



European Rare Blood
Disorders Platform

European Rare Blood Disorders Platform

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Learning objectives of the webinar

Main objective: The challenge of fragmentation of data in rare haematological disorders and how ENROL is addressing it at the EU level

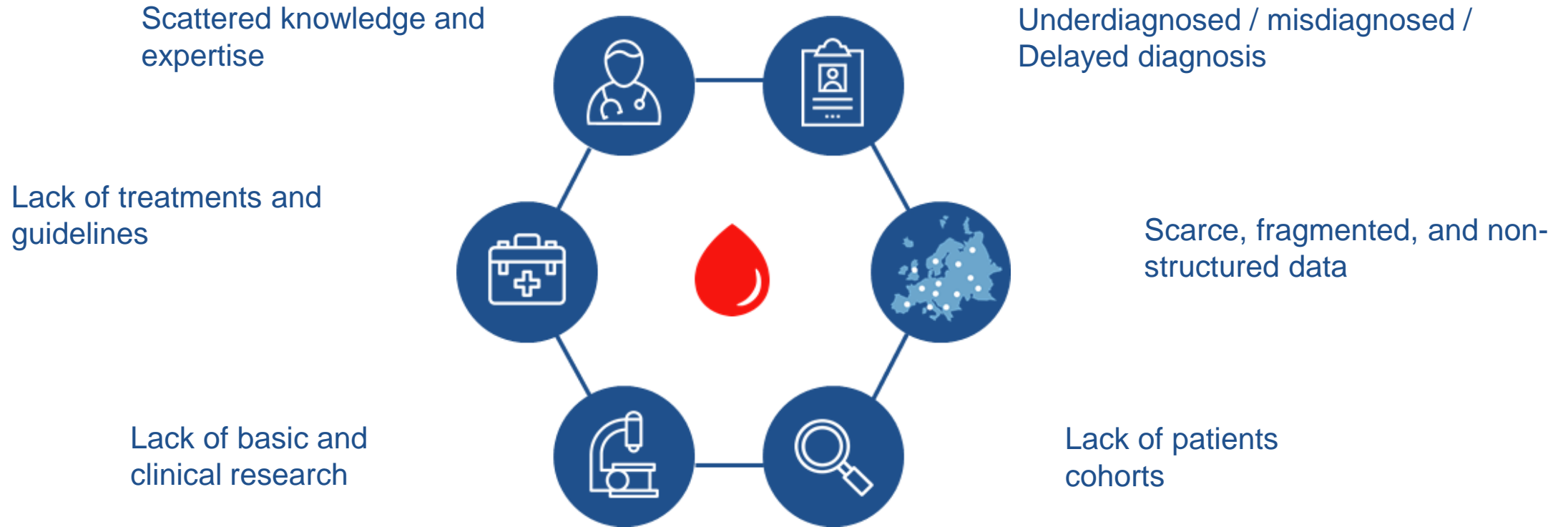
Addressed questions

- Data fragmentation in rare hematological disorders
- The EU context on patients' registries and ENROL Registry
- What does FAIR (Findable, accessible, interoperable and re-usable) mean
- ENROL strategy networking with existing patients' registries in RHD



The challenge of data fragmentation in RHD

Data fragmentation in Rare Hematological Diseases



Data fragmentation in Rare Hematological Diseases

Scattered knowledge and expertise

Underdiagnosed/misdiagnosed / Delayed diagnosis

Lack of treatments and guidelines

Scarce, fragmented, and non-structured data

Lack of basic and clinical research

Lack of patients cohorts



EU STRATEGY FOR PATIENTS REGISTRIES

EU Strategy for patients' registries

EU Platform on Rare Disease Registration (EU RD Platform)

Searchable, findable rare disease registry data



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

- ✓ Common data elements (16)
- ✓ **Pseudonymization tool** – GDPR Compliant



EU Strategy for patients' registries

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General Data Protection Regulation (GDPR)

✓ Personal Data:

- Data containing any identifiers that make possible to find out who the subjects are, including **codes or pseudonyms**.
- Data and/or factors that **in tandem allow the re-identification** of data subject, **although by indirect means**.

✓ Legal basis for Sharing of Personal Data (clinical practice and research):

- Informed consent (But not only! And not always!)
- Have to be done with the appropriate safeguards ----- **pseudonymisation tool**

The different stages of data de-identification

Personal data
Subject to GDPR

Not personal data
Not subject to GDPR



Direct identifiable data

Pseudonymous data

De-identified data

Anonymous data

Direct identifiers:
Claire Diot-Lefebvre
Passport Nb: ...
Address: ...

+ Clinical Data

Pseudonym: 5L7T replaces
direct identifiers

5L7T
+ Clinical Data

Remove pseudonym

Someone
+ clinical data
among some...

You need extra information
to re-identify

Minimization of clinical data

Someone
+ clinical data among
many...

You cannot re-identify

The European context

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European Reference Networks registries

EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW-PREVALENCE AND COMPLEX DISEASES
Share. Care. Cure.



