

# Deliverable

# D5.1 Bespoke Phenotips frontends for associated ERNs and undiagnosed disease programmes

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# Explanation according to GA Annex I:

Bespoke Phenotips frontends for collection of clinical information of unsolved patients from associated ERNs and undiagnosed disease programmes will be created.

# Abstract:

This report provides information on the new clinical submission forms designed and implemented in GPAP-PhenoStore, the phenotypic module of the RD-Connect Genome-Phenome Analysis Platform (GPAP, <u>https://platform.rd-connect.eu/</u>). These templates have been designed in collaboration with clinical experts from Solve-RD WP1 and in alignment with Genomics England data models. This implementation facilitates the collation and future portability of structured clinical information of unsolved patients from associated ERNs and undiagnosed disease programs.

## Introduction:

The collation of structured phenotypic data using standards and ontologies such as HPO (*https://hpo.jax.org*), OMIM (*https://www.omim.org*) and ORDO (*http://www.orphadata.org*) can be an important workload for clinicians and researchers. To facilitate phenotypic data entry, the RD-Connect GPAP offers a user-friendly phenotypic data entry tool, GPAP-PhenoStore (https://playground.rd-connect.eu/phenostore/), developed in the context of the EJP-RD project.

Herein and in collaboration with Solve-RD WP1 and clinicians from the core ERNs and undiagnosed rare disease programs, we have designed specific disease forms to facilitate data entry in the system. These forms are based on the Genomics England data model for Rare Diseases (*https://www.genomicsengland.co.uk/?wpdmdl=5500*) and provide a tailored list of relevant signs and symptoms for describing the patients' phenotypes in 20 types of disorders such as neurology and neurodevelopmental disorders or tumour syndromes. Specific disease-related fields such as the number of different types of polyps for ERN-GENTURIS have been included to corresponding forms. Disorders from all ERNs submitting data within Solve-RD are represented and mapped in these templates.

The reported system and design are interoperable and very flexible, enabling new additions and customizations by Solve-RD partners if required in the future. Data from all Solve-RD participants entering the system will then be exported into phenopackets (*http://phenopackets.org*) and used for downstream (meta)analyses.

## Report:

Phenotypic data in PhenoStore is collected through available forms for users. These forms are customizable and can be adapted to ease the introduction of information for certain diseases. Below is shown the main page with the disease forms to choose from:



	New Index Case Submisson	
	The following templates are based on Genomics England Clinical Data Models. Please, mind t	that displayed ERNs
	are only suggestions to recommend clinical scientists the best template to enter the	heir case
	Choose a Template:	
	21 Templates Available	
0	Default Template Standard PhenoStore Case	SELECTED
C	Cardiovascular disorders Disorders of the heart and blood vessels ERN GUARD-HEART,VASCERN,ERN EURO-NMD,ERN EuroBloodNet,ERNICA	
C	Ciliopathies Abnormal formation or function of cilia ERN LUNG,ERKNet,ERN EYE,ERNICA	
C	Dermatological disorders Conditions that affect the integumentary system ERN Skin,ERN RECONNET,ERNICA	

Through the Solve-RD project, and in collaboration with WP1, we were able to create new forms to facilitate the collection of data by clinicians/researchers from ERNs. Specifically, forms covering disorders for ERNs GENTURIS, ITHACA, NMD and RND were created.

C	Cardiovascular disorders Disorders of the heart and blood vessels ERN GUARD-HEART,VASCERNERN EURO-NMDERN EuroBloodNet,ERNICA
O	Dysmorphic and congenital abnormality syndromes Congenital structural abnormalities ERN EURO-NMD ERN CRANIO,ERNICA ERN ITHACA, ERN ReCONNET ERN-RND, MetabERN, Endo-ERN, ERKNet, ERN BOND
0	Endocrine disorders Disorders related to the endocrine glands of the body Endo-ERN,MetabERN,ERN EpiCARE ERN EURO-NMD, ERNICA
O	Dysmorphic and congenital abnormality syndromes Congenital structural abnormalities ERN EURO-NMD ERN CRANIO, ERNICA ERN ITHACA, ERN RECONNE [, ERN-RND, MetabERN, Endo-ERN, ERKNet, ERN BOND
O	Endocrine disorders Disorders related to the endocrine glands of the body Endo-ERN,MetabERN,ERN EpiCARE ERN EURO-NMD ERNICA
C	Growth disorders Disorders that affect height, weight and sexual development ERNICAERN ITHACA, ERN BOND, ERN CRANIOERN EURO-NMD, ERN RECONNET, ERN-RND, MetabERN, Endo-ERN



