ERICA

European Rare Disease Research Coordination and Support Action

ERICA GA 2024
Summary of WP2 activities

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Wednesday 11th December 2024

Udine - Italy

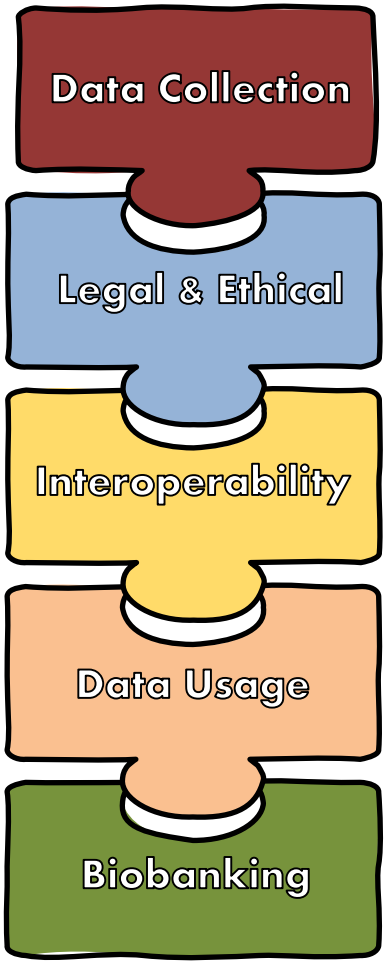
European Commission

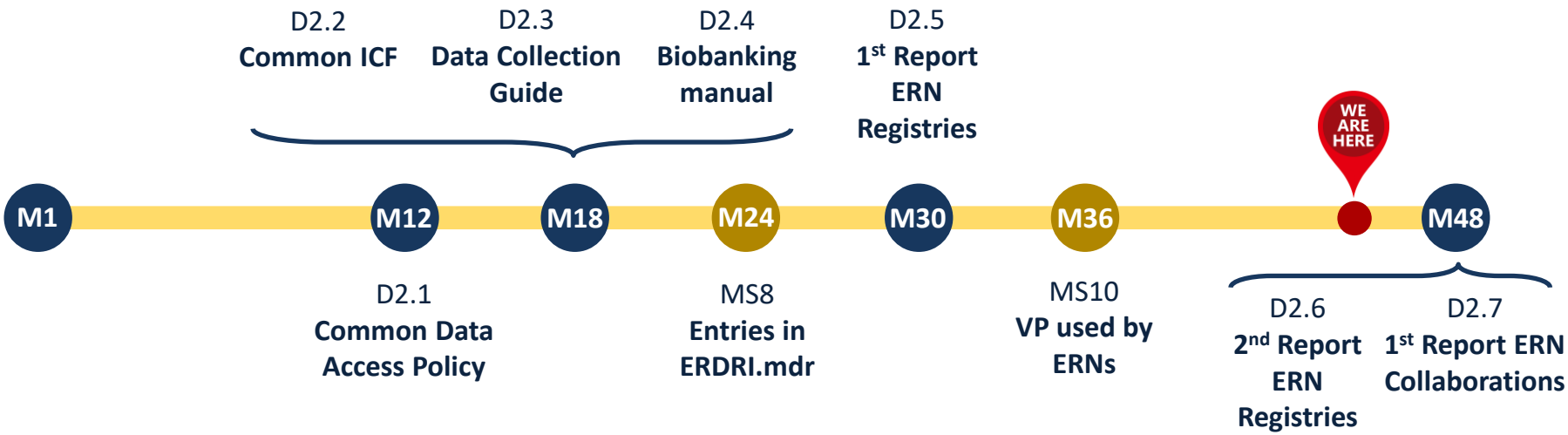
ERICA has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 964908

European Reference Networks

WP2 - Data Collection, Integration and Sharing

- Establish common guidelines for **collecting**, **reusing** and **sharing** data across ERNs and other stakeholders
- Encourage interoperability and standardisation
- Facilitate harmonised data capture across ERNs
- Maximise the usefulness of clinical data collection by promoting data **FAIR**ness (**F**indability, **A**ccessibility, **I**nteroperability and **R**e-usability
- Promote clinical research projects within and between ERNs





