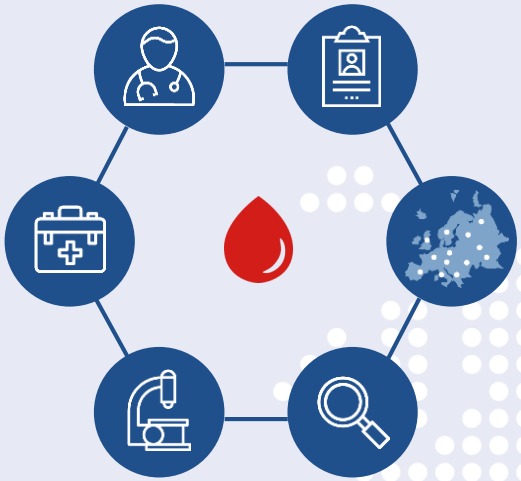
The European Rare Blood Disorders Platform

Kick off meeting 2nd July 2020



European Reference Network
for rare or low prevalence complex diseases

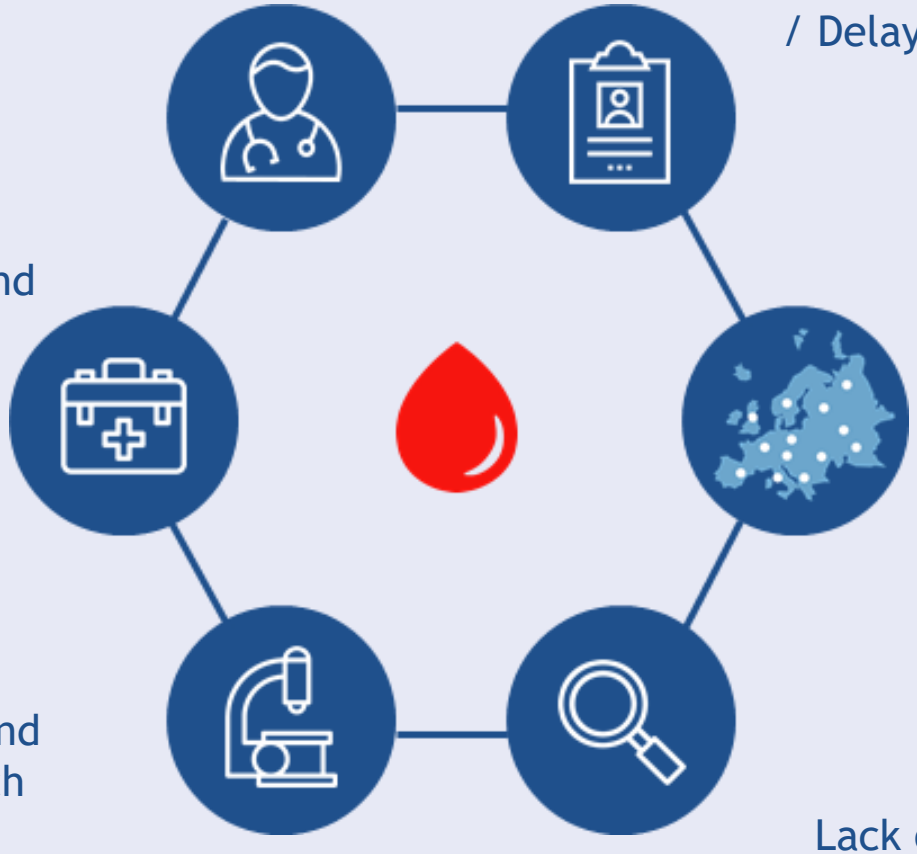
Network Hematological Diseases (ERN EuroBloodNet)

www.eurobloodnet.eu/enrol

Rare hematological diseases challenges

Scattered knowledge and expertise

Underdiagnosed / misdiagnosed / Delayed diagnosis



Lack of treatments and guidelines

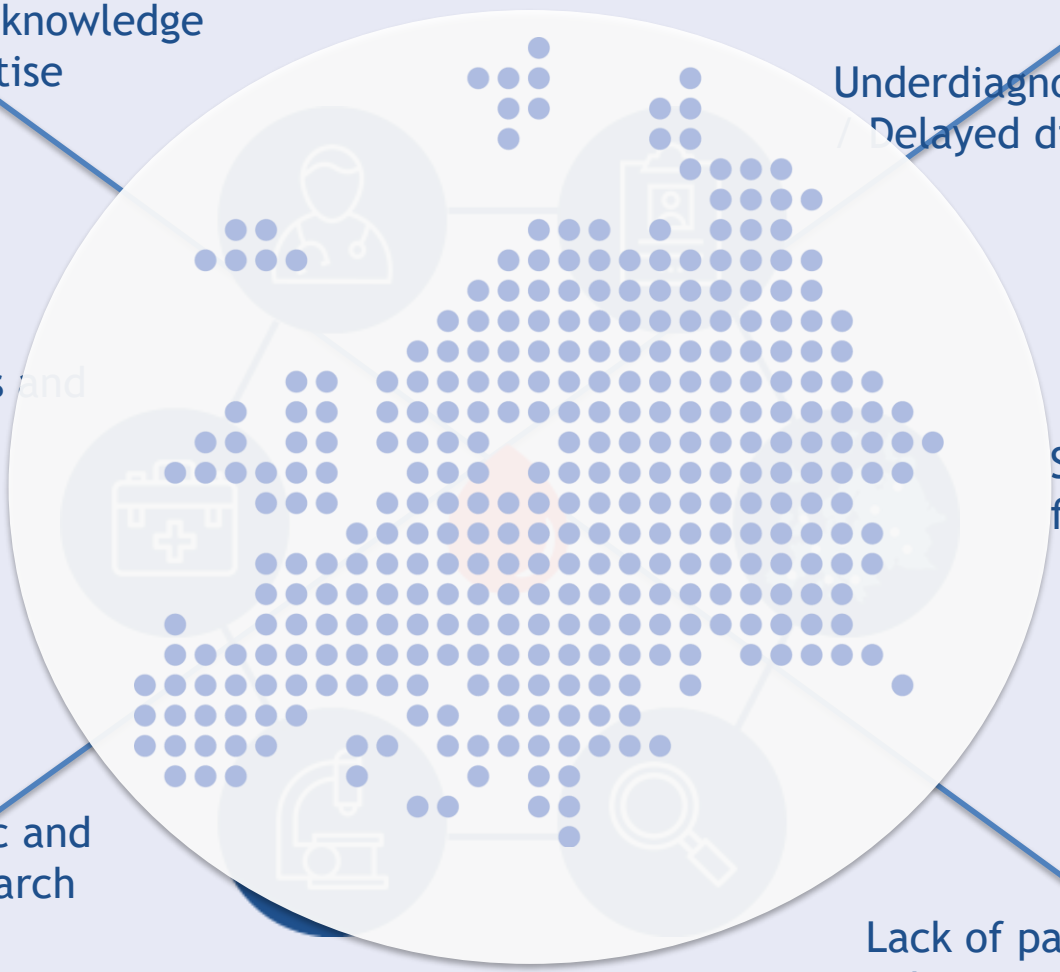
Scarce and fragmented data

Lack of basic and clinical research

Lack of patients cohorts

ENROL

Rare hematological diseases challenges



Scattered knowledge and expertise

Underdiagnosed / misdiagnosed / Delayed diagnosis

Lack of treatments and guidelines

Scarce and fragmented data

Lack of basic and clinical research

Lack of patients cohorts

ENROL

Rare hematological diseases challenges

Where are the patients?

- Lack of uniform standards for data collection during last decades
  → Scarce and unestructured data accross hundreds of databases in EU

- Codification challenges
  → Untraceable data – especial underrepresentation of ultrarare diseases

Rare diseases' registries

- National registries for RD: Belgium, Bulgaria, France, Italy, Latvia, Slovak Republic, Spain and UK

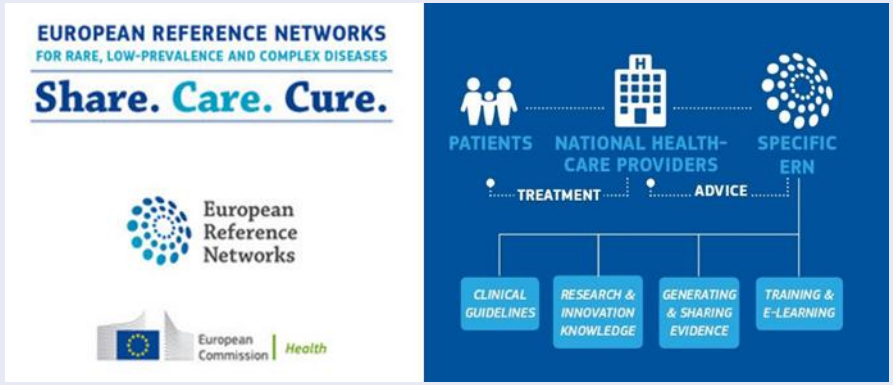
- 753 RD registries in Europe (Orphanet Report)

ENROL

European Commission strategy for RD registration

European Platform on Rare Disease Registration (EU RD Platform)

Copes with the fragmentation of RD patients data contained in hundreds of registries across Europe by releasing standards for interoperability



European Reference Networks registries

Grants for supporting RDs registries for ERNs to:

- ✓ Enable building
- ✓ Upgrading
- ✓ Linking and making interoperable

registries covering the diseases of each ERN following the standards defined by the EU RD Platform.

European Commission
Joint Research Centre

EUROPEAN JOINT PROGRAMME RARE DISEASES

ERNs Working group on Research includes a task force on registries with representatives of ERNs to align forces on transversal actions in colab. with **JRC and EJP-RD**, as:

- ✓ ERN registry data dictionary
- ✓ Domain specific Common Data Elements

European Rare Blood Disorders Platform (ENROL)

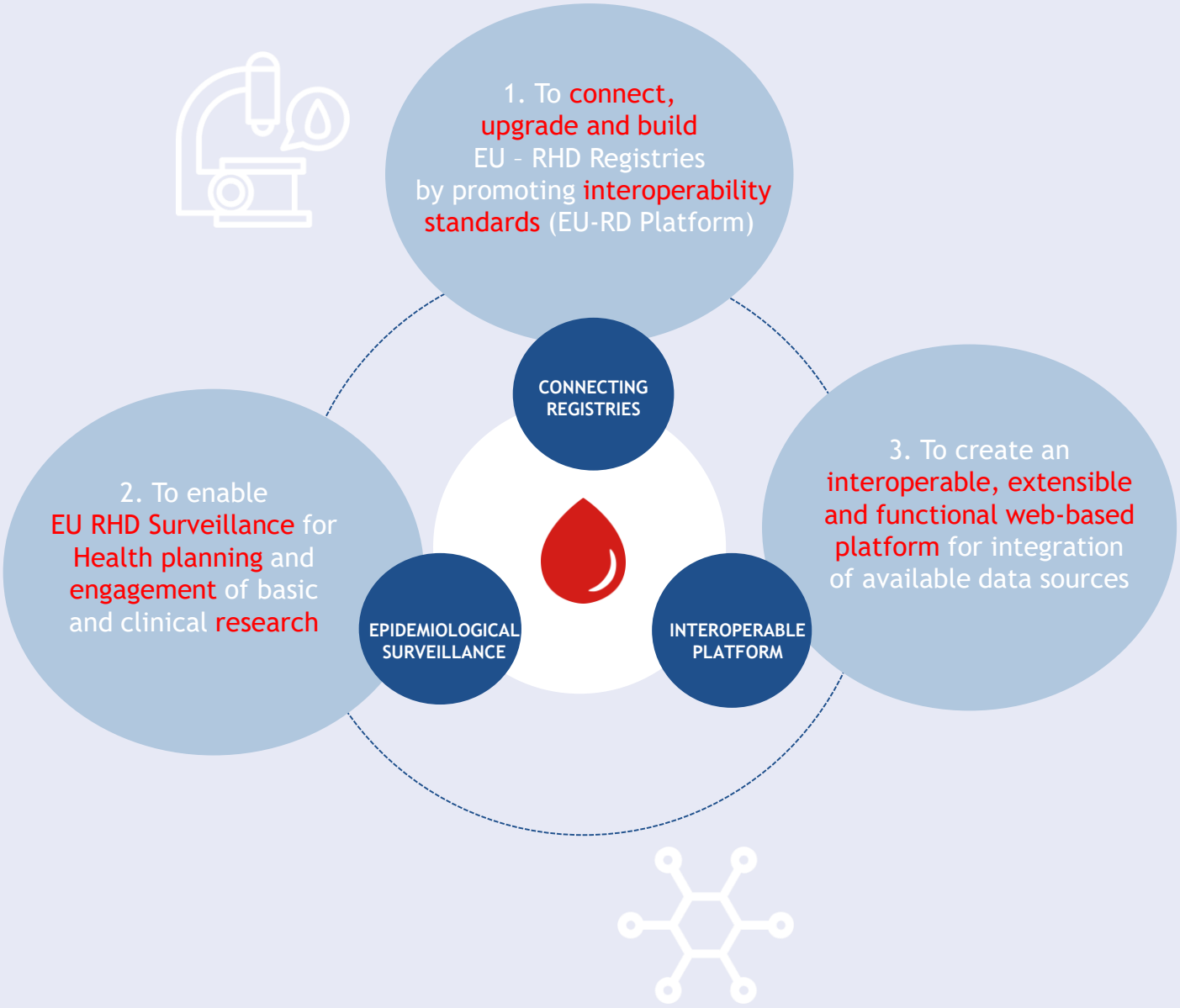
ENROL has been conceived in the core of ERN-EuroBloodNet as an umbrella for both new and already existing registries on rare hematological disorders (RHD) aiming at avoiding fragmentation of data by promoting the standards for patients registries' interoperability in line with the EU-RD-Platform

ENROL's principle is to maximize public benefit from data on RHD with the only restriction needed to guarantee patient rights and confidentiality, in agreement with EU regulations for cross-border sharing of personal data.