24 ERNs Central Registries:

- ✓ **Build**
- ✓ **Upgrade**
- ✓ **Link**

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



European Rare Blood Disorders Platform

European Rare Blood Disorders Platform

European Rare Blood Disorders Platform (ENROL)

ENROL has been conceived in the core of **ERN-EuroBloodNet** as an umbrella for: **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 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

Consortium



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ENROL is endorsed by the European Hematology Association



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Myeloma Patients
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MDS Alliance



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Lymphoma Coalition



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European Federation
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Jan Geissler,
Leukemia Patient
Advocates
Foundation



Pierre Aumont,
Ensemble Leucémie
Lymphomes Espoir &
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Jacqueline Dubow,
MDS Alliance and
Connaitre et
combattre les
myélodisplasies

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EU Platform on Rare Disease Registration (EU RD Platform)

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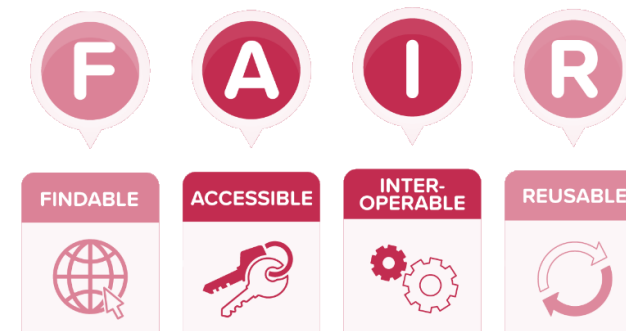
European Rare Blood Disorders Platform

ERICA & European Joint Program on Rare Diseases (EJP_RD)



24 ERNs Central Registries:

- ✓ Domain specific Common Data Elements
- ✓ Legal and Ethics issues
- ✓ FAIR Principles





What does FAIR Mean?

ENROL Directory of Registries in RHD

What does FAIR mean?