A	Hearing and ear disorders Abnormalies of the outer, middle, or inner ear
<b>U</b>	ERN-RND, ERN EURO-NMD, ERN CRANIO, ERNICA, MetabERN ERN ITHACA
	Metabolic disorders
U	MetabERN,Endo-ERN,ERN EpiCARE ERN EURO-NMD ERNICA ERN ITHACA,ERN-RND, ERN EpiCARE
	Neurology and neurodevelopmental disorders
U	ERN-RND, ERN EURO-NMD, ERN ITHACA, MetabERN, ERN EpiCARE, ERNICA
	Ophthalmological disorders
U	Eye and vision disorders ERN EYE ERN EURO-NMD, ERN-RND
	Psychiatric disorders
C	Mental health disorders
	Phoumatological disorders
C	Inflammation that affects the connecting or supporting structures of the body
	ERN RECONNE I, ERN BUND, ERN GRANIO, ERNIGA <mark>, ERN ITHACA, ERN-RND</mark>
	Skeletal disorders
U	Disorders that can affect <u>muscles, bones, and joints</u> ERN BOND, ERN CRANIO <mark>, ERN EURO-NMD, E</mark> RNICA, ERN ReCONNET, ERN RITA <mark>, ERN-RND, M</mark> etabERN
	Tumour syndromes
U	Higher risk of certain types of cancer ERN GENTURIS, ERN PaedCan, ERN EURACAN, Endo-ERN

We introduced mandatory fields to all these forms (see image below), which is necessary to provide a standard and robust phenotypic database.

In addition, we were able to provide a pre-defined list of mapped HPOs to the different diseases by using the data models generated by Genomics England, accessible at "<u>Rare Dis-</u> <u>ease Conditions Clinical Data Models</u>". Then, with the collaboration of the ERNs the HPOs were chosen and introduced in each form specific for each ERN.



# > Individual information

Alive				
Country of birt	h			
Unknown				
Date of birth*				
If day and month are	e left blank, it will take the 1st of J	anuary		
If day and month are	e left blank,it will take the 1st of J	day	~	
If day and month are year Sex*	e left blank,it will take the 1st of J	day	~	

Examples shown below are different forms for "Cardiovascular disorders" and "Endocrine disorders" with their respective specific disease types HPO trees to select from.

Template Selected: Cardiovascular disorders

Search for phenotypes	
scaren for priciocypes	
Browse the Human Phenotype Ontology (HPO)	
Browse Categories	
+ Arteriopathies	
+ Connective Tissues Disorders and Aortopathies	
<ul> <li>Connective Tissues Disorders and Aortopathies</li> <li>Cardiac arrhythmia</li> </ul>	
<ul> <li>Connective Tissues Disorders and Aortopathies</li> <li>Cardiac arrhythmia</li> <li>Cardiomyopathy</li> </ul>	
<ul> <li>Connective Tissues Disorders and Aortopathies</li> <li>Cardiac arrhythmia</li> <li>Cardiomyopathy</li> <li>Congenital heart disease</li> </ul>	
<ul> <li>Connective Tissues Disorders and Aortopathies</li> <li>Cardiac arrhythmia</li> <li>Cardiomyopathy</li> <li>Congenital heart disease</li> <li>Lymphatic disorders</li> </ul>	



Template Selected: Endocrine disorders

# Clinical symptoms

#### Search for phenotypes

Browse the Human Phenotype Ontology (HPO)

#### **Browse Categories**

+ Adrenal disorders
+ Disorders of calcium homeostasis
+  Gonadal and sex development disorders
+ Growth hormone disorders
+  Hypothalamic and pituitary disorders
+ Obesity syndromes
+ Rare subtypes of diabetes
+ D Thyroid disorders

Finally, a specific field was created (see below) with collaboration of ERN-GENTURIS, which allows submitters to introduce numbers of developed tumors in participants, a very important feature to improve the analyses performed for ERN-GENTURIS diseases.

# >Tumor Information

· Polyposis:
Adenomatous polyps
●none
Serrated polyps
none <10 10-20 20-50 50-100 100-1000 >1000 Not specified
Hyperplasic polyps
●none
luvenile polyps:
●none ●<10 ●10-20 ●20-50 ●50-100 ●100-1000 ●>1000 ●Not specified
· Tumor features:
Microsatellite instable
OYes ⊙No ●Unknown
Hypermutated
Yes No OUnknown



All these new features will be released in the new GPAP-PhenoStore platform. However, they are already accessible through the RD-Connect GPAP <u>Phenostore Playground</u> (https://playground.rd-connect.eu/phenostore/#/).

It is important to note that other forms outside Solve-RD project were also developed previously through other projects or under the EJP-RD project for other ERNs.

# **Conclusion:**

We successfully introduced new phenotypic forms specific for diseases related to the ERNs working in the Solve-RD project. These new forms will facilitate the collation of the participants' HPOs and other disease-specific relevant information and will improve phenotypic description and consistency of the introduced traits across the project.