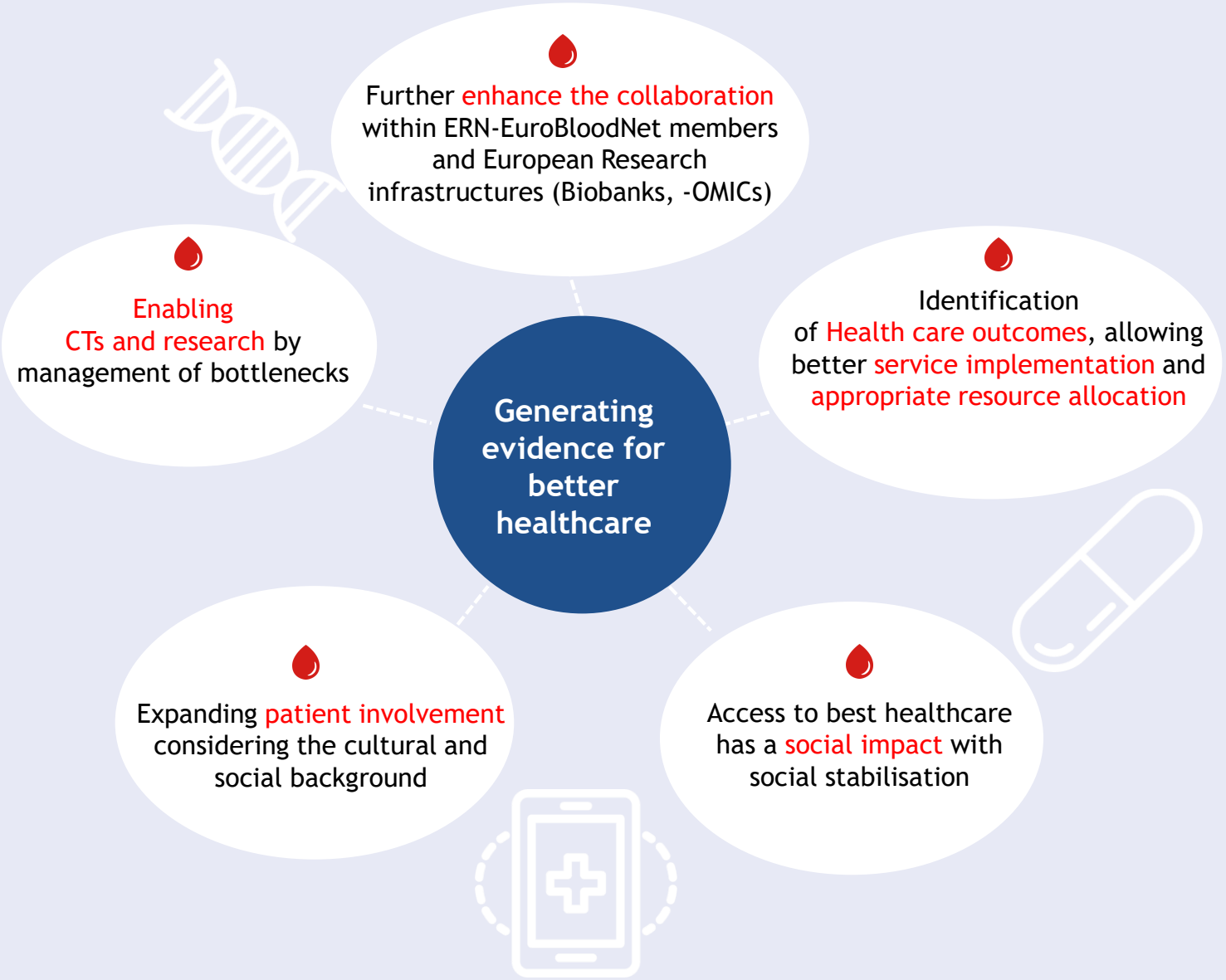
- possibility to share and pool data
- reach critical numbers
- analyse KPIs, perform clinical trials & research projects
- knowledge generation (evidence)
- **better healthcare for RHDs patients**

ENROL

Specific objectives



Expected outcomes



ENROL Consortium

Coordinator
Maria del Mar Mañú Pereira
Victoria Gutiérrez Valle
Vall d'Hebron University Hospital (HUVH) - Vall d'Hebron University Hospital Foundation - Research Institute (VHIR), Barcelona, Spain

Marina Kleanthous
Petros Kountouris
The Cyprus Foundation for muscular dystrophy research (CING), Nicosia, Cyprus

Béatrice Gulbis
Erasme University Hospital (ERASME) / LHUB-ULB, Brussels, Belgium

Pierre Fenaux
Mariangela Pellegrini
Assistance Publique - Hopitaux de Paris (AP-HP), Paris, France

ENROL Stakeholders

ENROL's collaborating partners:

EURORDIS RARE DISEASES EUROPE

EuroBloodNet

European Platform on Rare Disease Registration (EU RD Platform)

EUROPEAN JOINT PROGRAMME RARE DISEASES

Stakeholders to be approached shortly!

EHA EUROPEAN HEMATOLOGY ASSOCIATION

HARMONY
Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in Hematology

EBMT
European Society
for Blood and Marrow Transplantation

orphanet

Partner
Paediatric Rare Tumours Network - European Registry

www.genturis.eu

And...

- Existing registries curators
- Legal and ethical experts
- CEOs
- IT teams

ENROL

European Platform on Rare Disease Registration

European Commission
Joint Research Centre (JRC)

ENROL Kick-off meeting – 2 July 2020

European Commission's Strategy for Rare Diseases

Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on "Rare Diseases: Europe's challenges" (2008)

1. **To improve recognition and visibility on rare diseases**
2. **To support policies on rare diseases in the EU Member States**
3. **To develop European cooperation, coordination and regulation for rare diseases**

European Commission

European Commission's Strategy for Rare Diseases

Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on "Rare Diseases: Europe's challenges" (2008)

→ **European added value**

European Commission

Why an EU Platform on RD Registration?

- **To <u>cope with the extreme fragmentation</u> of data sources across EU Member States**

  Many RD registries exist, but

  - the **lack of interoperability** severely limits the registries' potential

  - no **standardised data collection** for most RDs

Source: EURORDIS

- **Benefits:**

  Reach the <u>critical number</u> of patients for

  - **studies (epidemiological, clinical, translational, pharmacolgical, etc.)**
  - **research**

European Commission

European Platform on Rare Disease Registration (EU RD Platform)

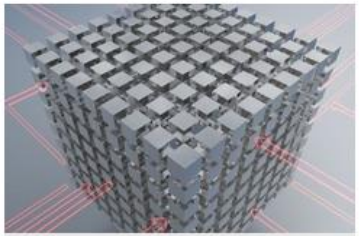
Searchable, findable rare disease registry data

European Rare Disease Registry Infrastructure (ERDRI)

European standards for data collection and data sharing

Trainings, Resources and Latest news

Data repository



European RD Registry Data Warehouse

eurocat

Surveillance of Congenital Anomalies in Europe

Surveillance of Cerebral Palsy in Europe

https://eu-rd-platform.jrc.ec.europa.eu

European Commission

European Platform on Rare Disease Registration (EU RD Platform)

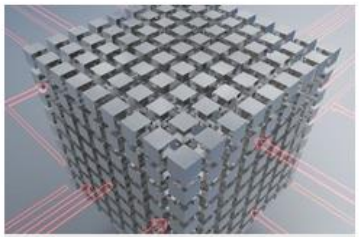
Searchable, findable rare disease registry data

European Rare Disease Registry Infrastructure (ERDRI)

European standards for data collection and data sharing

Trainings, Resources and Latest news

Data repository



European RD Registry Data Warehouse

eurocat

Surveillance of Congenital Anomalies in Europe

Surveillance of Cerebral Palsy in Europe

https://eu-rd-platform.jrc.ec.europa.eu

European Commission

The main components of the EU RD Platform

European Rare Disease Registry Infrastructure (ERDRI)

European Directory of Registries (ERDRI.dor)

Overview of rare disease registries in Europe including their characteristics

Central Metadata Repository (ERDRI.mdr)

Database containing the data elements used by rare disease registries

EUCERD-JA
Workpackage "Registries"
Univ. Frankfurt/Univ. Mainz

European Commission

The main components of the EU RD Platform

European Rare Disease Registry Infrastructure (ERDRI)

European Directory of Registries (ERDRI.dor)

Overview of rare disease registries in Europe including their characteristics

Central Metadata Repository (ERDRI.mdr)

Database containing the data elements used by rare disease registries

EUPID

Pseudonymisation tool

Service offering registries at local level the solution for patient pseudonymisation

Collaboration with

AIT AUSTRIAN INSTITUT OF TECHNOLOGY

European Commission

Interoperability by using the European Patient IDentity (EUPID)

Pseudonymisation tool

Service offering registries at local level the solution for patient pseudonymisation

Collaboration with

AIT AUSTRIAN INSTITUT OF TECHNOLOGY

- **EUPID offered to all registries joining the EU RD Platform**
- **Pseudonyms provided at registries' local level**
- **Prevention of patients' multiple registration**

European Commission

European Platform on Rare Disease Registration (EU RD Platform)

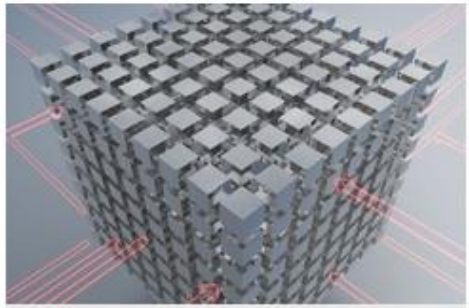
Searchable, findable rare disease registry data

European Rare Disease Registry Infrastructure (ERDRI)

European standards for data collection and data sharing

Trainings, Resources and Latest news

Data repository



European RD Registry Data Warehouse

eurocat

Surveillance of Congenital Anomalies in Europe

Surveillance of Cerebral Palsy in Europe

https://eu-rd-platform.jrc.ec.europa.eu

European Commission

EU RD Platform: Common Data Elements

Tools for semantic interoperability

Set of Common Data Elements (CDE)

Domain Specific Common Data Elements (DsCDE)

Work in progress

https://eu-rd-platform.jrc.ec.europa.eu/set-of-common-data-elements_en

European Commission

Setting up a registry using the EU RD Platform

The EU RD Platform provides:

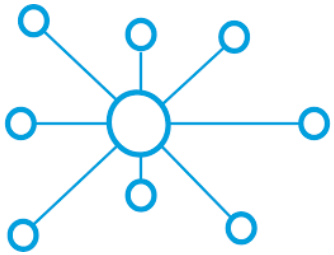
- **technical solution: open source software (University of Frankfurt)**
- **support**
- **assistance**