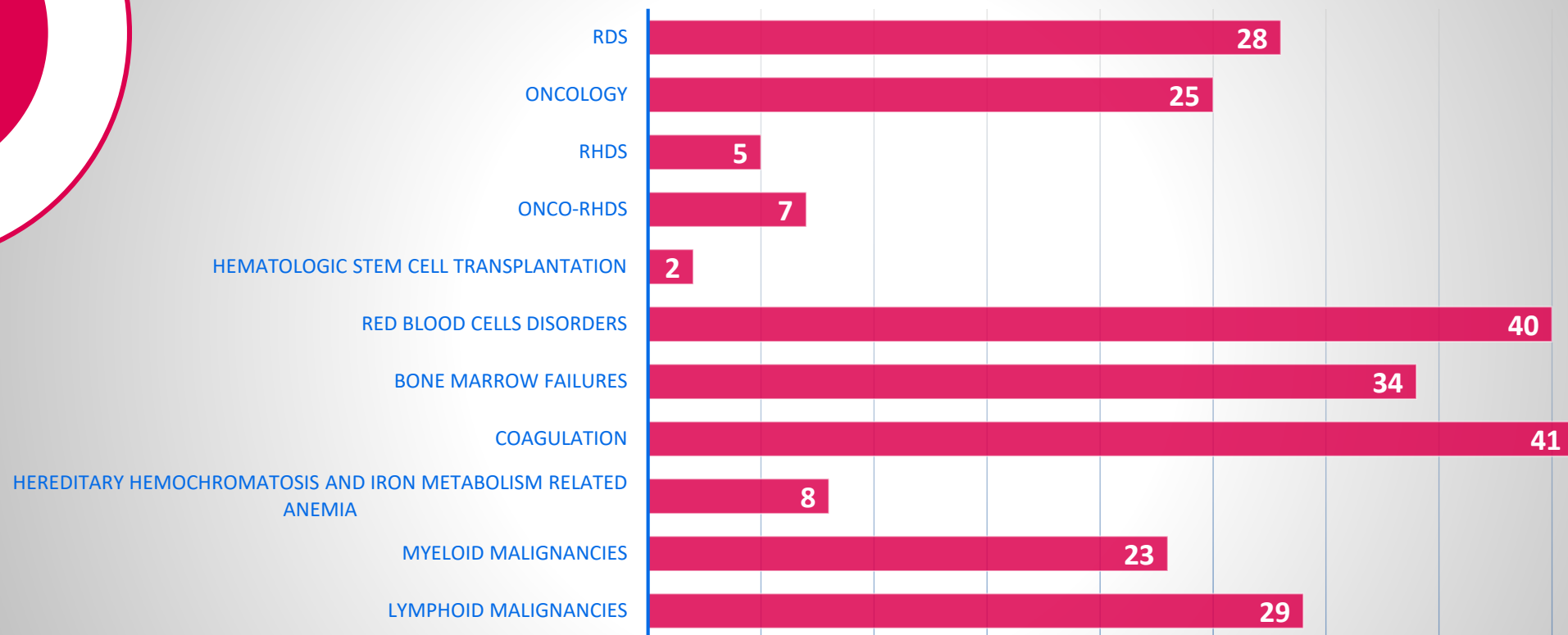


ENROL Directory of Registries in RHD

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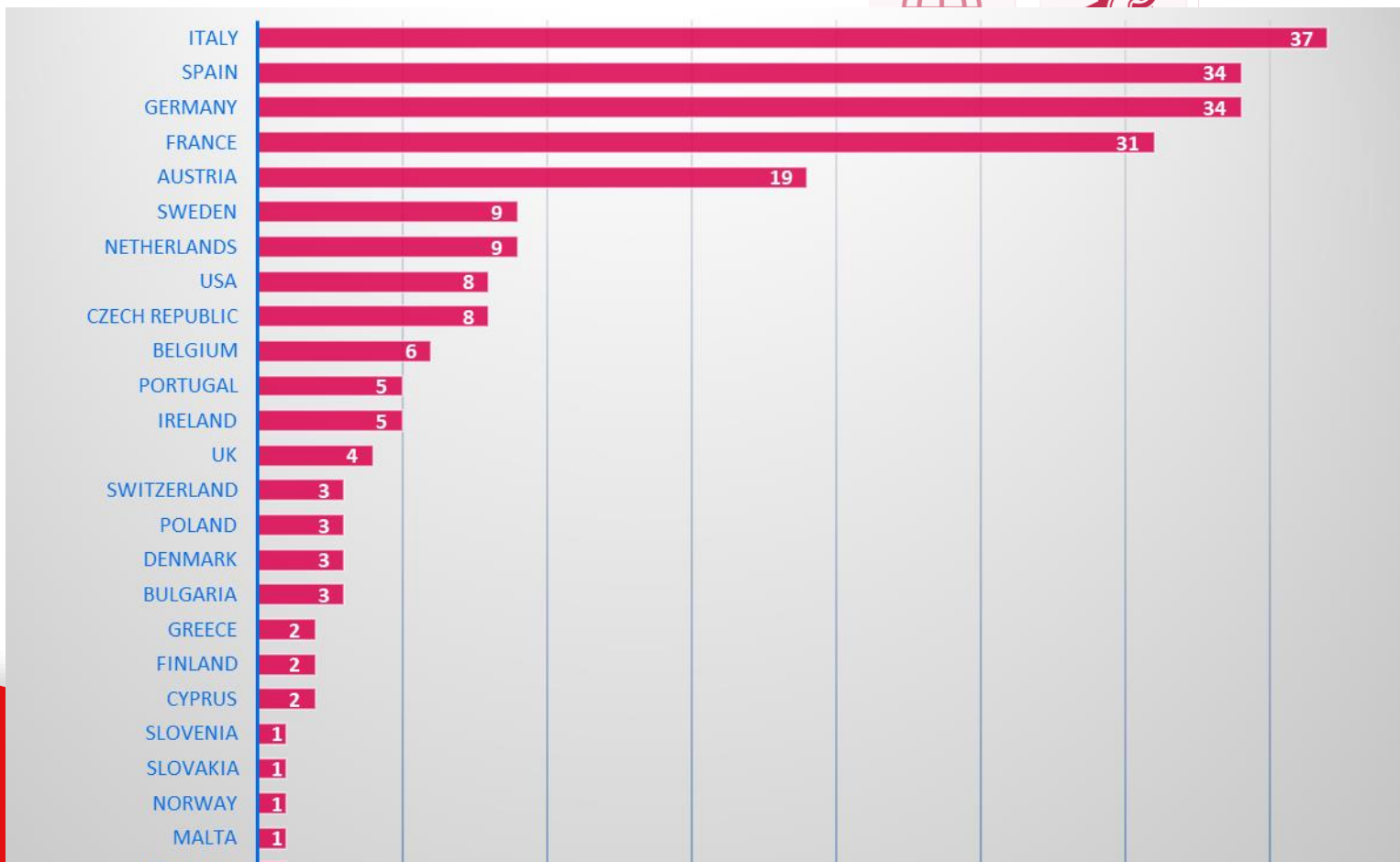
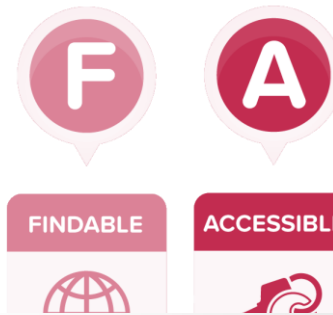


235
EU RHD
Registries



ENROL Directory of Registries in RHD

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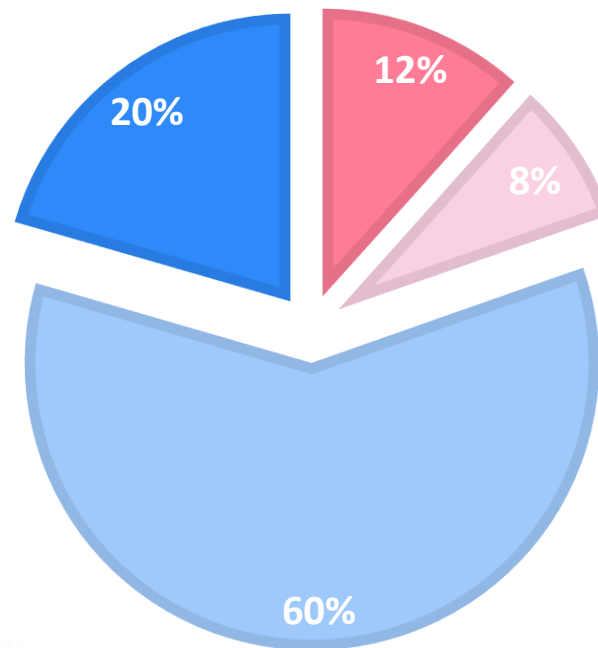


ENROL Directory of Registries in RHD

What does FAIR mean?



■ International ■ European ■ National ■ Regional



ENROL Directory of Registries in RHD

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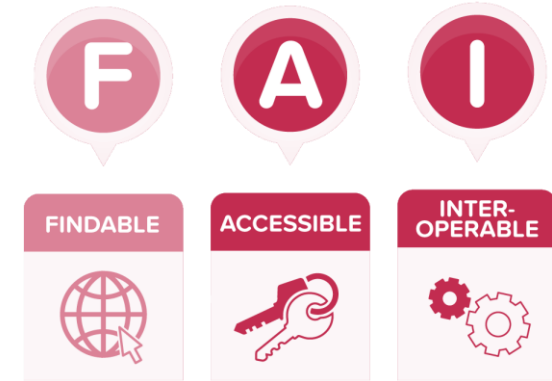


How many registries?
For which disorders?
Where they are?
Who is the curator/manager of the data (controller)?
What type of data (metadata)?
How can it be accessed?
By Whom?



ENROL Data standardization

What does FAIR mean?



