappings between ORPHAcodes and MeSH terms to test preliminary alignment and inventory. Afterwards, all existing tools for PCOMs/PROMs for RD were extracted from the PROQOLID™ database using ORPHANET alignments of RD nomenclature. This search resulted in the identification of **259 PCOMs/PROMs** designed specifically for RD and/or their subtypes.

2. Added PRO according to Domains

To increase the exhaustivity of the Repository, WP3 included all 10 Domains from the Orphanet Functioning Thesaurus[1], which is derived from the WHO International Classification of Functioning, Disability and Health (ICF)[2]. These 10 domains (Understanding and learning, Communication, Motor Skills, Self-care abilities, Sleep, Temperament

[1] https://www.orpha.net/orphacom/cahiers/docs/GB/Orphanet_Functioning_Thesaurus_EN.pdf
[2] World Health Organization. ICF: International Classification of Functioning, Disability and Health. Geneva, Switzerland: World Health Organization; 2001

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and behavior, Moving around, Interpersonal skills, Daily activities, Social life) were crossed with all available PCOMs/PROMs in PROQOLID™ to expand the list of viable PCOMs/PROMs in the Repository. This led to the identification of **151 PCOMs/PROMs** related to the functional consequences of RD, which were then added to the Repository.

3. ERN Workshop + Survey

The WP3 PROMs Repository Workshop was conducted over two days with the aim of setting expectations for the Repository while also identifying additional PCOMs/PROMs used by ERNs. **211 unique PCOMs/PROMs** were identified from the "Available PROMs and ObsRO in Rare Diseases" survey that was sent to each of the 24 ERNs. PCOMs/PROMs were added according to the ERNs survey responses, however this exercise required the establishment of several rules (listed below) when responses were either left blank or were considered not 'complete.'

- As a first step, only PCOMs/PROMs were selected
- PCOMs/PROMs developed for multiple diseases were reported, separately, in different rows.
- PCOMs/PROMs developed for rare diseases pertaining to multiple ERNs were associated with each of these ERNs, according to Orphanet based on information provided by ERNs.
- If a PCOM/PROM developed for a non-rare disease was reported by ERNs during the survey, the PCOM/PROM was included and marked as 'not a rare disease' in the appropriate columns.
- If the PCOM/PROM is a generic questionnaire, and hence applicable to any disease, it was included with the mention 'Not applicable' in the OrphaName, OrphaCode, Groups of diseases and ERNs columns.
- If an ERN provided the name of a PCOM/PROM for which no information was found, the PCOM/PROM was added and 'No information' was marked in the appropriate fields.

The WP3 PROMs Repository Workshop and survey also helped identify additional concepts that were important to ERNs, based on their input during the General Assembly. These concepts include: Burden, Self-efficacy, Adherence, Independence, amongst others. These terms were searched in PROQOLID™, resulting in the identification of an additional set of **160 PCOMs/PROMs**.

Note: These 160 PCOMs/PROMs were included in the preliminary Repository as part of our collaborative effort with ERNs, but merit further refinement to be more applicable for RD research. WP3 will soon establish these selection criteria based on ongoing discussions with ERNs.

Summary/Conclusions

The WP3 central Repository is a milestone in the Europe-wide standardization of Patient-Centered Outcome Measures (PCOMs) and Patient Reported Outcome Measures (PROMs) for rare diseases. Not only due its exhaustive (and accessible) list of **781** PCOMs/PROMs for RD, but also due to the collaborative approach between WP3 and European Rare Disease stakeholders. The central Repository, in fact, marks countless hours spent understanding ERNs aims to help determine: previous experiences using PCOMs/PROMs, ambitions for future PCOMs/PROMs studies, hopes to design PCOMs/PROMs as well as issues related to access and usability. The central Repository is the product of these conversations and will play a central role in helping document the impact of RD, in Europe.

As noted earlier, the WP3 central Repository is subject to change based on future user feedback, such as additional search criteria. WP3 will update the Repository accordingly and, in the upcoming months, will complete the following tasks to further meet our objectives:

- Continue the quality control of entries in the Repository

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- Include PCOMs/PROMs in PROQOLID™ when lacking
- Upgrade Repository content and functionalities according to users' feedback
- Further populate the Repository as new PCOMs/PROMs are identified and/or coded according to the WP3 work plan

Lastly, WP3 would like to thank the ERICA Coordinating team for their continued support, web development and coordination.

In conclusion, the ERICA PCOMs/PROMs Repository is the first attempt to identify and centralize Clinical Assessment Outcomes questionnaires of relevance for rare diseases and constitutes a milestone in the Europe-wide standardization of Patient-Centered Outcome Measures (PCOMs) and Patient Reported Outcome Measures (PROMs) for rare diseases. It has been made possible through the joint collaboration between Orphanet, Mapi Research Trust/ICON, ERN EuroBloodNet, and the active contribution of ERNs and ePAGs.

The central Repository is a dynamic and evolutive service and should be regarded as a centralized and standardized access gate to more in depth information contained in PROQOLID™.

Questions and access requests: info@erica-rd.eu

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