European Commission

Building an ERN central registry based on pre-existing registries

Metadata

Metadata



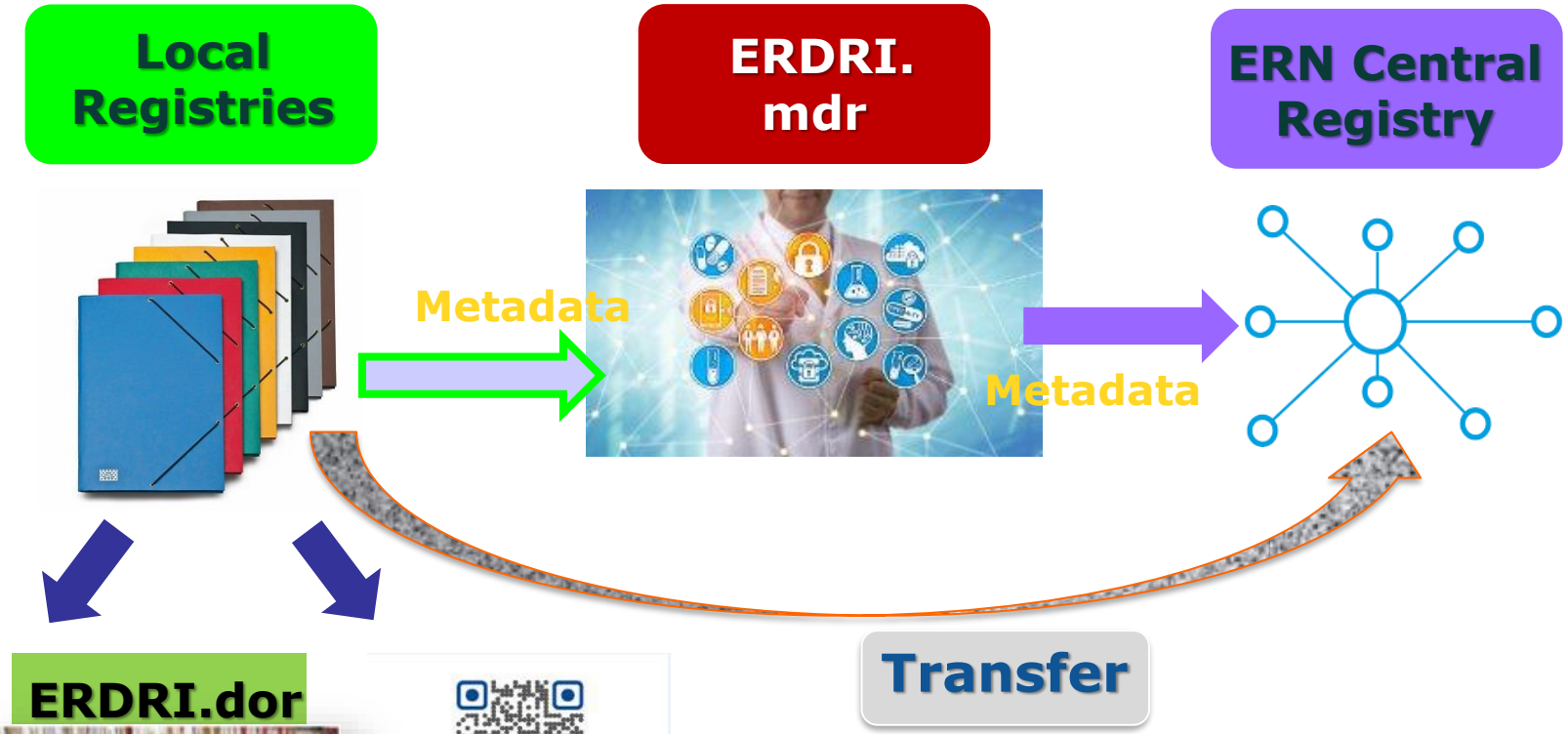
Local Registries

EU RD Platform

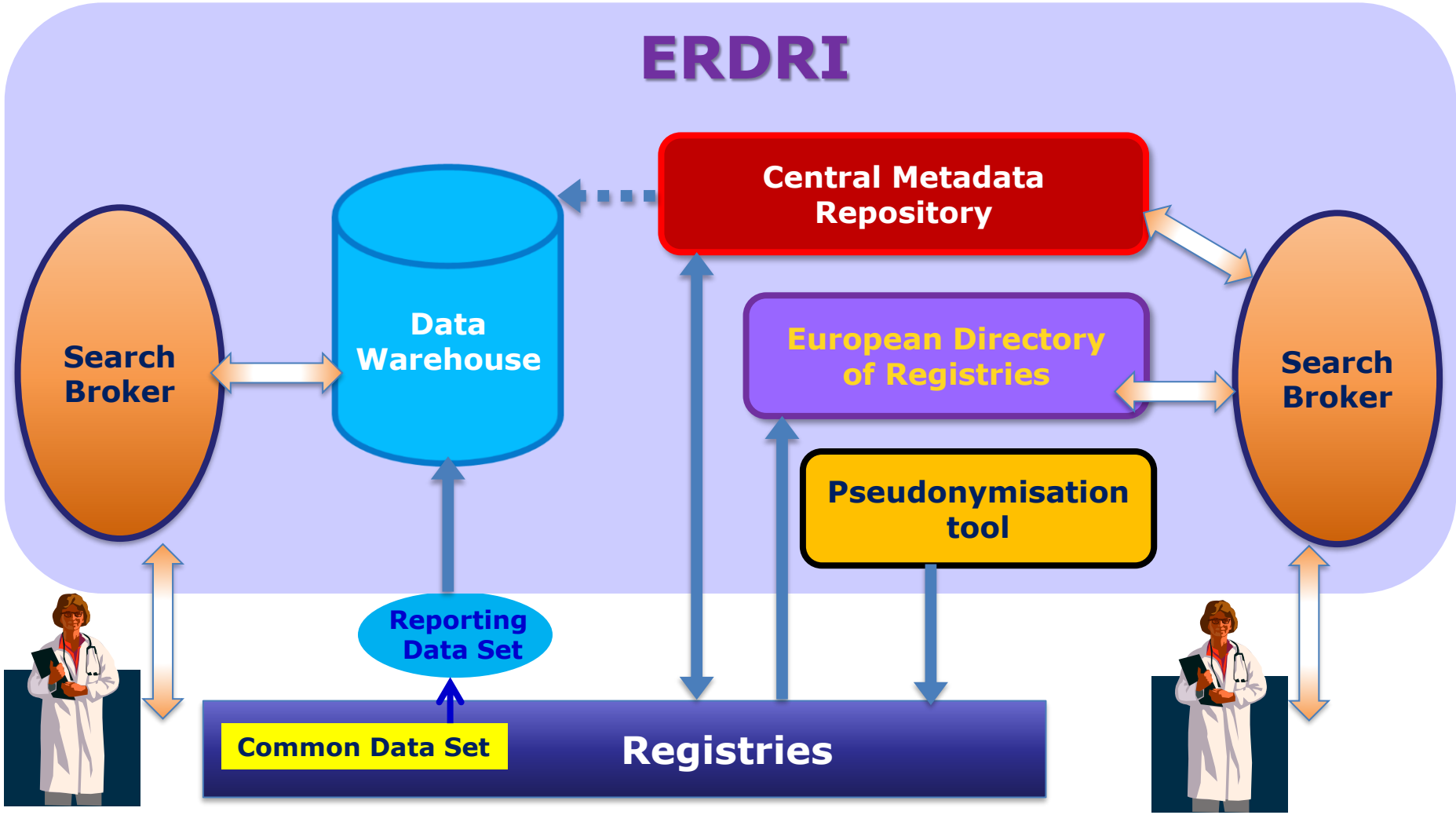
ERN Central Registry

European Commission

Building an ERN central registry based on pre-existing registries



EU RD Platform



European Commission

Join the EU RD Platform

knowledge generation centre for rare diseases

https://eu-rd-platform.jrc.ec.europa.eu

European Commission

EU RD Platform

JRC F.1 'Health in Society'

Simona Martin
Agnieszka Kinsner-Ovaskainen
Andri Papadopoulou
Monica Lanzoni
Alexander Binder
Stefano Adriani
Enrico Ben
Antonino Brunetti

University of Frankfurt

Holger Storf
Dennis Kadioglu
Jens Goebel
Torsten Panholzer
Michael Folz

Austrian Institute of Technology

Günter Schreier
Michael Nitzlnader
Markus Falgenauer

European Commission

European Platform on Rare Disease Registration (EU RD Platform)

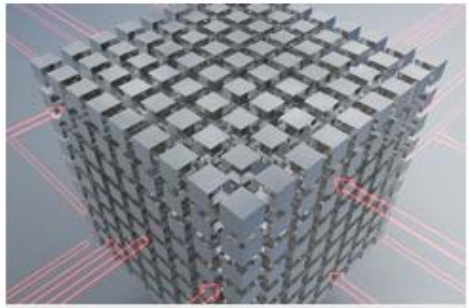
Searchable, findable rare disease registry data

European Rare Disease Registry Infrastructure (ERDRI)

European standards for data collection and data sharing

Trainings, Resources and Latest news

Data repository



European RD Registry Data Warehouse

eurocat

Surveillance of Congenital Anomalies in Europe

Surveillance of Cerebral Palsy in Europe

https://eu-rd-platform.jrc.ec.europa.eu

European Commission

EU RD Platform: Common Data Elements

Tools for semantic interoperability

Set of Common Data Elements (CDE)

Domain Specific Common Data Elements (DsCDE)

Work in progress

European Commission

SET OF COMMON DATA ELEMENTS FOR RARE DISEASES REGISTRATION

GROUP	ELEMENT N°	ELEMENT NAME	ELEMENT DESCRIPTION	CODING	COMMENT
1. Pseudonym	1.1.	Pseudonym	Patient's pseudonym	• String	https://eu-rd-platform.jrc.ec.europa.eu/erdri/eupid-intro
2. Personal information	2.1.	Date of birth	Patient's date of birth	• Date (dd/mm/yyyy)	
	2.2.	Sex	Patient's sex at birth	• Female • Male • Undetermined • Foetus (Unknown)	
3. Patient Status	3.1.	Patient's status	Patient alive or dead	• Alive • Dead • Lost in follow-up • Opted-out	If dead then answer question 3.2
	3.2.	Date of death	Patient's date of death	• Date (dd/mm/yyyy)	
4. Care pathway	4.1.	First contact with specialised centre	Date of first contact with specialised centre	• Date (dd/mm/yyyy)	

5. Disease history	5.1.	Age at onset	Age at which symptoms/signs first appeared	• Antenatal • At birth • Date (dd/mm/yyyy) • Undetermined	
	5.2.	Age at diagnosis	Age at which diagnosis was made	• Antenatal • At birth • Date (dd/mm/yyyy) • Undetermined	
6 Diagnosis	6.1.	Diagnosis of the rare disease	Diagnosis retained by the specialised centre	Orpha code (strongly recommended – see link) / Alpha code/ ICD-9 code/ ICD-9-CM code / ICD-10 code	http://www.orphadata.org/cgi-bin/inc/product1.inc.php
	6.2.	Genetic diagnosis	Genetic diagnosis retained by the specialised centre	International classification of mutations (HGVS) (strongly recommended – see link) / HGNC / OMIM code	http://www.hgvs.org
	6.3	Undiagnosed case	How the undiagnosed case is defined	• Phenotype (HPO) • Genotype (HGVS)	
7. Research	7.1.	Agreement to be contacted for research purposes	Patient's permission exists for being contacted for research purposes	• YES • NO	
	7.2.	Consent to the reuse of data	Patient's consent exists for his/her data to be reused for other research purposes	• YES • NO	
	7.3.	Biological sample	Patient's biological sample available for research	• YES • NO	If YES answer question 7.4
	7.4.	Link to a biobank	Biological sample stored in a biobank	• YES (if appropriate use link) • NO	https://directory.bbmri-eric.eu
8.Disability	8.1.	Classification of functioning/disability	Patient's disability profile according to International Classification of Functioning and Disability (ICF)	• Disability profile / Score	http://www.who.int/classifications/icf/whodasii/en/

EU RD Platform: Common Data Elements

Tools for semantic interoperability

Set of Common Data Elements (CDE)

Domain Specific Common Data Elements (DsCDE)

Work in progress

European Commission

Domain–Specific Common Data Elements

AIM

- **Extension of the Set of Common Data Elements (CDE) to increase semantic interoperability between rare disease registries.**
- **This will allow to meet the research needs of the ERNs**
- **Launch workshop organised by the JRC for 5-6 March had to be cancelled due to the global emengency.**
- **First Step:**

  Identification and definition of ERN medical domains

European Commission

The main components of ERDRI

European Rare Disease Registry Infrastructure (ERDRI)

European Directory of Registries (ERDRI.dor)

Overview of rare disease registries in Europe including their characteristics

Central Metadata Repository (ERDRI.mdr)

Database containing the data elements used by rare disease registries

EUPID

Pseudonymisation tool

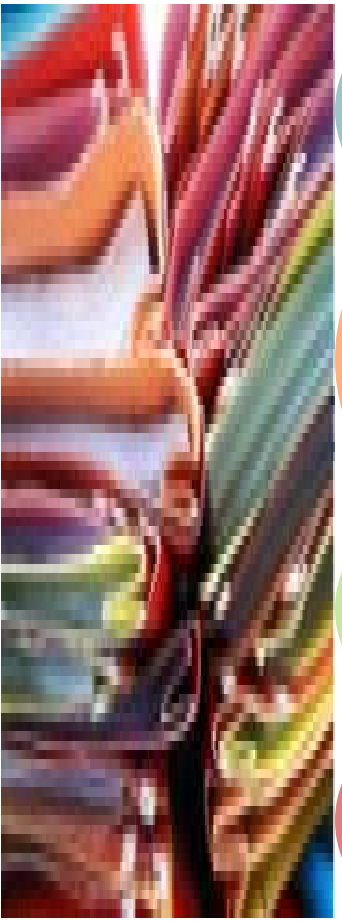
Service offering registries at local level the solution for patient pseudonymisation

EUCERD-JA Workpackage "Registries"
Univ. Frankfurt/Mainz

Collaboration with Austrian Institute of Technology

European Commission

The European Directory of RD registries ERDRI.dor



List of participating RD registries with their main characteristics and description

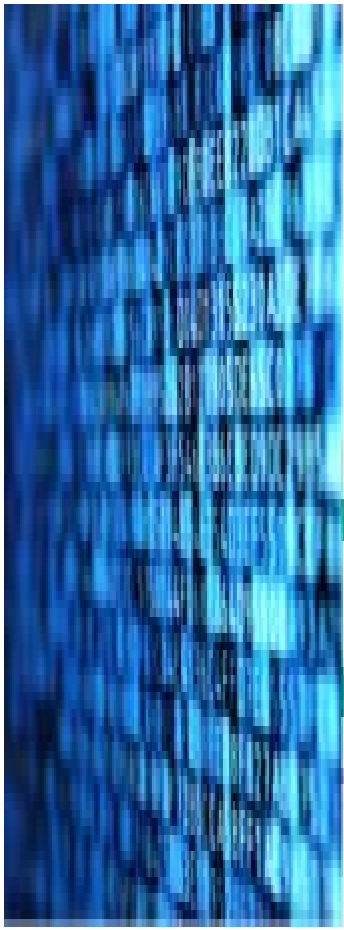
Descriptive information - eight sections with 38 data fields related to a registry of which 23 are obligatory

- **specific rare disease addressed**
- **scope**
- **operating institution**
- **contact information**

Data input is performed by registry owners

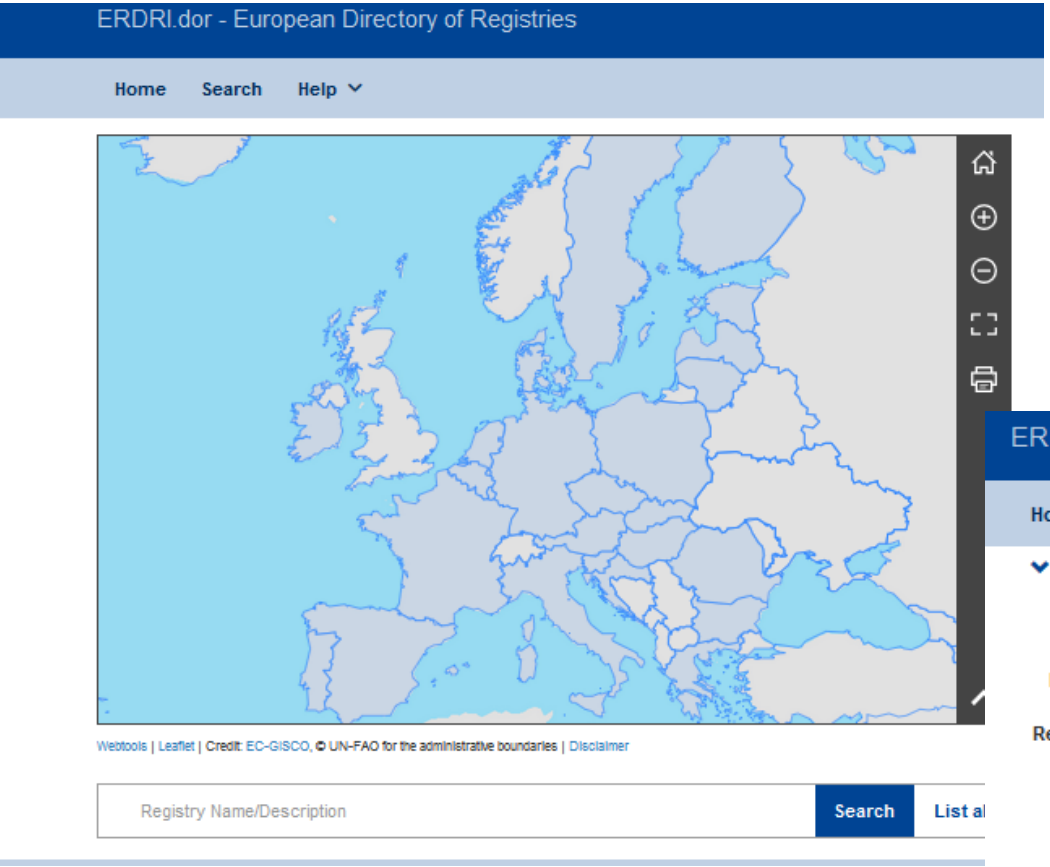
List of the data elements collected by the registries according to the ERDRI.mdr:

registry-specific data scheme

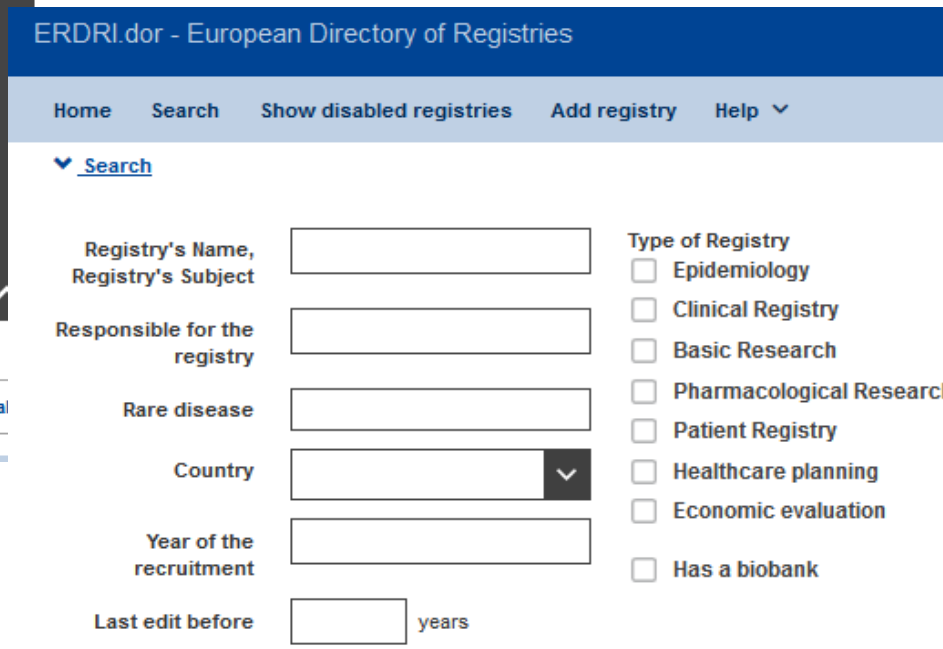


European Commission

The European Directory of RD registries - ERDRI.dor



- Clickable map
- "List all" function
- Search function



- ERN registry networks – have the obligation to introduce every single registry in the EU RD Platform

European Commission

The Central Metadata Repository – ERDRI.mdr

Central Metadata Repository ERDRI.mdr

=

Collection of metadata on all data elements collected by participating registries

- **Designation**
- **Definition**
- **Measurement unit + range**

Semantic Interoperability

common definitions for data elements

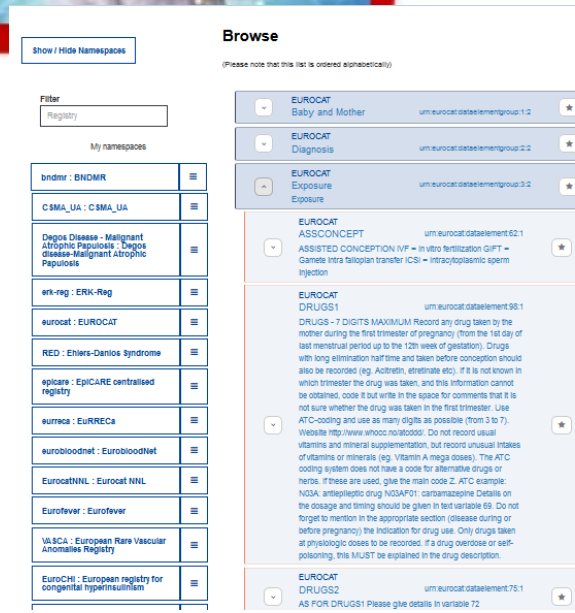
terms are understood in the same way by all data providers + data users

thesaurus of terms used by participating registries common format

European Commission

Role of ERDRI.mdr in building a registry

Import of metadata into ERDRI.mdr (software)



- **Implementation of the Set of CDE by each registry**
- **Domain Specific CDEs (work in progress) will also be included in ERDRI.mdr for registries to use**

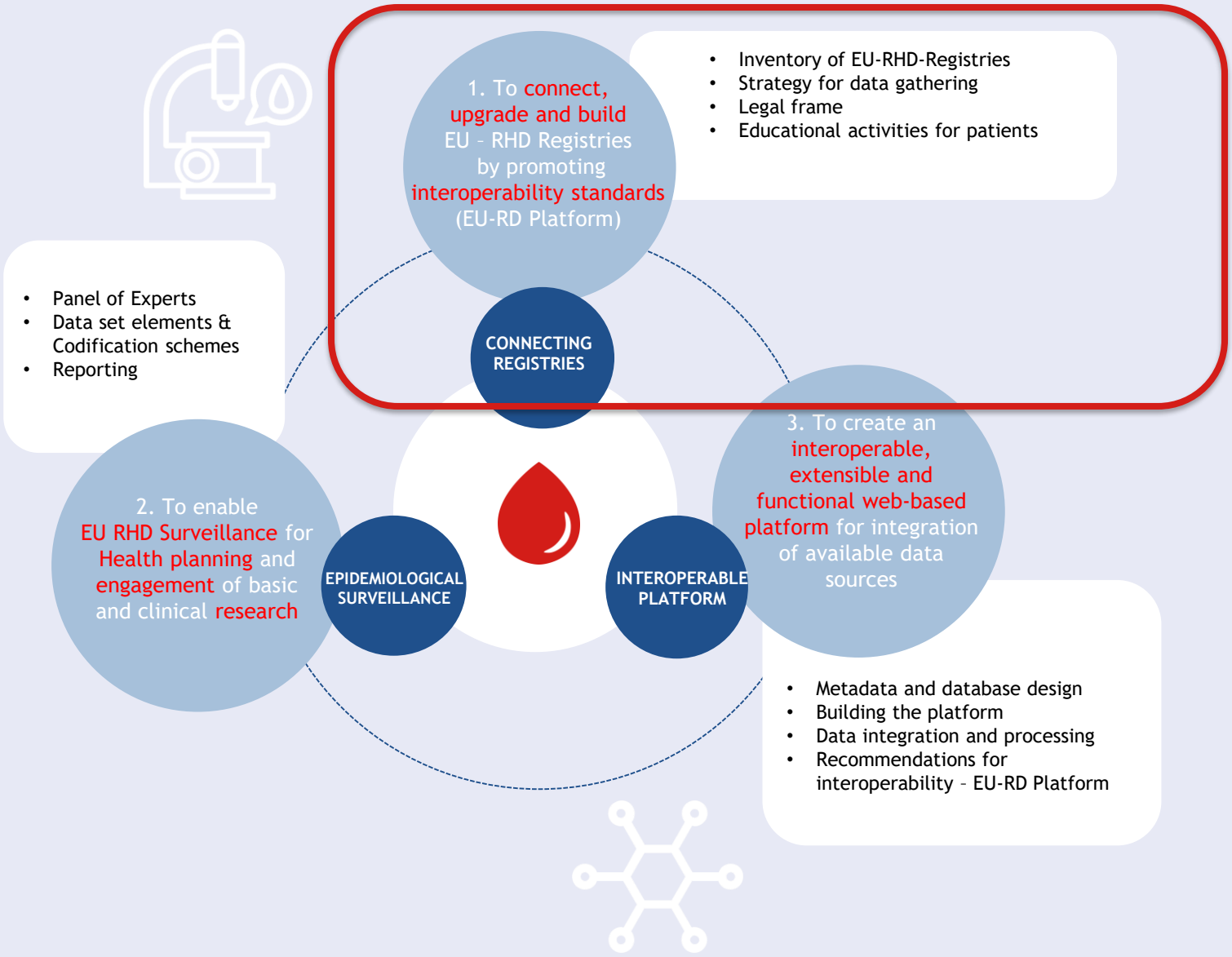
The European Rare Blood Disorders Platform

Kick off meeting 2nd July 2020

ENROL Implementation

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data



ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Actions undertaken to **connect EU-RHD Registries and Healthcare providers** within a **legal and ethical frame** enabling the sharing and re-use of RHD data, while ensuring the implementation of appropriate safeguards for secure transmission and respecting patient rights and privacy. It also includes **educational activities for patient empowerment.**

What is already in place?

Inventory of EU-RHD registries based on:

a) List of registries identified by ORPHANET covering RHD (Report May 2019)

b) EU-RHD registries identified by previous ERN-EuroBloodNet initiatives

c) Other EU-RHD registries identified by literature review and online search

ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Mapping exercise: preliminary data

184 Registries identified so far for RDs+RHDs: ORPHANET + ERN-EuroBloodNet survey

Rare diseases

- 18 Registries – Most of them at the regional level in Italy and Spain

Rare Hematological diseases

- 4 Registries – 3 National (Finland, France, Lithuania) + EBMT

Oncological RHD

- 70 Registries
  - 2 Global
  - 8 European
  - 46 National
  - 14 Regional / Institutional

Non-oncological RHD

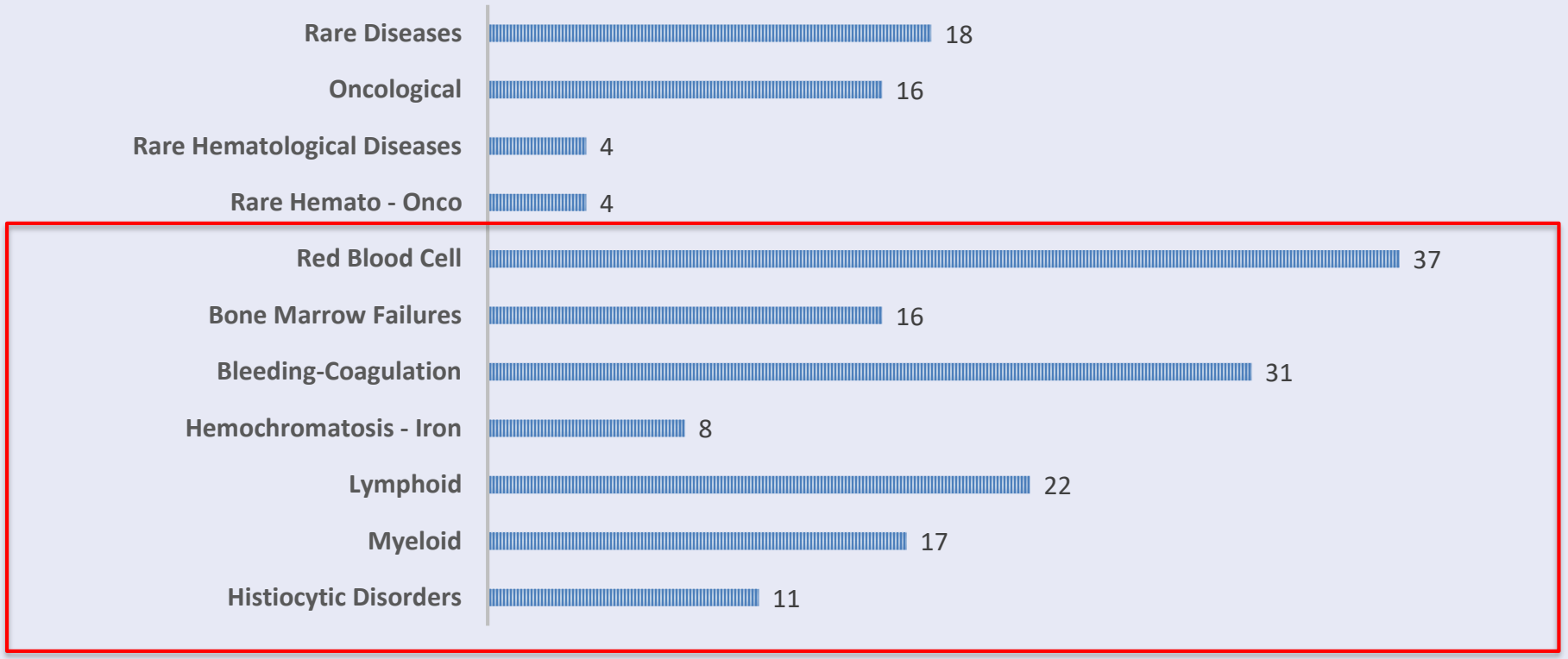
- 92 Registries
  - 14 Global
  - 8 European
  - 63 National
  - 7 Regional / Institutional

ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Mapping exercise: preliminary data

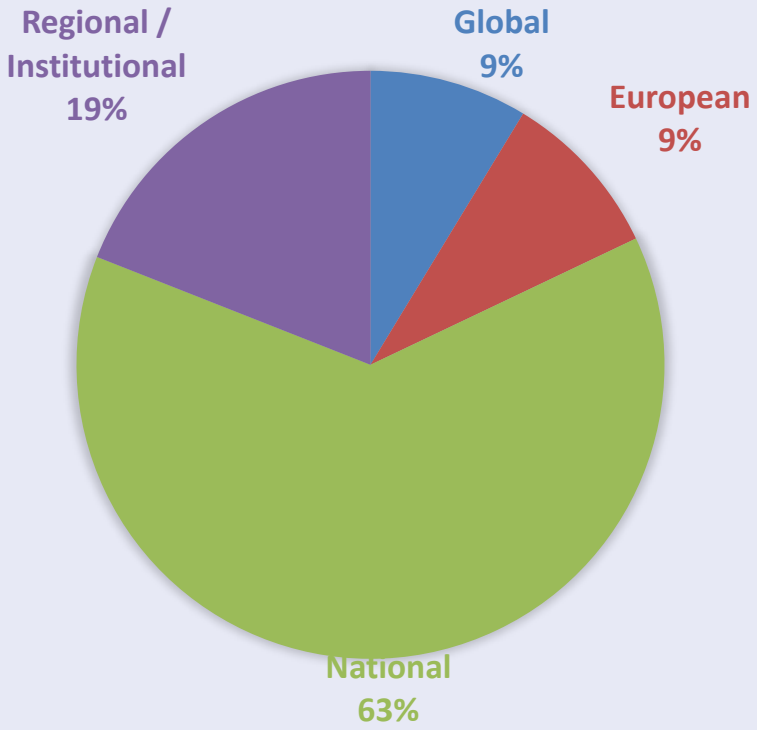
184 Registries identified so far for RDs+RHDs: ORPHANET + ERN-EuroBloodNet survey



WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Mapping exercise: preliminary data