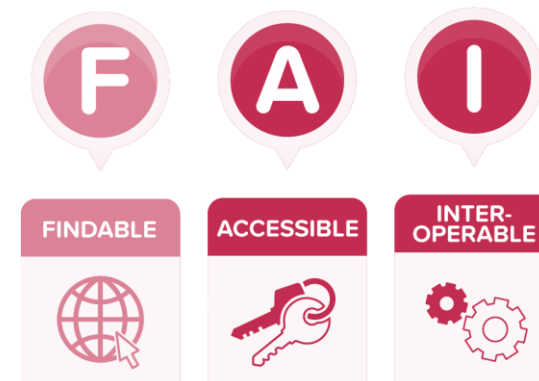
Comparable data on RHD at the EU level

- ✓ Epidemiological and clinical surveillance
- ✓ Promotion of basic and clinical research

- Number of patients affected by each RHD in EU-MS over time?
- Diagnosis delay? Methods used for diagnosis?
- Availability of Samples for research?
- Disease severity? Clinical manifestations and outcomes? Treatments?
- Possibility to include patients for research/clinical trials?



ENROL Data standardization



What does FAIR mean?

Research Q: Does the patient have anemia?

Element 1

Does the patient have anemia?

Yes / No

Element 2

Concentración de hemoglobina:
Número g/dL

Element 3

Does the patient have anemia?
Severe / Severe-Moderate/ Moderate /
Moderate- Mild / Mild / No

Element 4

Il paziente ha l'anemia?

Grave/moderato/lieve/

No

Element 5

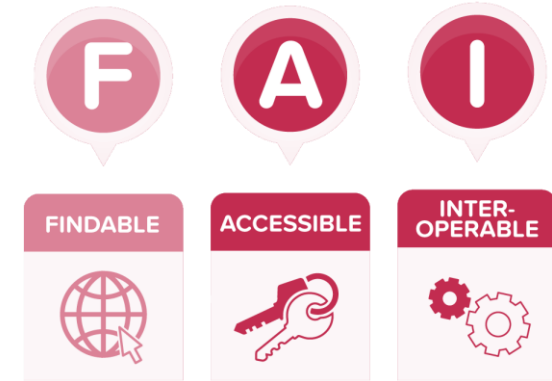
Concentration d'hémoglobine
Nombre mmol/L

Element 6

Concentration d'hémoglobine:
>120 g/L / 100-120 g/L / 80-100 g/L / <80 g/L



ENROL Data standardization



What does FAIR mean?

Research Q: Does the patient have anemia?

How the element is defined? Definition based on international recommendations

World health organization: blood hemoglobin (Hb) concentration <130 g/L (<13 g/dL) in adult males; Hb <120 g/L (<12 g/dL) in adult females.

✓ We also need to collect element: sex

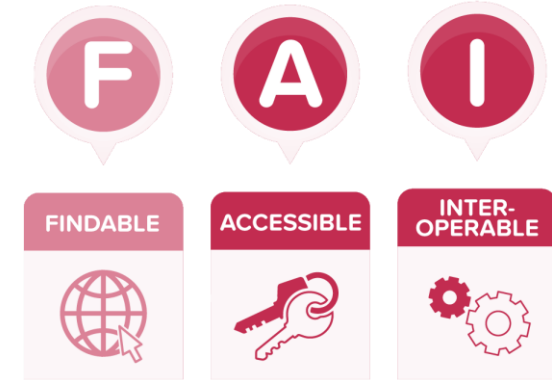
How the element is collected? Units based on international recommendations

**World health organization's recommendation is to use SI units for laboratory test, preparation of reagents, and reporting of the results.
SI Unit for Hb Concentration: g/L**

✓ Ranges (severe/moderate/mild) need to be also based on recommendations



ENROL Data standardization



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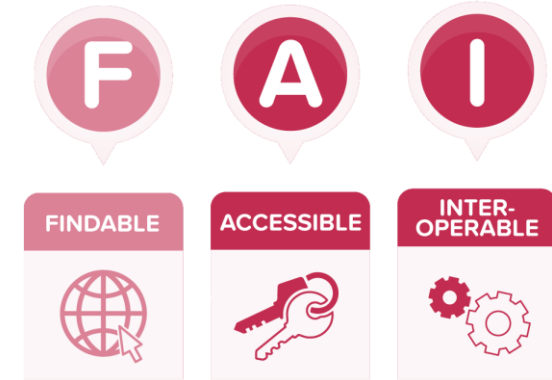


Clear...for Humans!!! But...What about machines?



ENROL Data standardization

What does FAIR mean?