T2.1 Coordination and Support of ERN registry activities

T2.1.1 Harmonisation of data protection and access policies for secondary use

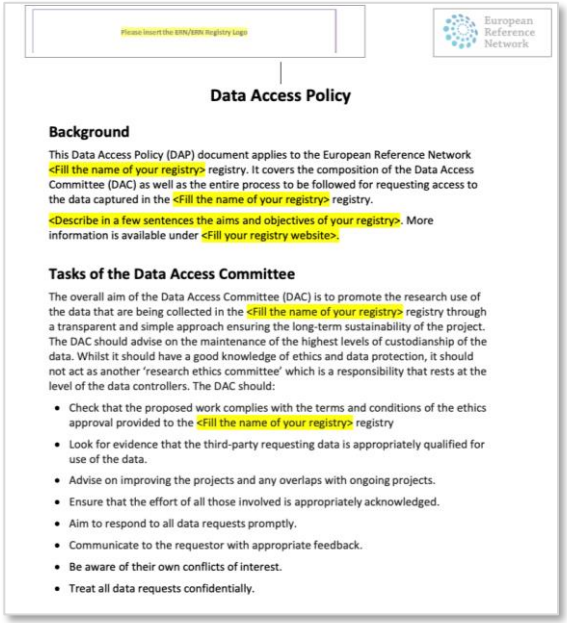
T2.1.2 Promotion of efficient RD data collection and management strategies

T2.1.2 Promotion of registry FAIRness

T2.2 Facilitation of biobanking

T2.3 Contribution to development/utilisation of EJP RD (ERDERA) Virtual Platform

Common Data Access Policy



Please insert the ERN/ERN Registry Logo

European Reference Network

Data Access Policy

Background

This Data Access Policy (DAP) document applies to the European Reference Network <Fill the name of your registry> registry. It covers the composition of the Data Access Committee (DAC) as well as the entire process to be followed for requesting access to the data captured in the <Fill the name of your registry> registry.

<Describe in a few sentences the aims and objectives of your registry>. More information is available under <Fill your registry website>.

Tasks of the Data Access Committee

The overall aim of the Data Access Committee (DAC) is to promote the research use of the data that are being collected in the <Fill the name of your registry> registry through a transparent and simple approach ensuring the long-term sustainability of the project. The DAC should advise on the maintenance of the highest levels of custodianship of the data. Whilst it should have a good knowledge of ethics and data protection, it should not act as another 'research ethics committee' which is a responsibility that rests at the level of the data controllers. The DAC should:

- Check that the proposed work complies with the terms and conditions of the ethics approval provided to the <Fill the name of your registry> registry
- Look for evidence that the third-party requesting data is appropriately qualified for use of the data.
- Advise on improving the projects and any overlaps with ongoing projects.
- Ensure that the effort of all those involved is appropriately acknowledged.
- Aim to respond to all data requests promptly.
- Communicate to the requestor with appropriate feedback.
- Be aware of their own conflicts of interest.
- Treat all data requests confidentially.

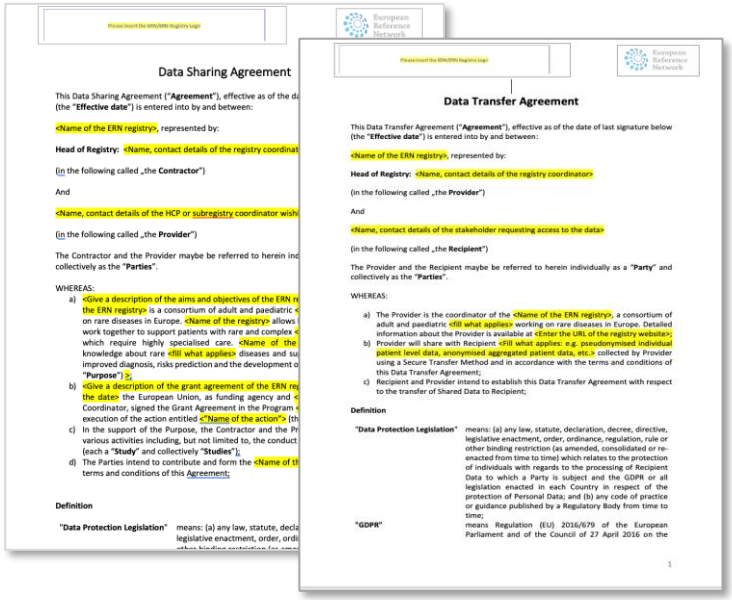
Background:

- Need to address discrepancies in interpretation and application of the GDPR regulation to process healthcare data for secondary purpose across EU member states.
- Lack of standardisation of consent documents for data processing and data access policy for ERN databases prevents efficient reuse of collected data.