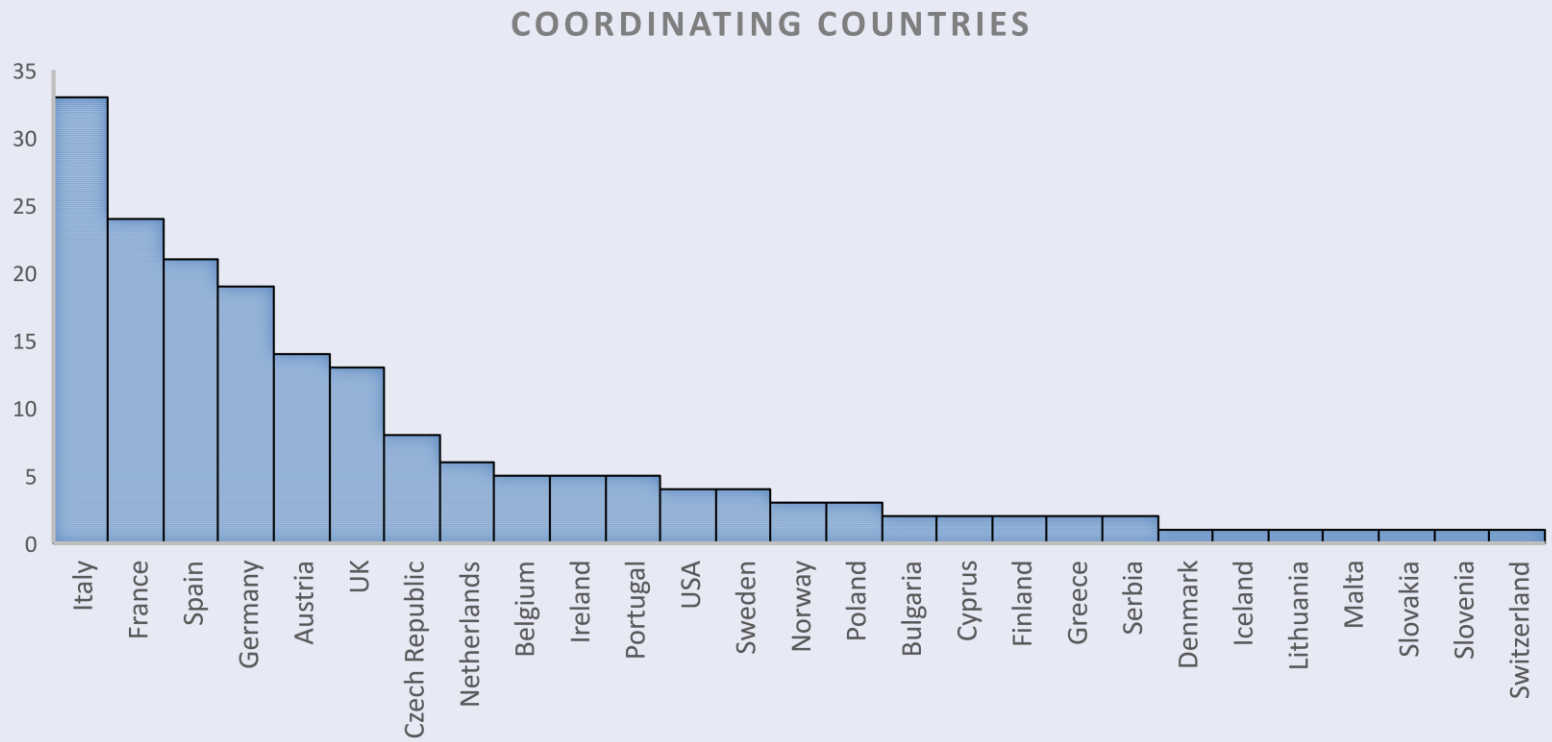
184 Registries identified so far for RDs+RHDs: ORPHANET + ERN-EuroBloodNet survey



WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Mapping exercise: preliminary data

184 Registries identified so far for RDs+RHDs: ORPHANET + ERN-EuroBloodNet survey



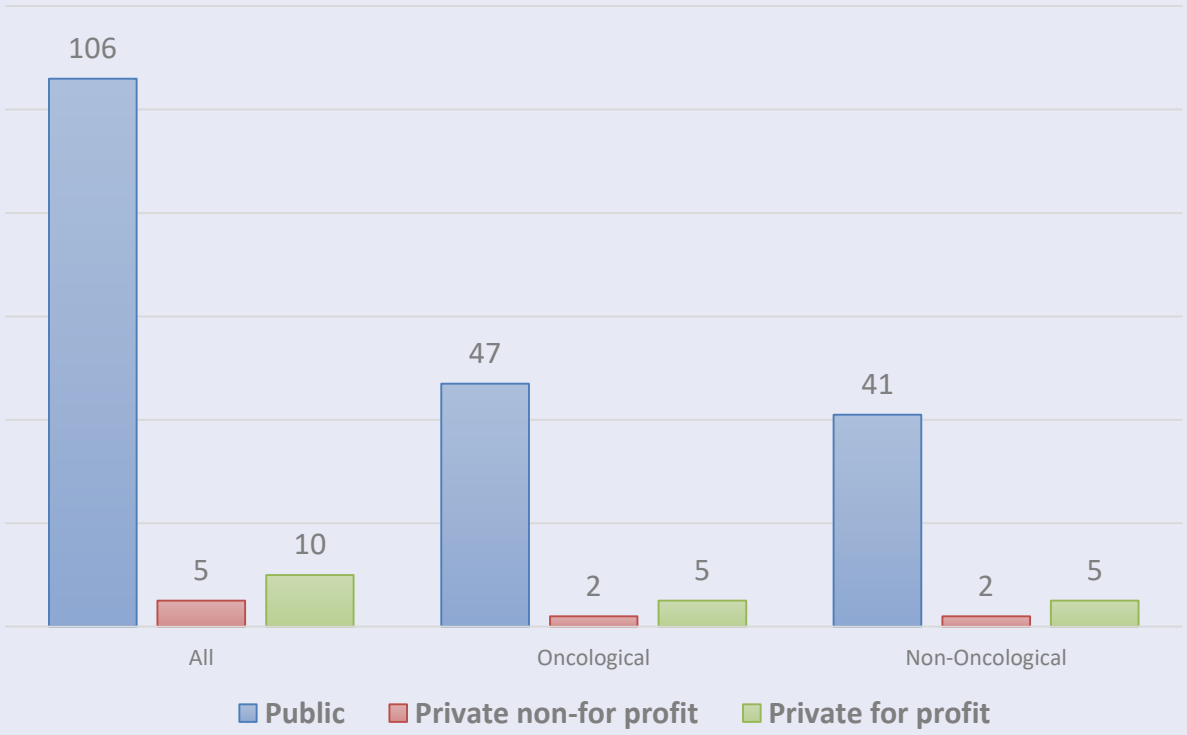
Croatia, Estonia, Hungary, Latvia, Luxembourg, Romania: 0 registries identified so far

ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Mapping exercise: preliminary data

184 Registries identified so far for RDs+RHDs: ORPHANET + ERN-EuroBloodNet survey



WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Actions undertaken to **connect EU-RHD Registries and Healthcare providers** within a **legal and ethical frame** enabling the sharing and re-use of RHD data, while ensuring the implementation of appropriate safeguards for secure transmission and respecting patient rights and privacy. It also includes **educational activities for patient empowerment.**

What is already in place?

Inventory of EU-RHD registries based on:

a) List of registries identified by ORPHANET covering RHD (Report May 2019)

b) EU-RHD registries identified by previous ERN-EuroBloodNet initiatives

c) Other EU-RHD registries identified by literature review and online search

Are existing registries/databases able to share data? In collab with WP6

Survey to assess their level of FAIRification:

a) Types of data stored

b) Coding systems

c) Possibility to export batch data and available data formats

d) Information on policies and if existing consents allow sharing of data

Synergies with EURACAN to assess HCPs standards

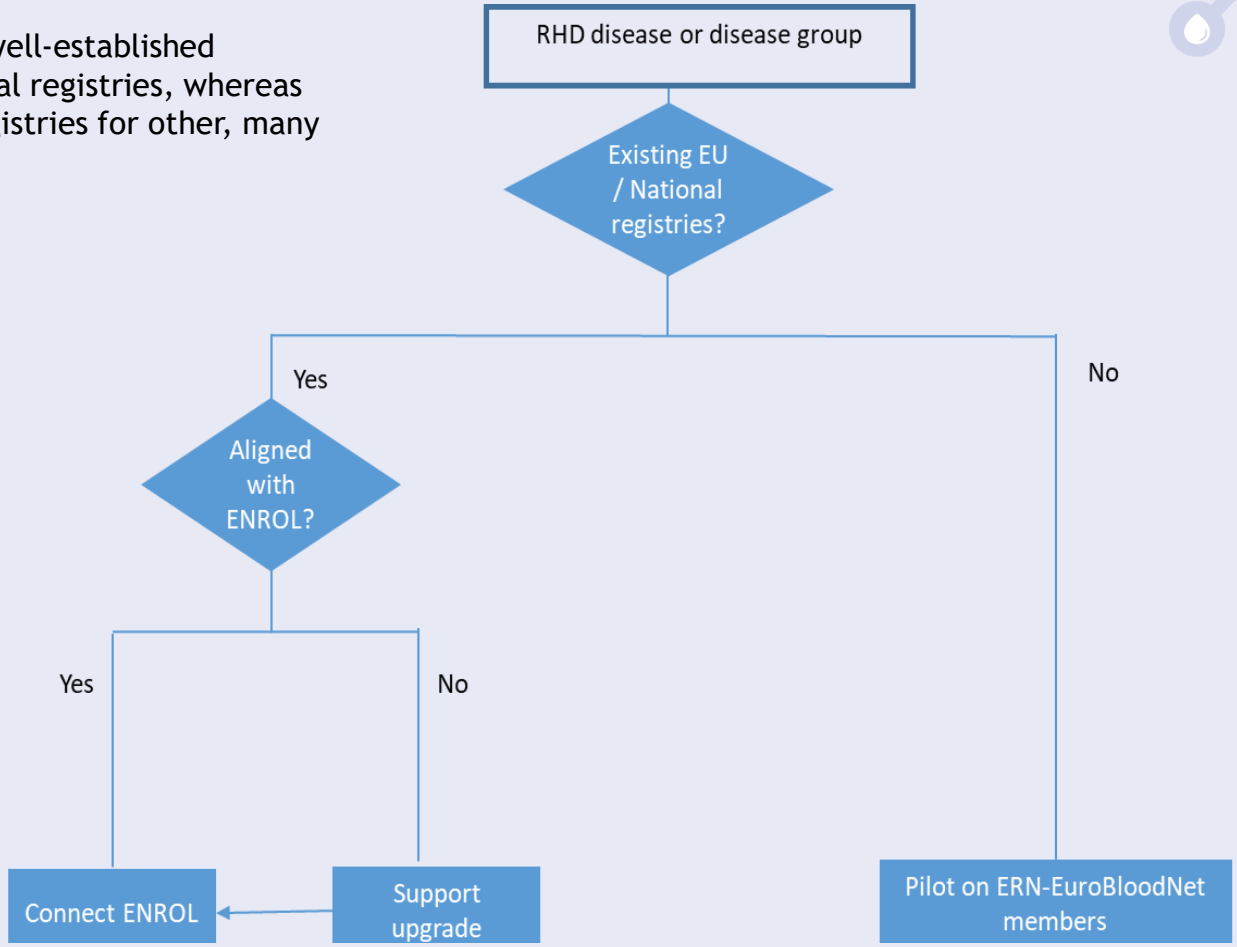
ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

How to gather data?

Strategical approach for comprehensive gathering of data at the EU level based on results from the FAIRification survey considering the following points for each group of RHDs:

- ✓ For some disorders there are well-established European networks and national registries, whereas there is a complete lack of registries for other, many of them, ultra-rare disorders



ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

Patients' Educational program

- Collaboration with EURORDIS
- 2 Educational activities

Webinar Program

Target: RHD Patients Advocates and Patients Organizations

Educational Video

Target: RHD Patients Community

Objectives

- To empower patients in the decision making regarding registries participation
- To raise awareness on ENROL Platform and the EU strategy on sharing of data for RDs

PRIORITISE TOPICS

CONTENTS TO DEVELOP

IDENTIFY SPEAKERS

Coordinators

- ERN-EuroBloodNet Coordination
- EURORDIS
- ePAGs and Patients Representatives

ENROL

WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

How to?

1

Analysis of potential topics to be addressed

- Eurordis Survey "The Voice of Rare Disease Patients: Experiences and Expectations of over 3,000 Patients on Rare Disease Patient Registries in Europe" (EPIRARE project).
- EURORDIS Rare Barometer survey "Share and protect our health data: an evidence based approach to rare disease patients' perspectives on data sharing and data protection - quantitative survey and recommendation".
- Potential topics derived from projects on registries based on proposals by the Program Committee.

2

Topics Classification

Topics will be classified in: topics for expert patients/community patients, transversal topics/diseases specific topics.

3

Survey

Survey conducted among ePAGs and/or patients community for prioritizing topics.

4

Shape programs

A draft for both programs Webinar/Educational Videos programs.

5

Identify speakers

Final programs + Identification of the speakers for both programs Webinar/Educational Videos.

