Deliverable

D5.2 3.500 collected data sets from associated ERNs and undiagnosed disease programmes	
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Explanation according to GA Annex I:
Collect standardized phenotypic and genotypic information of a large number of undiagnosed RD from associated ERNs and undiagnosed disease programmes.

Abstract:

Solve-RD has four core European Reference Networks (ERNs): ITHACA, EURO-NMD, RND and GENTURIS. The core ERNs have provided the bulk of data for re-analysis within Solve-RD. Solve-RD has also worked since its conception with the Undiagnosed Disease Programmes/Networks (UDPs/UDNs) from Spain and Italy. During the project, two ERNs have become associated with Solve-RD: EpiCare and RITA. 2,932 datasets in total have been provided by UDN-Spain, ERN-EpiCare, ERN-RITA and other ERNs as part of data freezes 1 to 3. This data has already been processed and is available to the consortium members. Further data is still being submitted as part of data freeze 4.

Introduction:

During the Solve-RD proposal phase, it was estimated after consultation with the European Research Networks (ERNs) and other Solve-RD partners, that approximately 3,500 datasets would be collected from the associated ERNs excluding the four core ERNs (ERN-ITHACA, ERN Euro-NMD, ERN-GENTURIS and ERN-RND). UDN-Spain has been a partner of Solve-RD since the beginning, integrating most of its activities within ERN-ITHACA. During the project ERN-EpiCare and ERN-RITA have been associated with Solve-RD, allowing them to participate in some of the Solve-RD activities, including the submission and re-analysis of exome/genome data and the corresponding phenotypic and clinical information from undiagnosed rare disease patients and relatives.

Report:

When starting submission to the RD-Connect GPAP for the Solve-RD project, the user can indicate under which ERN the dataset should be associated. The user can choose any ERN, and some users submitting data to Solve-RD have chosen ERNs other than the core ERNs (ITHACA, Euro-NMD, RND, GENTURIS), the associated ERNs (EpiCare, RITA) or UDN-Spain. The data has been collected with the same procedure used for the four core ERNs (see deliverable D1.7).

To facilitate the submission of the phenotypic and clinical data of rare disease patients and relatives, the RD-Connect GPAP PhenoStore module has several forms aligned with the Genomics England data models. Those forms cover most “usual” rare diseases, including those from Solve-RD associated ERNs and other ERNs (Figure 1). Starting in 2021, we evaluated the disease-specific forms created in the context of H2020 EJPR-RD and available in PhenoStore to ensure they covered the needs from new ERNs (RITA and EpiCare). This work was done in collaboration with new Solve-RD associated partners involved in the project. We have provided continuous user support on phenotypic data upload to the RD-Connect GPAP through individual entries (forms) or bulk upload (Excel format). All phenotypic data is available to export using the PhenoPackets format.

New Index Case Submisson

The following templates are based on Genomics England Clinical Data Models. Please, mind that displayed ERNs are only suggestions to recommend clinical scientists the best template to enter their case

Choose a Template:

21 Templates Available

Default Template
Standard PhenoStore Case
SELECTED

Cardiovascular disorders
Disorders of the heart and blood vessels
ERN GUARD-HEART, VASCERN, ERN EURO-NMD, ERN ReCONNET, ERN LUNG

Ciliopathies
Abnormal formation or function of cilia
ERN LUNG, ERKNet, ERN EYE, ERNICA, ERN BOND

Dermatological disorders
Conditions that affect the integumentary system
ERN Skin, ERN ReCONNET

Dysmorphic and congenital abnormality syndromes
Congenital structural abnormalities
ERN eUROGEN, ERN CRANIO, ERNICA, ERN ITHACA, ERN BOND, ERN-RND, MetabERN, Endo-ERN, ERKNet,

Endocrine disorders
Disorders related to the endocrine glands of the body
Endo-ERN, MetabERN, ERN ITHACA

Gastroenterological disorders
Disorders that occur within the gastrointestinal tract
ERN RARE-LIVER, ERNICA

Growth disorders
Disorders that affect height, weight and sexual development
ERN ITHACA, ERN BOND, VASCERN, Endo-ERN

Haematological and immunological disorders
Inflammatory and immune disorders
ERN EuroBloodNet, ERN RITA

Hearing and ear disorders
Abnormalies of the outer, middle, or inner ear
ERN CRANIO, ERN ITHACA

Infectious diseases
Disorders caused by organisms — such as bacteria, viruses, fungi or parasites from the inner body
NA

Metabolic disorders
Rare inherited metabolic disorders
MetabERN, Endo-ERN, ERN EpiCARE, ERN EURO-NMD, ERN RND, ERN ITHACA