Comparable data on RHD at the EU level

We need to pool data in a centralized repository for analysis

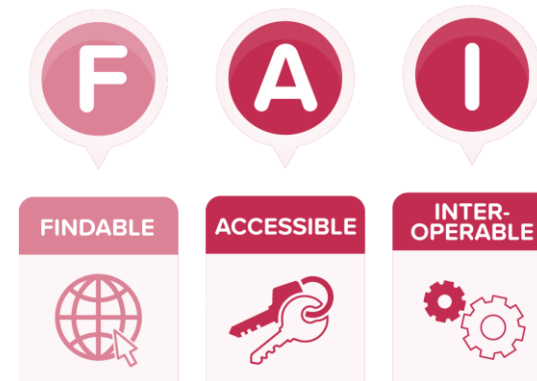
- ✓ **Centralized registries**

We need to analyse data at each local site and centralized the result

- ✓ **Federated registries**



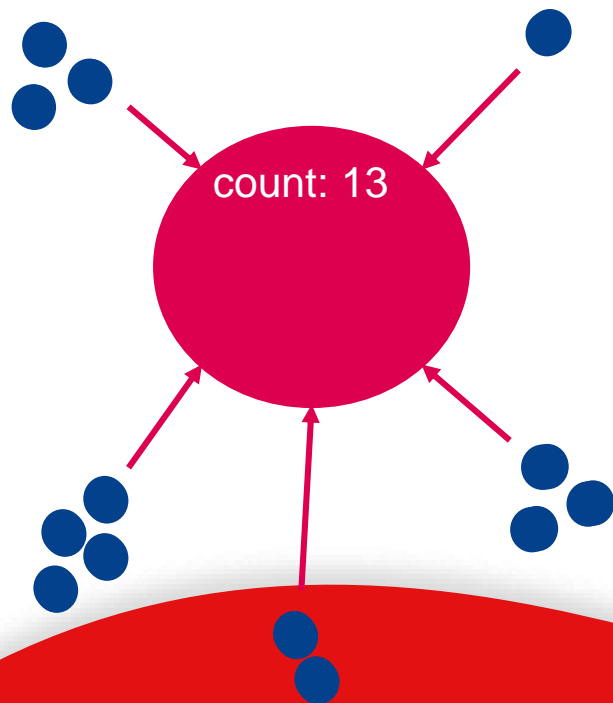
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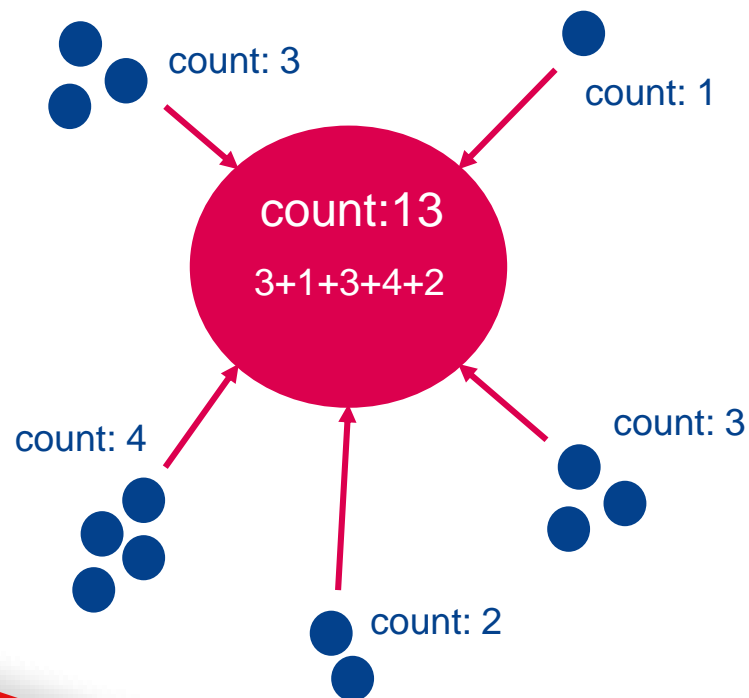
What does FAIR mean?

How many blue ballons we have?

✓ Centralized registries

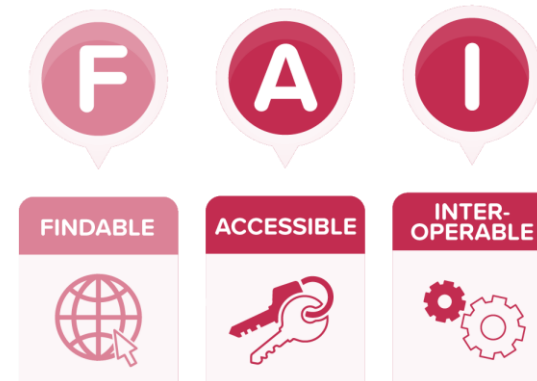


✓ Federated registries





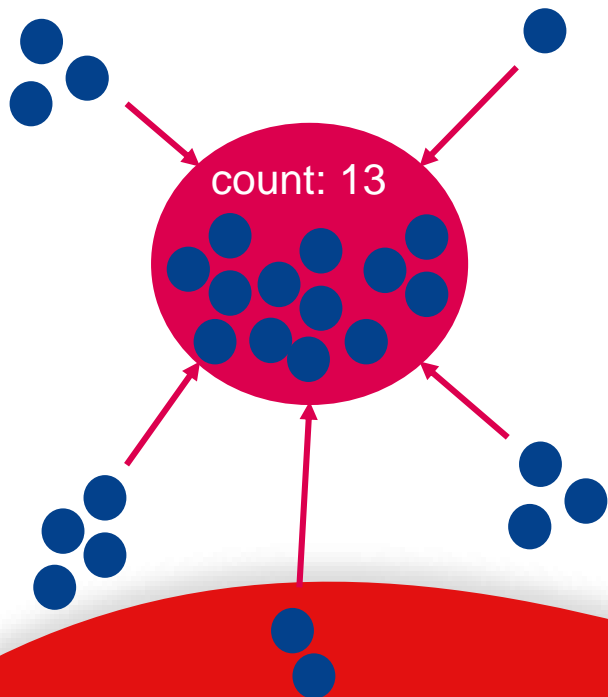
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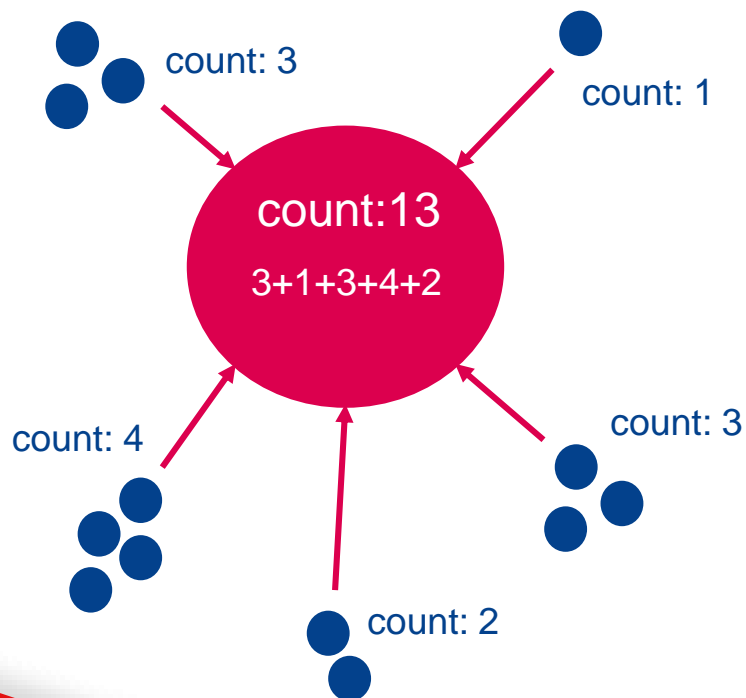
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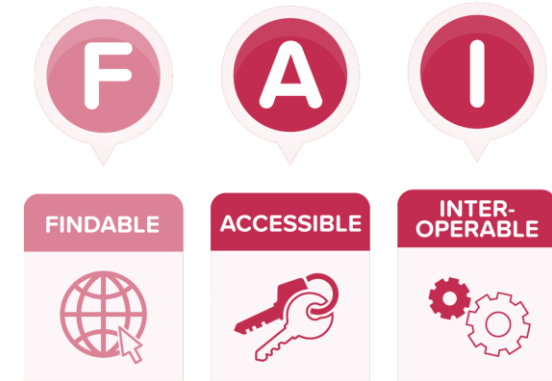
Challenges:

- Automatic data transfer
- Interoperability platforms
- Federated Platforms

Coding Systems!



ENROL Data standardization



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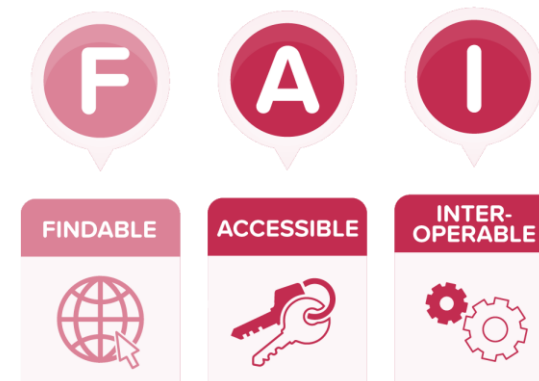
Comparable data on RHD at the EU level

Coding systems: assign codes to elements definitions and variables

- ✓ **Definition of diseases: Beta thalassaemia (umbrella)**
 - International classification of diseases ICD-9: 282.44 ICD-10: D56.1
 - ORPHANET classification for rare diseases: 848
 - OMIM classification for inheritance disorders:613985
 - SNOMED Nomenclature of medicine – clinical terms: 65959000
- ✓ **Phenotypes & clinical terms: anemia**
 - Human Phenotype Ontology (HPO): 0001903 + 44 terms
 - SNOMED: 191268006 + 41 terms for chronic anemia
- ✓ **Genes and variations:**
 - OMIM:613985
 - ClinVar: mutation
 - HGVS: mutation



ENROL Data standardization



What does FAIR mean?



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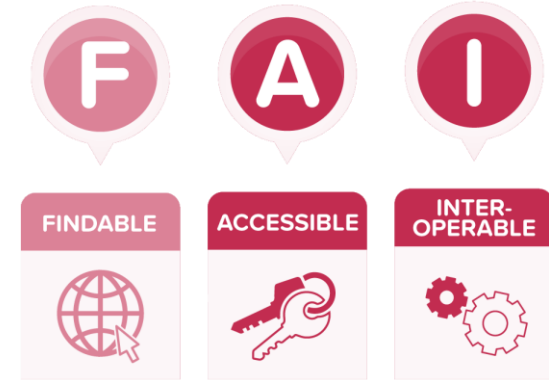
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Interoperability platforms based on common data models:

- FHIR (Fast Healthcare Interoperability Resources)
- OMOP Observational Medical Outcomes Partnership



ENROL Data standardization



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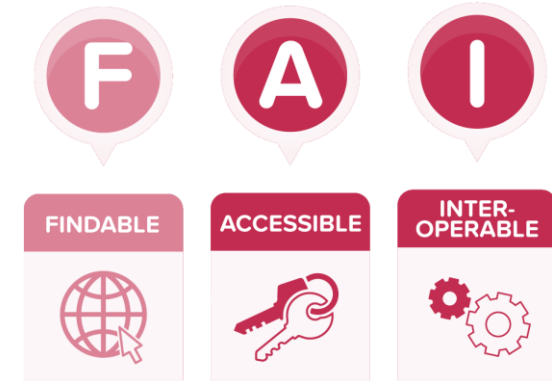
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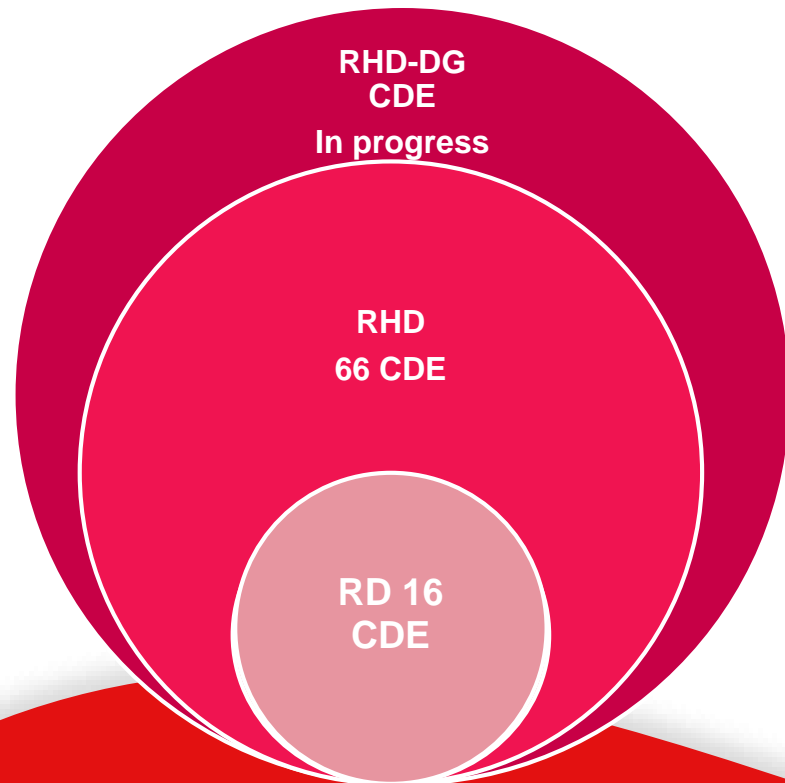
**Clear for Humans and machines!!!
(or more or less)**