ENROL

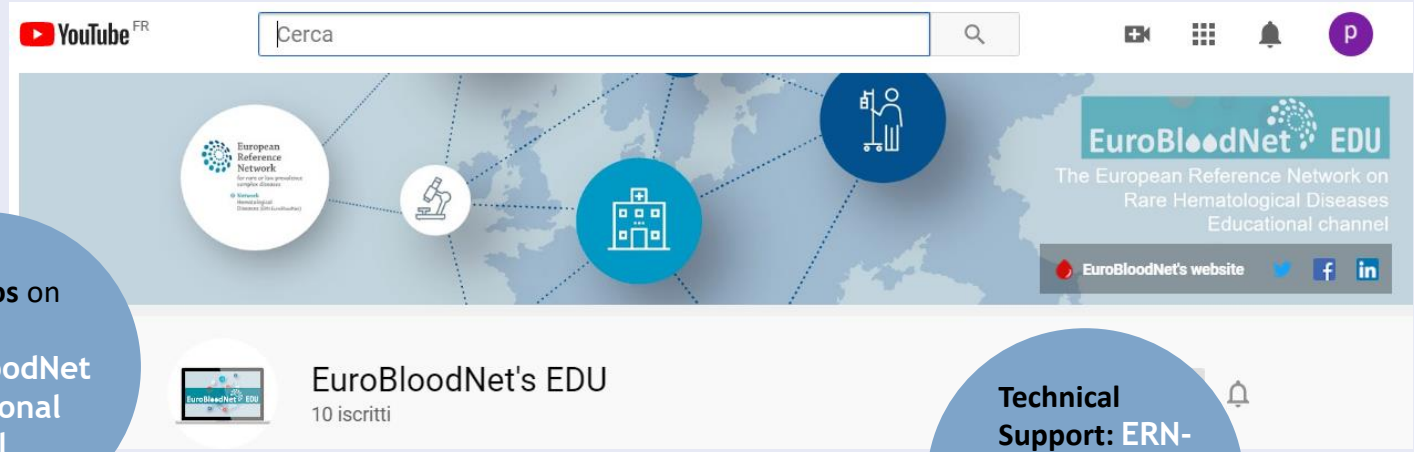
WP 4 Connecting EU-RHD Registries and Healthcare providers for secure sharing and re-using of data

WEBINARS

- **Webex** Platform provided by the EC
- **Speech** + Visual aid of **a Power Point**.
- **45 minutes**: 30 min for speech and 15 minutes for hearers' questions.

EDUCATIONAL VIDEOS

- **Video**: Expert speech +Visual Graphics.
- **Subtitles** in different languages.
- From **5** to **10** minutes.

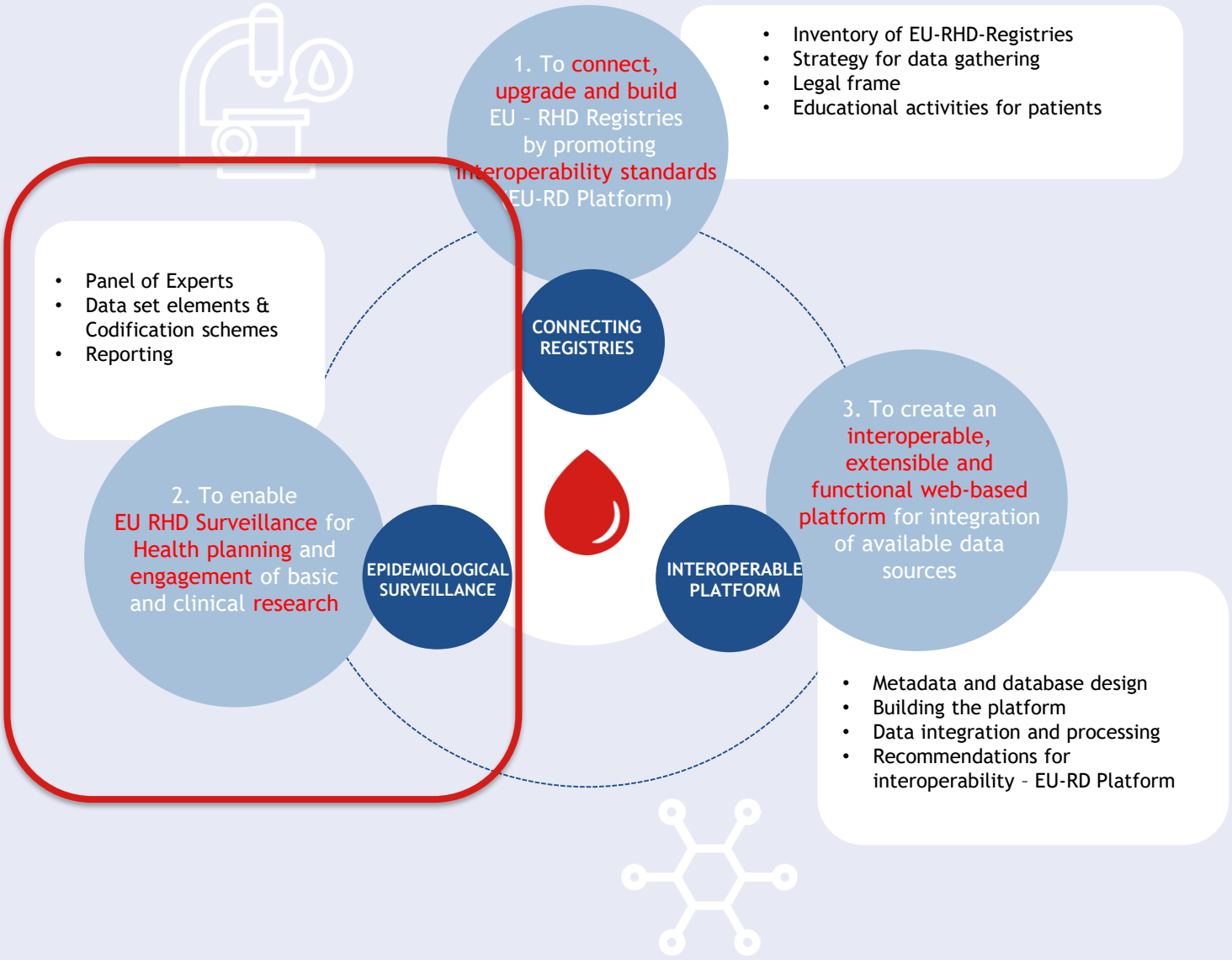


All Videos on **ERN-EuroBloodNet Educational Channel**

Technical Support: ERN-EuroBloodNet Coordination Team

ENROL

WP 5 Facilitating epidemiological surveillance, research and access to new treatments for RHD



WP 5: Facilitating epidemiological and clinical surveillance

OBJECTIVE Comparable data on RHD at the EU level

Epidemiological and clinical surveillance

Promotion of basic and clinical research

RESEARCH QUESTIONS?

- Population **frequency** of each RHD disease group and disease **survival**?
- Diagnosis delay?
- Attractiveness of Rare Disease centres in the health professionals community and the care pathway?
- Method used for diagnosis ?
- Samples for research/clinical trials ?
- Disease severity ? Stratification of patients based Clinical manifestations and Treatments
- Use of specific treatments and possibility to include patients for research/clinical trials?

An extended panel of experts will be established
including different groups of expertise according to RHDs disease grouping

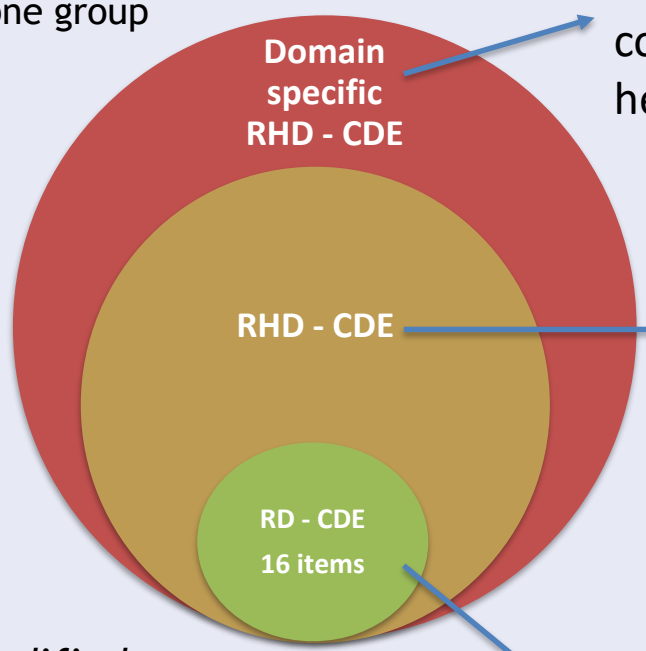
ENROL

WP 5: Facilitating epidemiological and clinical surveillance

HOW? Implement a **protocol for collection and processing of data** on RHDs

Rare haematological disease:

- 7 subnetworks / 13 domains / 58 disease groups (RHD-DG)
- Any RHD is covered by one group
- Each RHD is only covered by only one group



Domain specific expert committees including health professionals and ePAGs

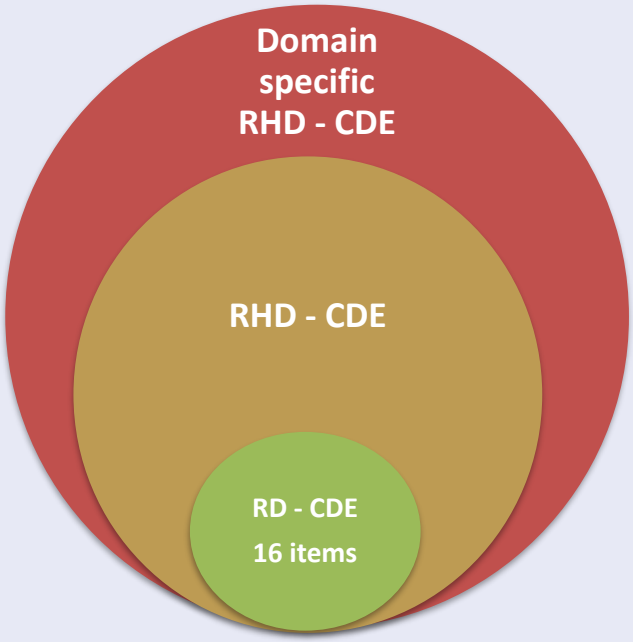
Patients' stratification according to severity and treatment options
Data dictionary for rare cancer registries (collaboration between ERNs+EJP-RD)

European common data set

*All Data elements need to be codified through existing standards to ensure interoperability - **Colab. With WP6***

ENROL

WP 5: Facilitating epidemiological and clinical surveillance



→ **Codification schemes**

- ✓ Definition of diseases (e.g. ICD-10 or ICD-11),
- ✓ Clinical trials (e.g. SNOMED),
- ✓ Observed phenotypes (e.g. HPO),
- ✓ Genes and variations (e.g. OMIM, HGNC, ClinVar and HGVS).

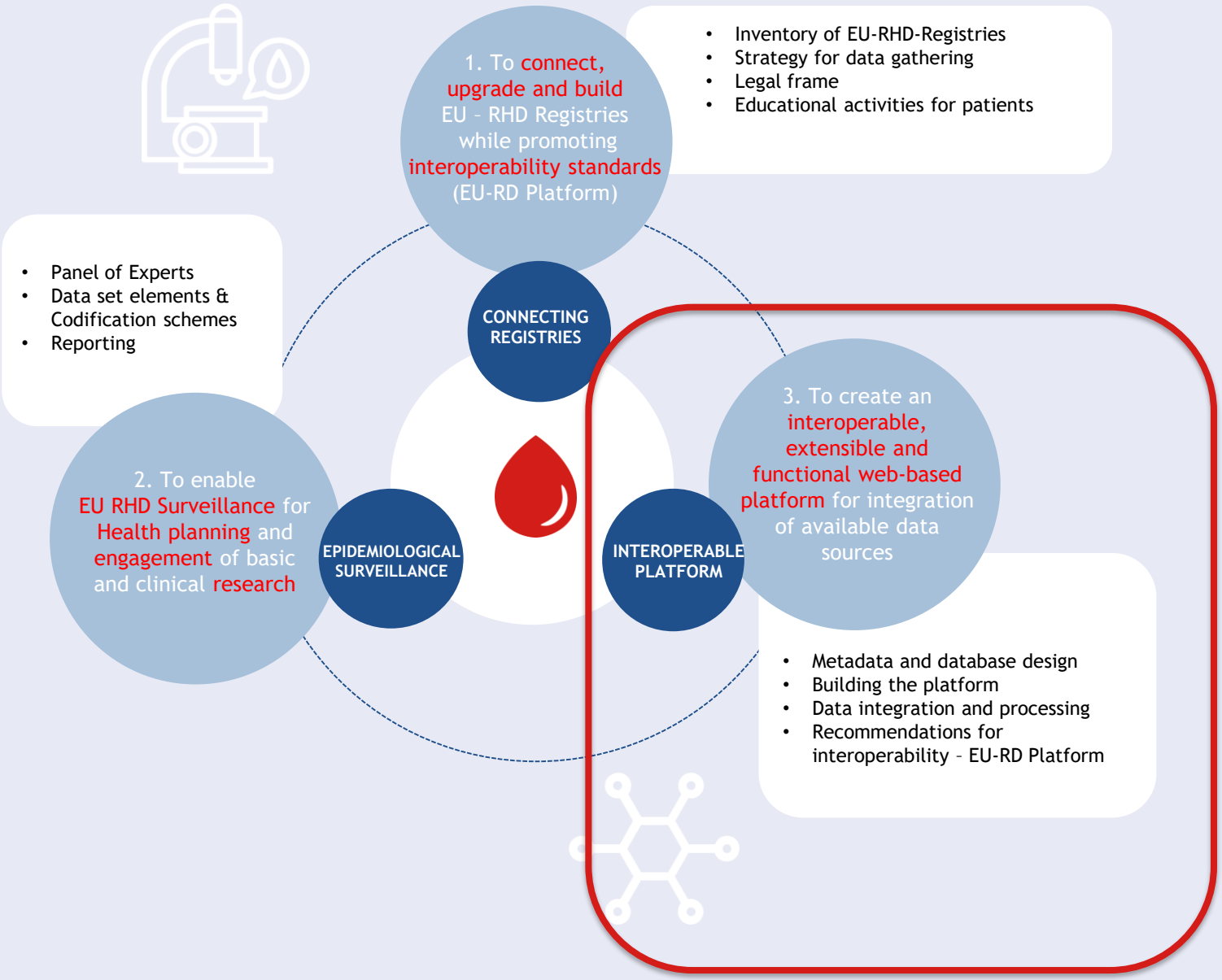
→ **Disparities and gaps between RHDs**

Annual reports

- ✓ Number of registries and patients enrolled by disease / group of diseases.
- ○ Policy reports addressing needs at the European and National level for better allocation of resources
- ○ Peer-review publications

ENROL

WP 6 Setting-up ENROL's Platform in line with the EU-RD Platform



WP6 – ENROL platform development: overall approach

Scope: To create an interoperable, extensible and functional web-based platform, which will enable entering and integration of certified patient data from available sources.