Contribution:

- Collaboration with legal experts from EJPRD, EURORDIS, the EU commission and national authorities
- Customisable Data Access Policy template was developed, based on existing ERN data access policy
- Request feedback forms templates allowing to request access to the data in a way that is compliant with the data access policy were also developed

Common Data Sharing/Transfer Agreements



Data Sharing Agreement

This Data Sharing Agreement ("**Agreement**"), effective as of the d
(the "**Effective date**") is entered into by and between:

<Name of the ERN registry>, represented by:

Head of Registry: <Name, contact details of the registry coordinat

(in the following called „the **Contractor**")

And

<Name, contact details of the HCP or subregistry coordinator wish

(in the following called „the **Provider**")

The Contractor and the Provider maybe be referred to herein ind
collectively as the "**Parties**".

WHEREAS:

a) <Give a description of the aims and objectives of the ERN r
the ERN registry> is a consortium of adult and paediatric <
on rare diseases in Europe. <Name of the registry> allows
work together to support patients with rare and complex <
which require highly specialised care. <Name of the
knowledge about rare <fill what applies> diseases and su
improved diagnosis, risks prediction and the development o
"**Purpose**") >;

b) <Give a description of the grant agreement of the ERN re
the date> the European Union, as funding agency and <
Coordinator, signed the Grant Agreement in the Program <
execution of the action entitled <"Name of the action"> (th

c) In the support of the Purpose, the Contractor and the Pr
various activities including, but not limited to, the conduct
(each a "**Study**" and collectively "**Studies**");

d) The Parties intend to contribute and form the <Name of t
terms and conditions of this Agreement;

Definition

"**Data Protection Legislation**" means: (a) any law, statute, decla
legislative enactment, order, ordi

Data Transfer Agreement

This Data Transfer Agreement ("**Agreement**"), effective as of the date of last signature below
(the "**Effective date**") is entered into by and between:

<Name of the ERN registry>, represented by:

Head of Registry: <Name, contact details of the registry coordinator>

(in the following called „the **Provider**")

And

<Name, contact details of the stakeholder requesting access to the data>

(in the following called „the **Recipient**")

The Provider and the Recipient maybe be referred to herein individually as a "**Party**" and
collectively as the "**Parties**".

WHEREAS:

a) The Provider is the coordinator of the <Name of the ERN registry>, a consortium of
adult and paediatric <fill what applies> working on rare diseases in Europe. Detailed
information about the Provider is available at <Enter the URL of the registry website>;

b) Provider will share with Recipient <Fill what applies: e.g. pseudonymised individual
patient level data, anonymised aggregated patient data, etc.> collected by Provider
using a Secure Transfer Method and in accordance with the terms and conditions of
this Data Transfer Agreement;

c) Recipient and Provider intend to establish this Data Transfer Agreement with respect
to the transfer of Shared Data to Recipient;

Definition

"**Data Protection Legislation**" means: (a) any law, statute, declaration, decree, directive,
legislative enactment, order, ordinance, regulation, rule or
other binding restriction (as amended, consolidated or re-
enacted from time to time) which relates to the protection
of individuals with regards to the processing of Recipient
Data to which a Party is subject and the GDPR or all
legislation enacted in each Country in respect of the
protection of Personal Data; and (b) any code of practice
or guidance published by a Regulatory Body from time to
time;

"**GDPR**" means Regulation (EU) 2016/679 of the European
Parliament and of the Council of 27 April 2016 on the