ENROL Data standardization



What does FAIR mean?



- ✓ **RD CDE: 16 Common Data Elements on rare diseases from the EU-RD-Platform**
 - Date of birth, sex, diagnosis, survival,
- ✓ **RHD CDE: 66 Common Data Elements on Rare Hematological diseases**
 - Hematological Stem Cell Transplant, Blood transfusion, participation in clinical trials, laboratory tests, splenomegaly, treatments



ENROL Platform

What does FAIR mean?



Interoperable centralized web-based platform

It enables entering and integration of certified patient data from available sources

Data description & database design

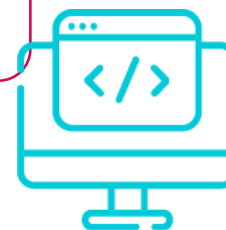
- Data elements
- Metadata description
- Codification

Platform development

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

Data collection & integration

- Standardisation of data transfer
- Link with EU-RD-Platform



EU RD PLATFORM

What does FAIR mean?

ENROL Data governance and flow

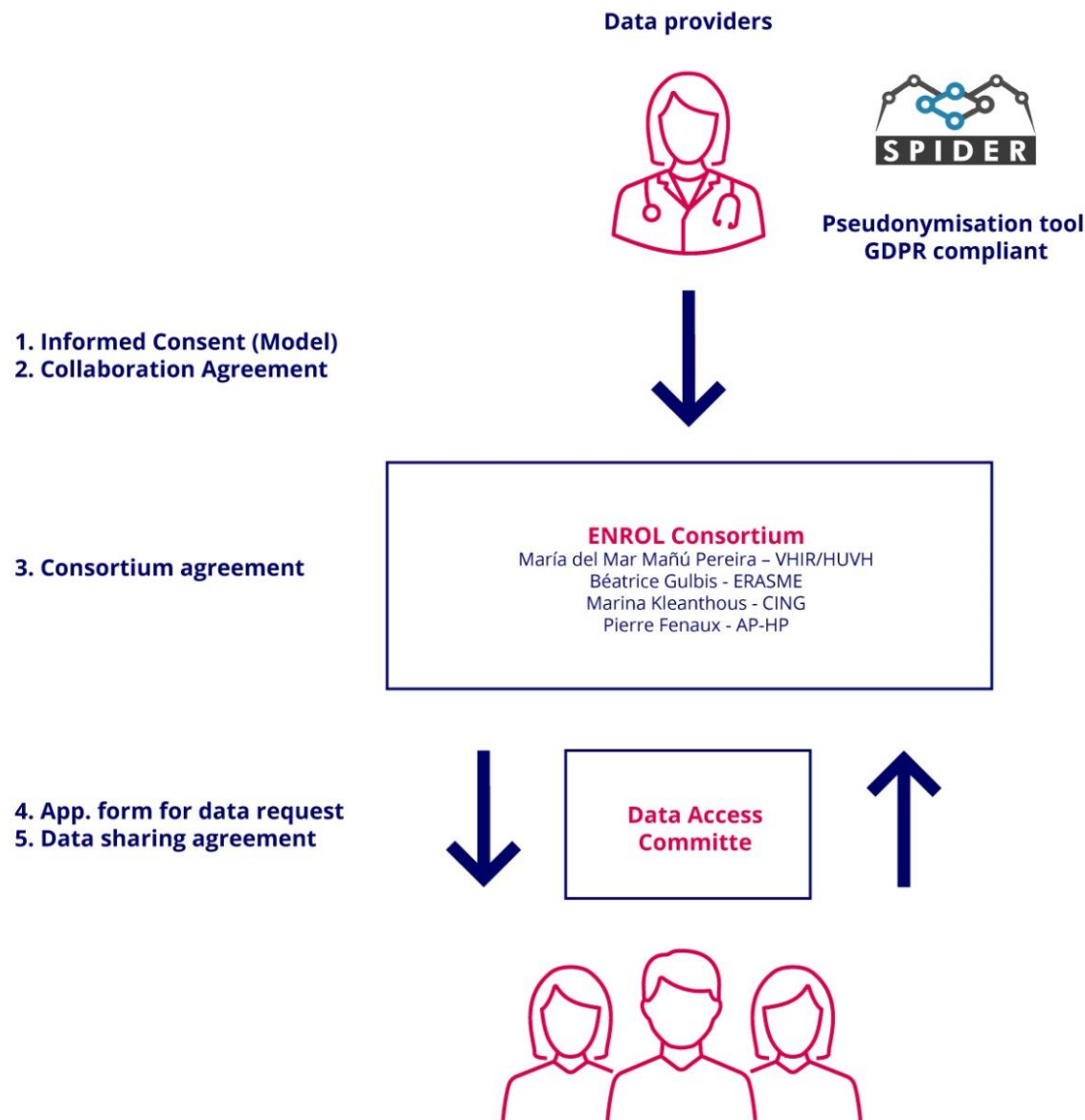


Steering and Data Access Committees



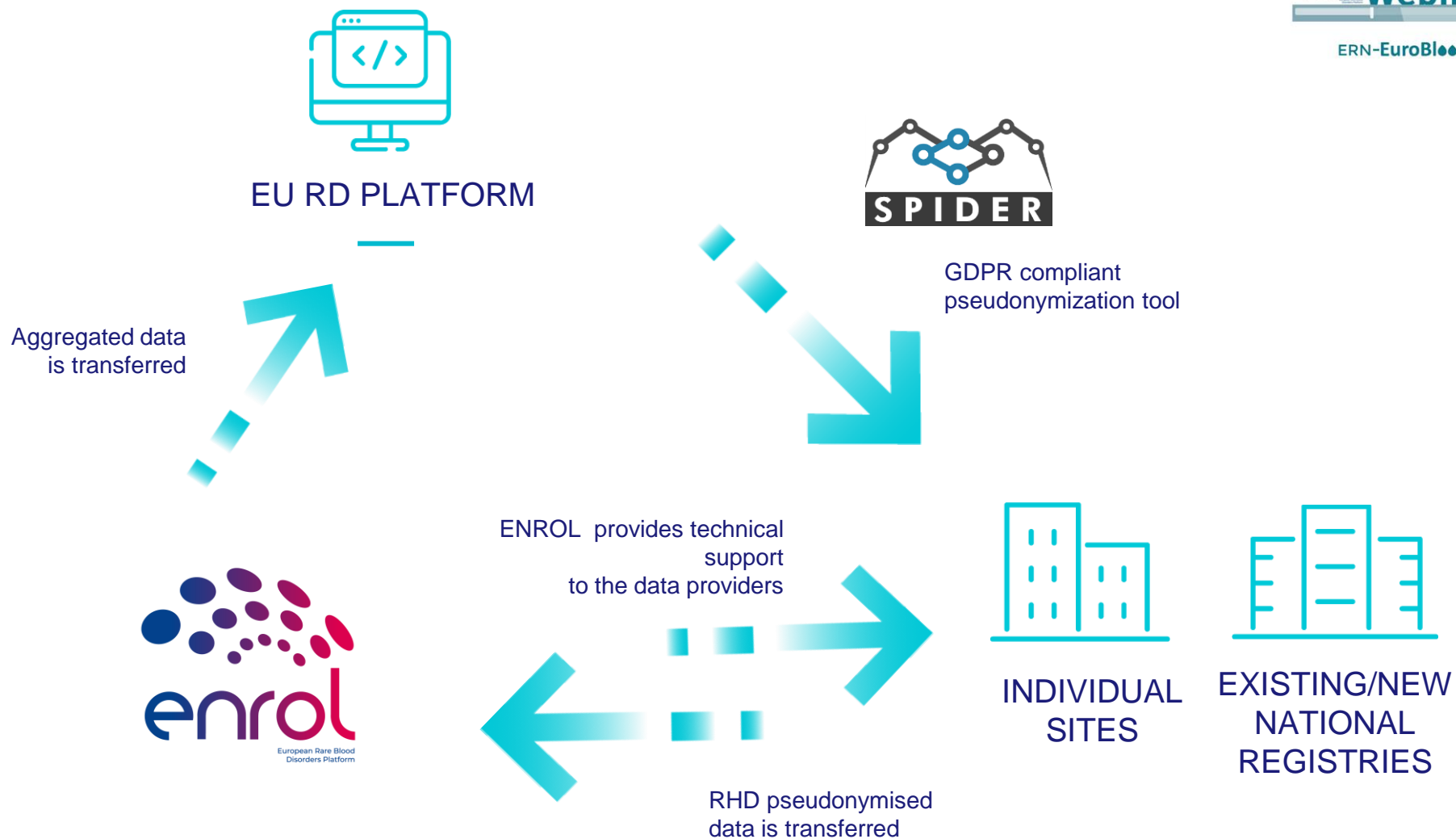
What does FAIR mean?

ENROL Data governance and flow



Legal frame:

- Informed consent