Data description & database design

- Codification
- Metadata description

Platform development

- Pseudonymisation
- Access control
- Encryption
- Visualisation
- Web services

Data collection & integration

- Standardisation of data transfer
- Link with ERDRI

WP6 – Data description and database design

Data description & database design → Platform development → Data collection & integration

In collaboration with WP5

Codification using:

- ✓ Definition of diseases (ICD-10, ORDO)
- ✓ Phenotypes & clinical terms (HPO, SNOMED)
- ✓ Genes and variations (OMIM, ClinVar, HGVS)

Source: https://xkcd.com/927/

Metadata description:

- ✓ Description of data and their interaction (ER model)
- ✓ Linked to ERDRI.mdr

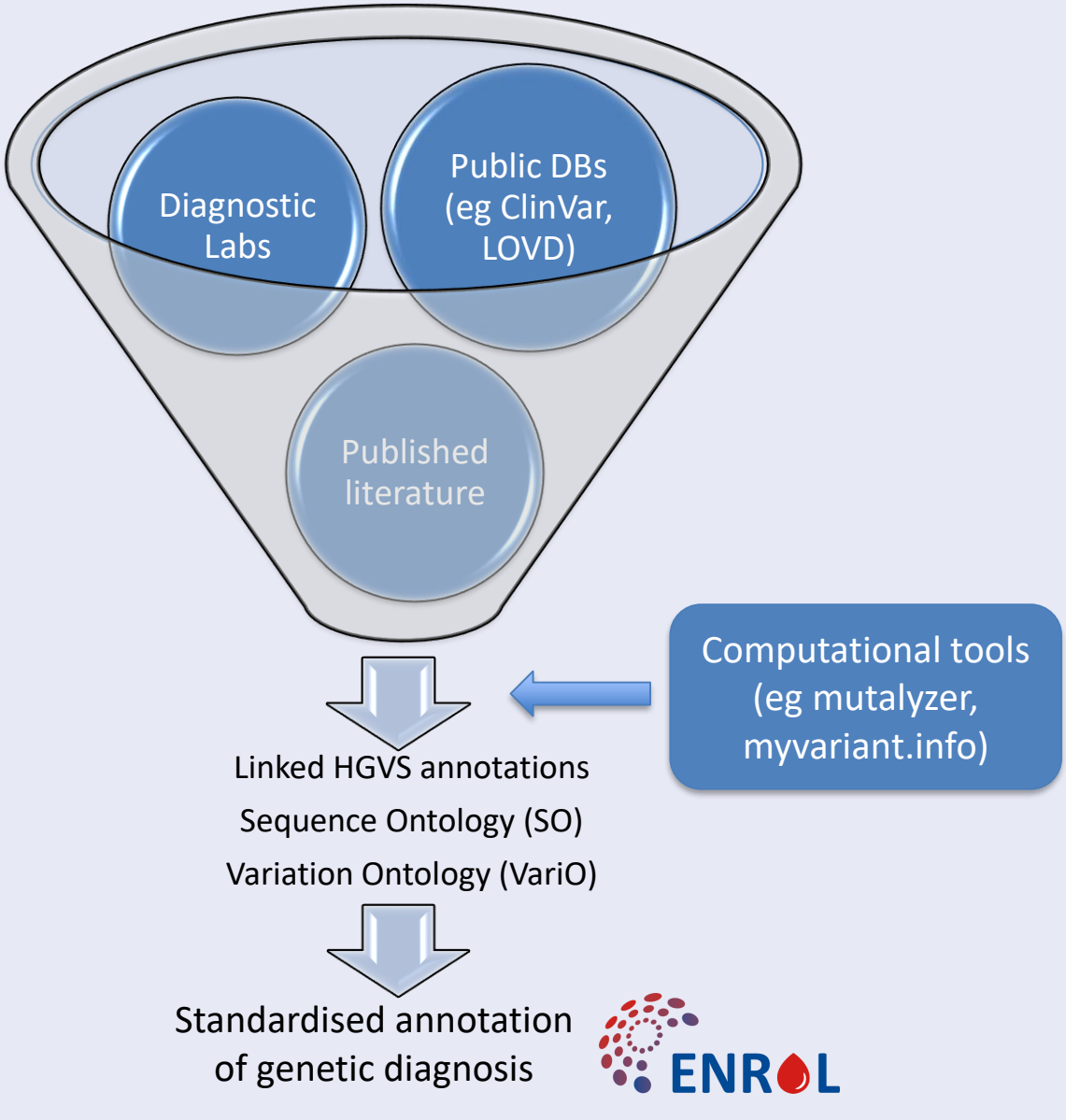
Release of recommendations on codification schemes for RHD

ENROL

WP6 – Standardisation and interoperability of genetic diagnosis

Problem:

- Multiple representations of identical variant: different HGVS names, non-standardised common names etc.
- Adherence to the HGVS nomenclature can be laborious for diagnostic labs
- Highlighted as a common problem for different ERNs



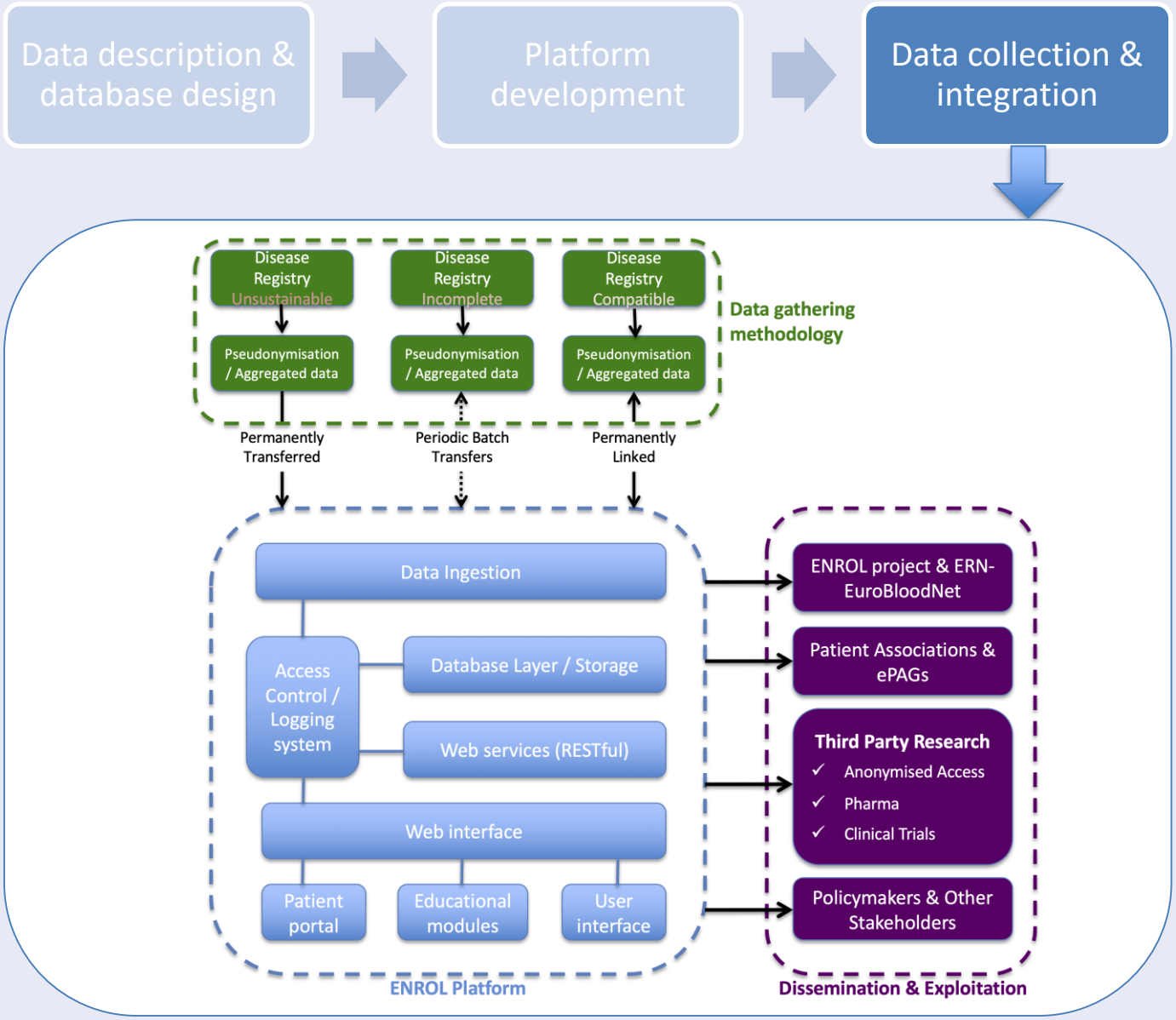
ENROL

WP6 – Platform development

- ✓ Pseudonymisation: EUPID, recommended by the ERDRI
- ✓ Access-control lists (ACLs): granular access granular access to different information depending on the user credentials and the consent provided by the patient (e.g. Data Manager/Curator, Clinician, Nurse, Patient)
- ✓ Encryption: Sensitive data will be encrypted
- ✓ Visualisation: user-friendly presentation of collected data using graphs and infographics, e.g. using javascript tools such as HighCharts and plotly
- ✓ Web services: REST interface for exchanged of anonymised data

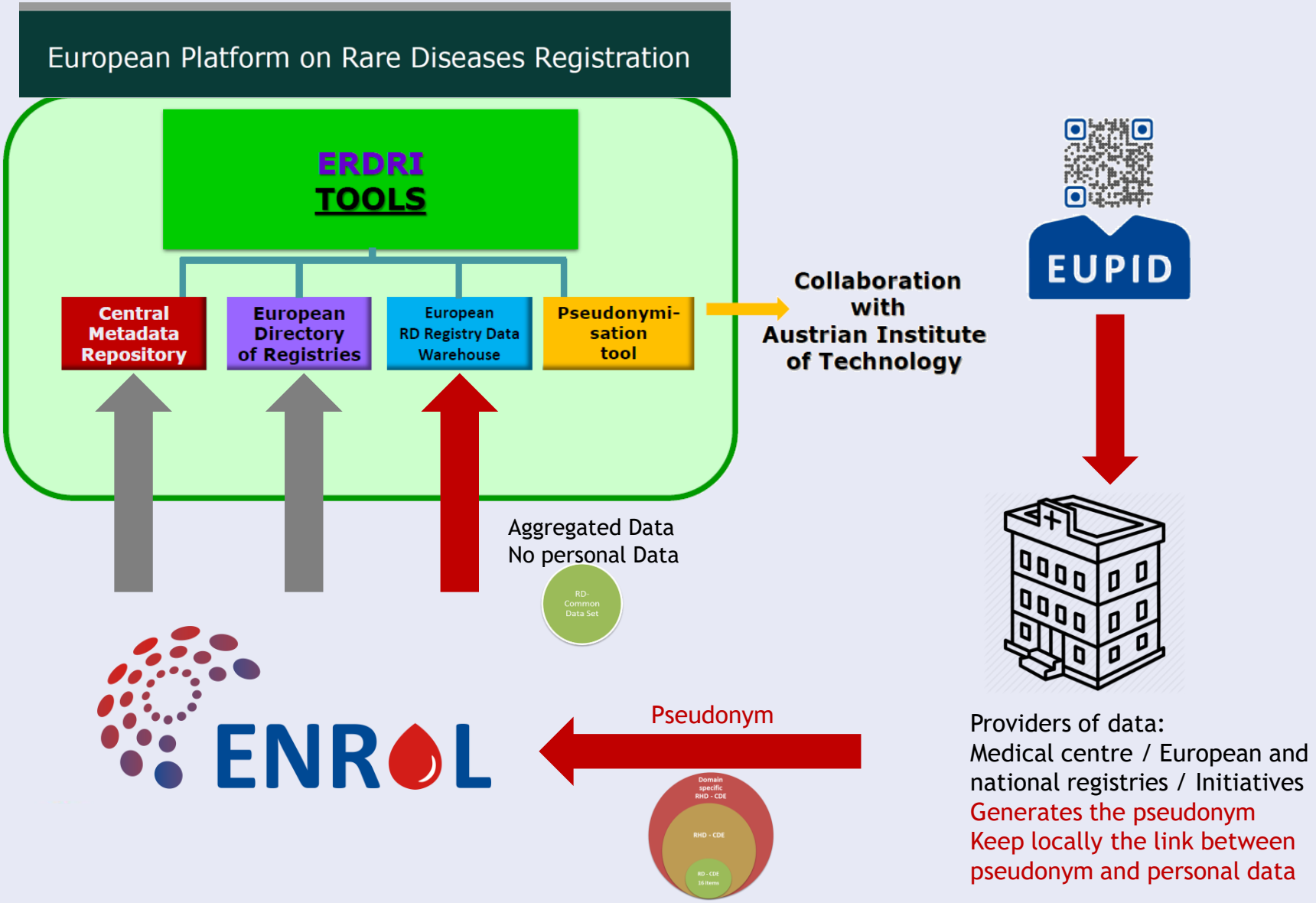
ENROL

WP6 – Data collection and integration



How data will be integrated from the different sources

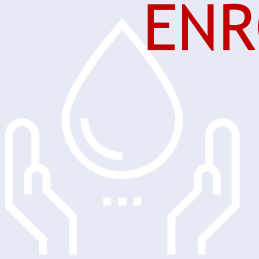
WP6 – How ENROL will contribute to the EU RD Platform



The European Rare Blood Disorders Platform

Kick off meeting 2nd July 2020

ENROL Governance and stakeholders involvement



European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

Governance and stakeholders involvement – WP4

How to ensure a legal and secure sharing and processing of data?