Neurology and neurodevelopmental disorders
Disorders that affect the development of the nervous system
ERN RND, ERN EURO-NMD, ERN ITHACA, MetabERN, ERN EpiCARE

Ophthalmological disorders
Eye and vision disorders
ERN EYE

Psychiatric disorders
Mental health disorders
ERN ITHACA, ERN-RND, Endo-ERN, ERN EpiCARE

Renal and urinary tract disorders
Disorders that affect the urinary system
ERKNet, ERN eUROGEN

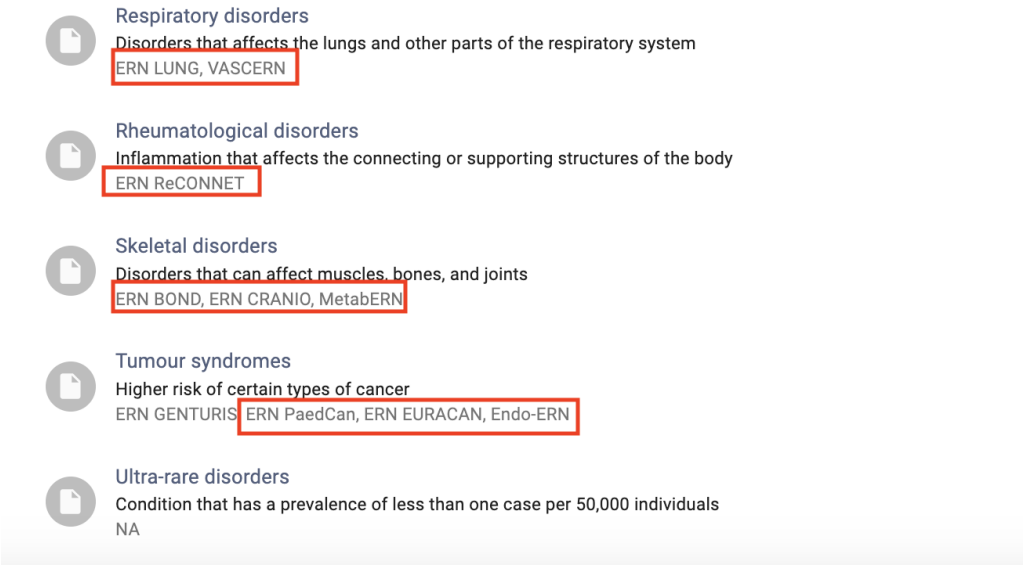

Figure 1: Templates in the GPAP to support submission of phenotypic data for non-core Solve-RD ERNs.

Data freezes 1 to 3 included a total of 2,932 datasets (phenotypic and clinical data, metadata and sequencing data) submitted by non-core ERNs: 2,402 from the associated ERNs (RITA and EpiCare), 342 from other ERNs, 136 from UDN-Spain, and 52 for which the ERN was not specified (see *Table 1)*.

Table 1: Number of datasets submitted by non-core ERNs in data freezes 1 to 3. Note that the number of datasets from data freezes 1 to 3 are included also in deliverable D1.7.

ERN/UDN name	Number of datasets
ERN-EpiCARE	1,866
ERN-RITA	536
ERN-PaedCan	201
UDN-Spain	136
ERNICA	39
Endo-ERN	35
ERN-GUARD-HEART	14
ERKNet	13
ERN-ReCONNET	10
MetabERN	10
ERN-EYE	8
ERN-EuroBloodNet	8
VASCERN	3
ERN-CRANIO	1
ERN not specified	52
TOTAL	**2,932**

All the aforementioned datasets have been processed with the RD-Connect GPAP standard analysis pipelines in order to harmonise the output, and were released for analysis and interpretation in the RD-Connect GPAP and submitted to the EGA in the same way as done for the datasets from the Solve-RD core ERNs (see deliverable D2.7).

Conclusion:

The coordination team at EKUT and CNAG-CRG have worked in a coordinated and continuous manner to facilitate data submission, reaching out to and following-up with partners that had committed to contribute data to Solve-RD. We have collated 2,538 datasets from associated

ERN-EpiCare, ERN-RITA and UDN-Spain, 342 datasets from other ERNs and 52 datasets with an ERN not specified. The data has been collected with the same procedure used for the four core ERNs (see deliverable D1.7). The standard data processing pipelines have been successfully applied to the datasets as described in deliverable D2.7, and the data is available to Solve-RD partners through the RD-Connect GPAP and the EGA as described also in D2.7. Further data is still being submitted as part of data freeze 4.