1

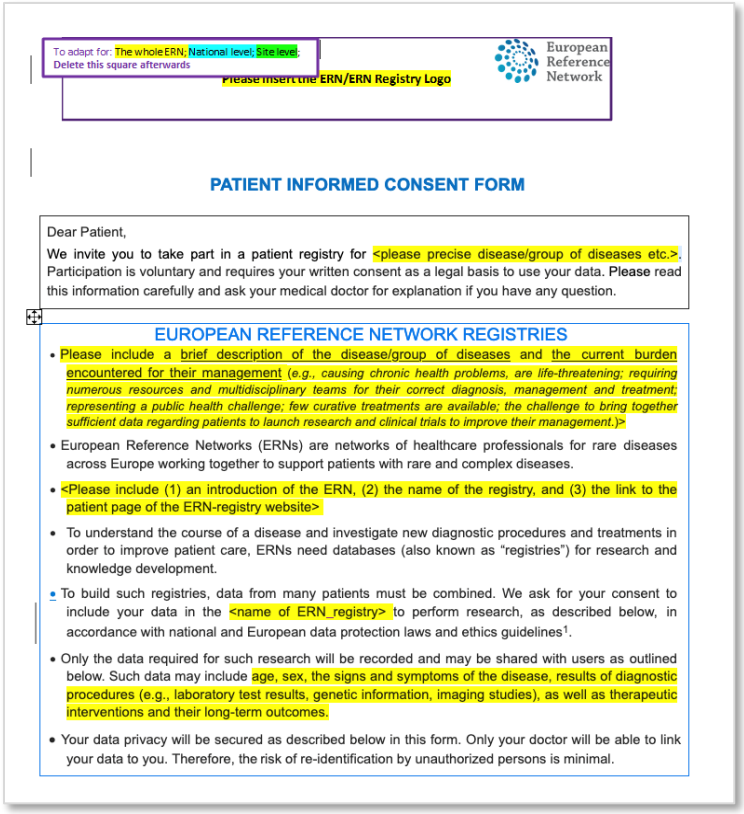
Background:

- In **centralised** registries, all data collected by HCPs is transferred to a centralised server
- **Data Sharing Agreements** need to be drafted and signed between the registry and every participating HCP
- If DAC decides to grant access to the registry data to a stakeholder, a **Data Transfer Agreement** needs to be signed
- **Lack of standardisation** drags these processes out

Contribution:

- Collaboration with legal experts from EJPRD, EURORDIS, the EU commission and national authorities
- Customisable Data Sharing and Transfer agreements were developed
- Request feedback forms templates allowing to request access to the data in a way that is compliant with the data access policy were also developed.

Common Informed Consent Policy



To adapt for: The whole ERN; National level; Site level.
Delete this square afterwards

Please insert the ERN/ERN Registry Logo

European Reference Network

PATIENT INFORMED CONSENT FORM

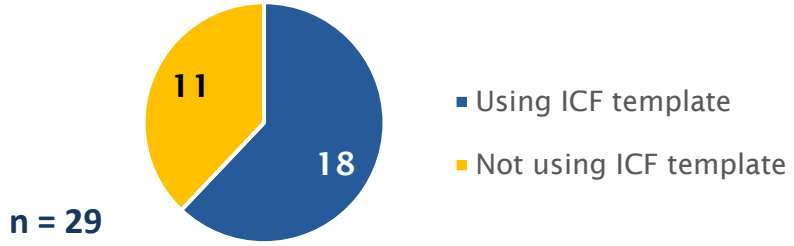
Dear Patient,

We invite you to take part in a patient registry for <please precise disease/group of diseases etc.>. Participation is voluntary and requires your written consent as a legal basis to use your data. Please read this information carefully and ask your medical doctor for explanation if you have any question.