- Data providers collaboration agreement
- Request form for accessing data
- Data Access Committee review
- Sharing agreement with third party



- ▶ Module I: Mandatory elements for RHDs
- ▶ Module II: Optional elements for RHDs
- ▶ Module III: Mandatory elements for RHDs disease groups



Data transfer agreement between Data provider and ENROL



Networking of EU Registries in RHD

ENROL sub registries: what is transferred?



EU RD PLATFORM



RD CDE

ENROL RHD-CDE

ENROL CDE
Onco

ENROL CDE
RAD

ENROL CDE
Bleeding

BPDCN

MDS / AML

Rare anaemia
disorders

Von Willebrand

NEW EU-BLAST

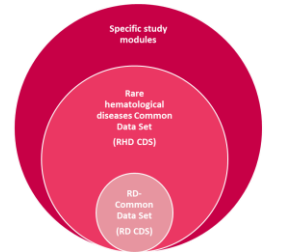
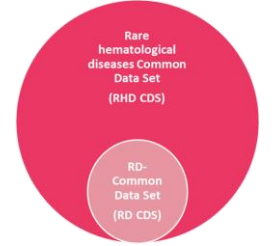


GENOMED4ALL



TWIST **NEW**

NEW IMPACT- AML




Thank You!!

Q&A Time

The logo for the European Rare Blood Disorders Platform (enrol). It features the word "enrol" in a lowercase, sans-serif font. Above the letter "n", there is a decorative graphic consisting of a cluster of small white dots arranged in a semi-circular pattern.

European Rare Blood
Disorders Platform



 Network
Hematological
Diseases (ERN EuroBloodNet)



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