ENROL's Policy and Legal and ethical documents for regulating the legal actors and the sharing of data among the different stakeholders in agreement with the General Data Protection Regulation

Providers of data
- Hospitals
- Registries
- Networks

Steering and Data Access Committee

- Coordinators
- Domain specific Experts Committees & EBN Coordinators on Research and Guidelines
- ePAGs
- Legal and Ethical experts

Users of data
- Hospitals
- Researchers
- Pat. Assoc.
- Industry
- Policy makers

Involvement of stakeholders & Long-term Sustainability

ENROL

European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

Steering and Data Access Committee (SDAC)

- To define ENROL's Policy for data sharing
- To define domain specific CDE and Research questions
- Formal collaborations of ENROL with external organizations and sponsors
- Ensures ENROL makes good use of assets;
  - Approve aggregated figures to be publically published by ENROL
  - Approve application forms from users of data
- Rules for publication

Coordination team

- To define ENROL's global strategy
- To collaborate with the EU – RD – Platform and ERNs WG on Registries & EJP-RD
- To develop the IT solution with adequate safeguards for secure data exchanging
- Data processing of assets for protocols / application forms approved by SDAC

ENROL

Legal and Ethical issues – WP4

EUPID

1. Informed Consent (Model)
2. Transfer agreement A

ENROL Coordinators
Maria del Mar Mañú Pereira – HUVH/VHIR
Béatrice Gulbis - ERASME
Marina Kleanthous – CING
Pierre Fenaux – AP-HP

3. Consortium agreement

4.a App. form for data request
4.b Transfer agreement B

Steering & Data Access Committe

Informed consent

- Processing / Re-use in other projects / Re-contacted

Transfer agreement

- Data providers: regulating processor role, responsibilities and rights

Consortium agreement

- Joint Controller: roles, rights and responsibilities
- Data ownership and Intellectual property

Data request form & Transfer agreement

- Users of data: regulating terms and conditions for use of data

Public registry of Users of Data

- Including type of data shared

ENROL

Legal and Ethical issues – WP4

General Data Protection Regulation

✓ Personal Data definition:

- **Data containing any identifiers** that make possible to find out who the subjects are (including **codified data and pseudonymized data**).
- **Data and/or factors that in tandem allow the re-identification of data subject**, although by indirect means.
  - Specially relevant for ultra-rare diseases

Question 1. Can Personal Data be shared and re-used? YES, if done with the appropriate safeguards.

✓ Share and re-use of Personal Data (for both clinical practice and research):

- **Informed consent is required for sharing Personal Data. However, Art89 GDPR includes the possibility that National legal provisions regulate the need for informed consent for research.**

Question 2. A specific informed consent for ENROL is mandatory? Yes, in principle, but national legal provisions may avoid it, with appropiate safeguards.

ENROL

Legal and Ethical issues – WP4

General Data Protection Regulation

✓ Safeguards:

1) Pseudonymization tool: EUPID
   - avoid creating a transparent universal patient ID
   - preserve the possibility for re-identification by a trusted third party

2) Legal Contract (Transfer agreement B) with users of data including clauses aiming to protect data confidentiality:
   - Not to attemp to re-identify the patient
   - Not to attempt to directly contact the patient
   - Not to share the research data with non authorized persons or external Institutions

3) Steering and Data access committee: Ensures good use of assets

4) Registry of Users of data, data shared, authorized persons

5) IT platform security measures

ENROL

The European Rare Blood Disorders Platform

Kick off meeting 2nd July 2020

Involvement of Patient Representatives/ ePAG Advocates in ENROL

Ariane Weinman
EURORDIS – Rare Diseases Europe

ePAG Advocates and EURORDIS' involvement in ENROL

- The European Patient Advocacy Group (ePAG) Advocates are nominated to represent their disease area in the ERN EuroBloodNet as well as the interests of the wider patient community affected by rare hematological diseases.

- They are the voice of the patients in the EuroBloodNet Board of the Network.

- EURORDIS - Rare Diseases Europe ensures a transversal coordination.

https://eurobloodnet.eu/patientsadvocacy/epag/

ENROL

ePAG Advocates and EURORDIS' involvement in ENROL

Sub-network	ePAG name	Function	Organisation
Myeloid malignancies	Sophie Wintrich	Chief Executive Trustee & Director Patient Liaison	MDS UK Patient Support Group & MDS Alliance
Myeloid malignancies	Jan Geissler	Co-founder as well as co-founder of CML Advocates Network	Leukemia Patient Advocates Foundation
Lymphoid malignancies	Pierre Aumont	Board member SILLC and Vice-President CLLAN	Association de Soutien et d'Information à la Leucémie Lymphoïde Chronique et la maladie de Waldenström (SILLC) & CLL Advocates Network (CLLAN)
Lymphoid malignancies	Ananda Plate	Chief Executive Officer	Myeloma Patients Europe (MPE)

https://eurobloodnet.eu/patientsadvocacy/epag/

ENROL

ePAG Advocates and EURORDIS' involvement in ENROL

Sub-network	ePAG name	Function	Organisation
Rare Red blood cell defects	Angelo Loris Brunetta	Board member	Thalassaemia International Federation (TIF)
Bone marrow failure and hematopoietic disorders	Maria Piggin	Founder and Trustee	PNH Support
Rare bleeding-coagulation disorders and related diseases	Baiba Ziemele	Member of EHC (and President of Latvia Hemophilia Society)	European Haemophilia Consortium (EHC)
Hemochromatosis and other rare genetic disorders of iron metabolism and heme synthesis	Dag Erling Stakvik	Member of the Executive Committee / Treasurer	European Federation of Associations of Patients with Haemochromatosis (EFAPH)

https://eurobloodnet.eu/patientsadvocacy/epag/

ENROL

ePAG Advocates and EURORDIS' involvement in ENROL

- **Why Rare Disease Registries matter to patients?**

"Rare Disease Patient Registries (RDPR) […] constitute key instruments for increasing knowledge on rare diseases (RD) by pooling adequate thresholds of data for fundamental, clinical research, and epidemiological research. RDPR are vital to the assessment of the feasibility, planning and design of clinical trials and facilitate the enrolment of patients for real-life post-marketing observational studies.

It has been demonstrated that RDPR are a major determinant for successful translational research in the field of RD. **Where well-implemented registries and active patient organizations exist, the likelihood for developing a treatment for the disease in question is increased.**"

Quoted from: *The Voice of Rare Disease Patients: Experiences and Expectations of over 3,000 Patients on Rare Disease Patient Registries in Europe (EPIRARE EU Project, 2011-2014)*

ENROL

ePAG Advocates and EURORDIS' involvement in ENROL

- **Patient organisations / ePAGs can bring a significant expertise in the development of patient registries**
- ePAG Advocates represent European federation of patients in RHD who all have a significant expertise in the development of patient/disease registries and have contributed to European policy recommendations
- EURORDIS:
  - Published the experiences and expectations of over 3,000 patients on RD patient registries in the frame of the EU-funded project EPIRARE (2011-2013)
  - Contributed to the EUCERD recommendations on RD patient registration and data collection
  - Active partner of the European Joint Programme for RDs, in which patient registries is an important component

ENROL

ePAG Advocates and EURORDIS' involvement in ENROL

- **Specific role of ePAGs & additional patient representatives not yet represented in ENROL:**
  - Contributing to the definition of specific core data set for their disease area, teaming up with the clinicians;
  - Ensuring the good use of data set:
  - Defining informed consent;
  - Contributing to the development of the educational programme

EURORDIS will provide its support throughout the project.

CEOs Involment Vall d'Hebron

Yolima Cossio Gil

Director Information and Management Systems

PROVIDERS POINT OF VIEW

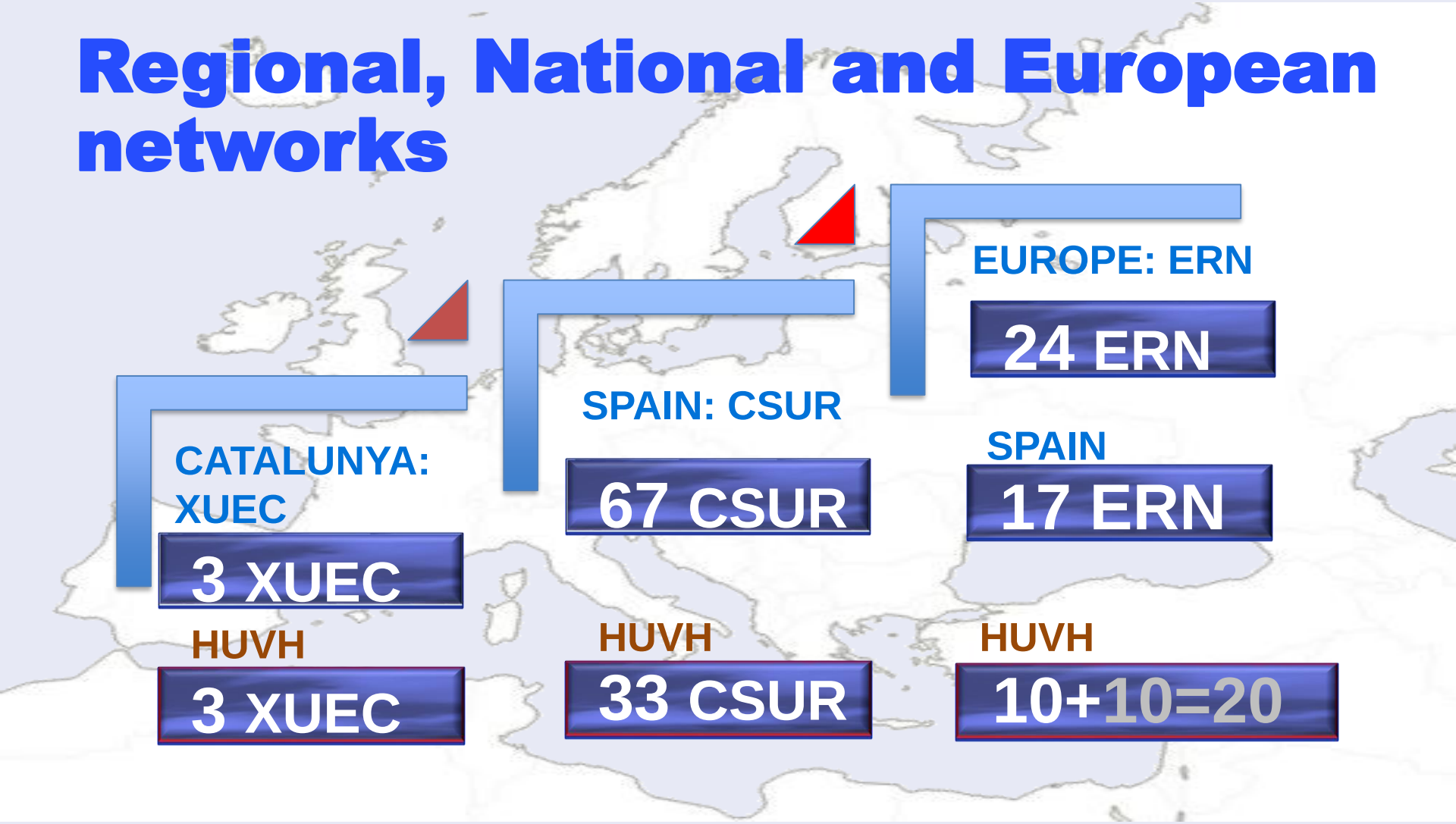
ENROL

Vall d'Hebron Campus
A glance

- **9,000** professionals
- **1.2 million people seen (adults and children)**
- **1,100** beds
- **80** research groups
- **2,000** researchers
- **1200** clinical trials
- Training in **47** specialisations and in biomedical research
- **531** residents
- **22** buildings

ENROL

Regional, National and European networks



Strategy

- ✓ Commitment with the rare diseases and excellence
- ✓ Provide expertise and best care for our patients
- ✓ **Data is a driving force to improve healthcare and knowledge**

ENROL

Challenges and Opportunities

Challenges

Detection and tracking

- Coding system

Sustainability

- Individual registers: burden the professional
- Multiple registration (EU, National, Regional, Hospital)
- Data protection

ENROL

Challenges

Generation of knowledge

- Limited data
- Best practices/ Clinical outcomes?

Healthcare planning

- Real needs
- Costs
- forecasting

ENROL

Opportunities

- Standardized classification for the EU (**Universal coding**)
- Integrate the registres with the electronical health record **EHR**
- Natural language processing → artificial intelligence
- **Automated extraction** clinical data, allocated resources.
- Harmonized data for **interoperability.**

ENROL

Key points

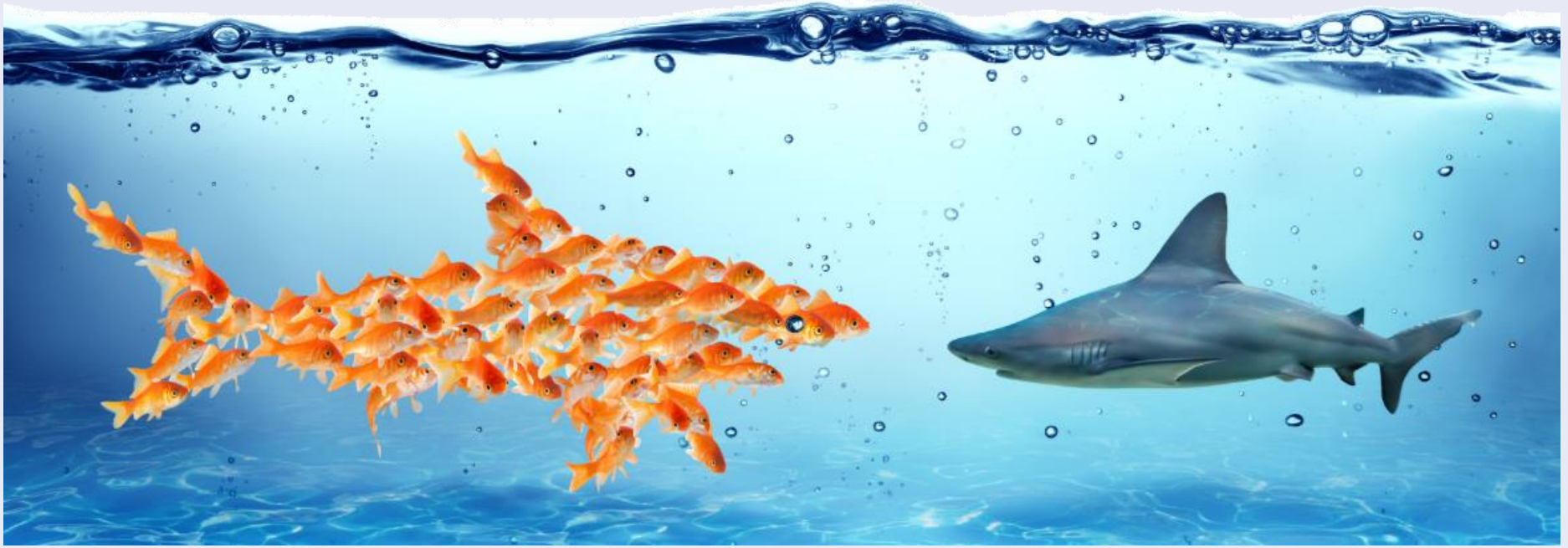
- ✓ Data and RD as part of the hospital strategy
- ✓ Commitment of the CEOs
- ✓ Adapt the EHR and invest in new technology and data innovation

ENROL

Thanks

ENROL

Working together is better than alone



ENROL