EUROPEAN REFERENCE NETWORK REGISTRIES

- Please include a brief description of the disease/group of diseases and the current burden encountered for their management (*e.g., causing chronic health problems, are life-threatening; requiring numerous resources and multidisciplinary teams for their correct diagnosis, management and treatment; representing a public health challenge; few curative treatments are available; the challenge to bring together sufficient data regarding patients to launch research and clinical trials to improve their management.*)>
- European Reference Networks (ERNs) are networks of healthcare professionals for rare diseases across Europe working together to support patients with rare and complex diseases.
- <Please include (1) an introduction of the ERN, (2) the name of the registry, and (3) the link to the patient page of the ERN-registry website>
- To understand the course of a disease and investigate new diagnostic procedures and treatments in order to improve patient care, ERNs need databases (also known as "registries") for research and knowledge development.
- To build such registries, data from many patients must be combined. We ask for your consent to include your data in the <name of ERN_registry> to perform research, as described below, in accordance with national and European data protection laws and ethics guidelines[1].
- Only the data required for such research will be recorded and may be shared with users as outlined below. Such data may include age, sex, the signs and symptoms of the disease, results of diagnostic procedures (e.g., laboratory test results, genetic information, imaging studies), as well as therapeutic interventions and their long-term outcomes.
- Your data privacy will be secured as described below in this form. Only your doctor will be able to link your data to you. Therefore, the risk of re-identification by unauthorized persons is minimal.

- Collaboration between Legal & Ethical WG and EJP RD
- **Two customisable ICFs**, for adult patients and patient representatives, were developed
- Translations in the 26 European languages are available



- Majority of ERN registries use the ICF template
- **Less than 15%** of the local Ethic Committees **requested modifications** to the ICF template prior to providing approval
- Reasons for not using the common template:
  - Specific ICFs had already been developed
  - Consent not required for some registries

https://erica-rd.eu/work-packages/data-collection-integration-and-sharing/generated-documents/

Recommendations on Registry Data Collection

Dataset:
- Balanced
- Consistently defined

Data Capture System:
- Comprehensive
- Scalable

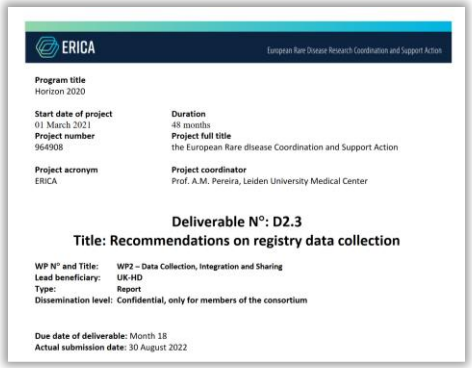
Data validation:
- At input and periodic
- As automatised as possible

Registry

Monitoring:
- Definition of KPIs
- Evaluation of objectives

Patients:
- Clear inclusion criteria
- Data protection considerations

Interaction with HCPs:
- Definition of KPIs
- Operational aspects


ERICA
European Rare Disease Research Coordination and Support Action

Program title
Horizon 2020

Start date of project
01 March 2021
Project number
964908

Duration
48 months
Project full title
the European Rare dIsease Coordination and Support Action

Project acronym
ERICA

Project coordinator
Prof. A.M. Pereira, Leiden University Medical Center

Deliverable N°: D2.3
Title: Recommendations on registry data collection

WP N° and Title: WP2 – Data Collection, Integration and Sharing
Lead beneficiary: UK-HD
Type: Report
Dissemination level: Confidential, only for members of the consortium

Due date of deliverable: Month 18
Actual submission date: 30 August 2022

D2.3 facilitates:
- Technical aspects
- Legal considerations
- Registry sustainability

Biobanking EWG

Ana Martinez-Feito & Eduardo López-Granados

- **Objective:** to provide methodological and operational guidance for ERN-wide biobanking projects

- A Biobanking EWG – Survey among ERNs members was launched in march 2022, >130 HCP responded

- We mapped the current ecosystem and available resources and recommendations for Biobanking activities in biomedical research that could be useful for Rare Diseases

Biobanking EWG

Ana Martinez-Feito & Eduardo López-Granados

- We went through existing available resources of major European biobanking framework
  - Telethon Network of Genetic Biobanks (in collaboration with Luca Sangiorgi)

    Charter for governance, ethical guidelines, technological information, quality assurance, Sample SOPs, MTAs, Consent forms, catalogue access.
  - Orphanet,

    Catalogue of biobanks: Melania Cruciani
  - Eurobiobank network of RD-Connect (databases, registries, biobanks, …)

    RD-Sample: Catalogue of Biobanks: Esther van Enckevort
  - BBMRI-ERIC.

    Knowledge hub: international standards, quality management (German Biobank node manual

    Research related to Ethical, Legal and Societal Issues (ELSI Knowledge base) and training.

    General data protection and regulation (GDPR)

- Existing scientific literature and RARE 2030 Knowledge base documents

Biobanking EWG

Ana Martinez-Feito & Eduardo López-Granados

All along, a close collaboration was maitained with Biobanking training initiatives developed by the EJP-RD

EJP RD Pillar 3: Capacity Building & Empowerment

EUROPEAN JOINT PROGRAMME RARE DISEASES

-Rare Disease Biobanks: Roles in Research Networks and International Collaborations
Online Training Workshop. 10-11 May 2021. ELG **ATTENDED**

-ERN biological samples in Rare Diseases research: Added value and usefulness
On site Training Workshop. 12 – 14 June 2023. Madrid. ELG and AMF **PARTICIPATED**

-Managing RD biological sample data in Biobanks: lessons learned from the EJP RD training workshops", **ATTENDED**

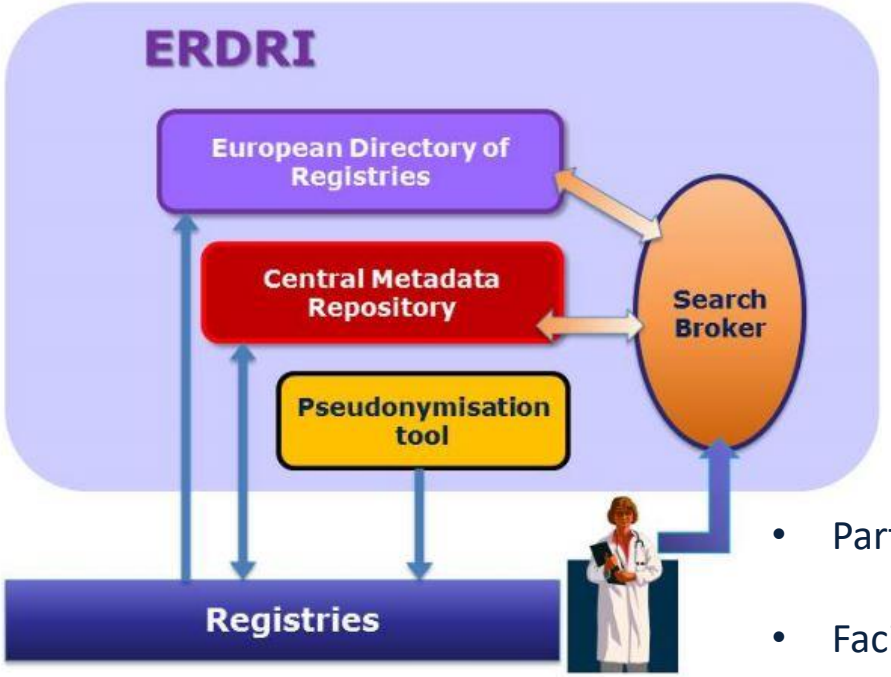
On site Training Workshop to be held 13-14 December 2023, Milan, Italy AMF **PARTICIPATED**

Biobanking EWG

Ana Martinez-Feito & Eduardo López-Granados

- Deliverable D2.4: RD biobanking manual with all SOPs and legal documents.
- **Compilation of RD biobanking manual** with all SOPs and legal documents.
  https://erica-rd.eu/work-packages/data-collection-integration-and-sharing/biobanking/
  We worked aligned with WP4 activities in Clinical Research
- We drafted a manuscript (*Orphanet Journal of rare diseases*)
- The manual will be discussed and improved after a webinar / online workshop.
- We will provide afterwards support for the use and implementation of the manual recommendations

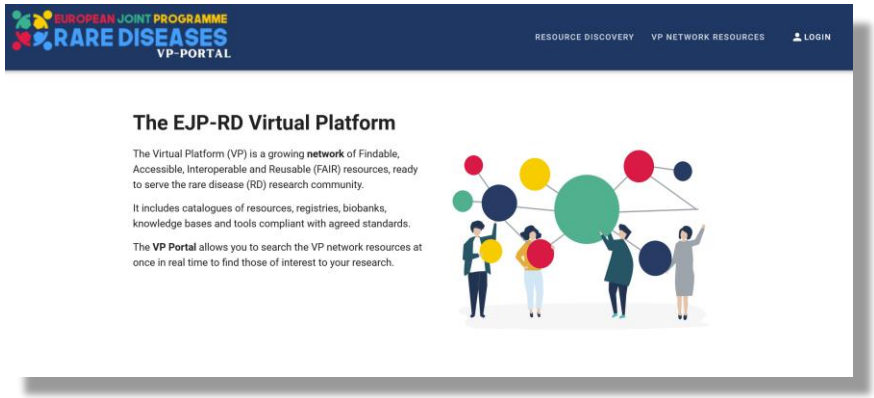
Milestone: ERN Registry Data in ERDRI.mdr



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

- Part of EU RD Platform on Rare Disease Registration
- Facilitates metadata discovery of RD resources
- **ERDRI.mdr features all 25 operational ERN registries**
- Regularly updated (19 entries updated in 2024)

Milestone: ERN use of EJPRD/ERDERA VP



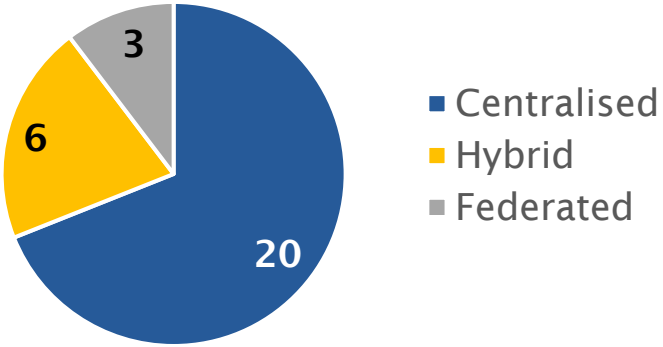
- Ecosystem of RD research-ready data resources
- Supports research and policy making
- Allows rare disease stakeholders to easily **find**, **access**, and **use** data for their purposes
- Currently features data/metadata from 11 ERNs, more to follow in ERDERA

Funded by the European Union
GA n° 825575

Monitoring Reports on ERN DC – Registries Overview

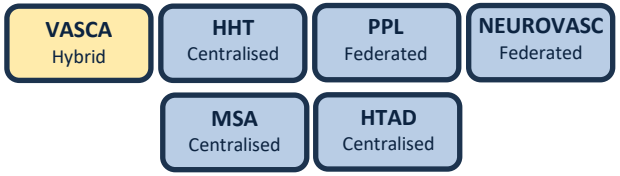
29 Registries - 24 ERNs, several ERNs manage disease-specific registries in addition to their core registries:

Types of ERN registries



n=29

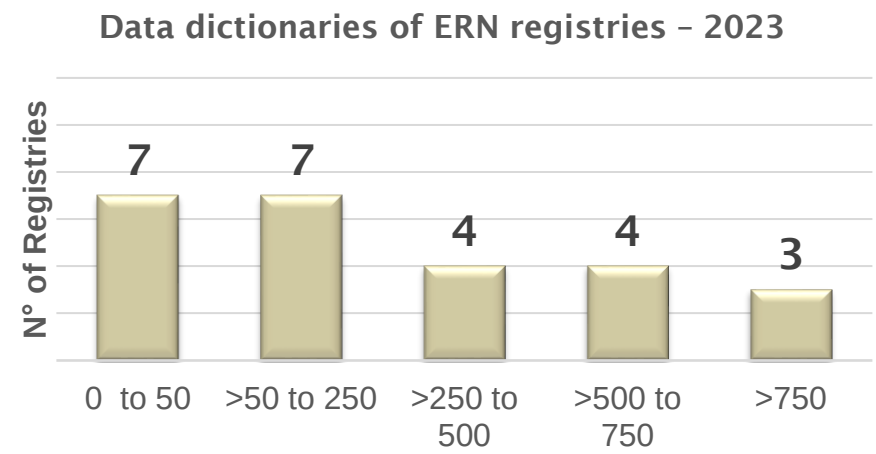
- Separate from the core registry, with different approaches (e.g. VASCERN)



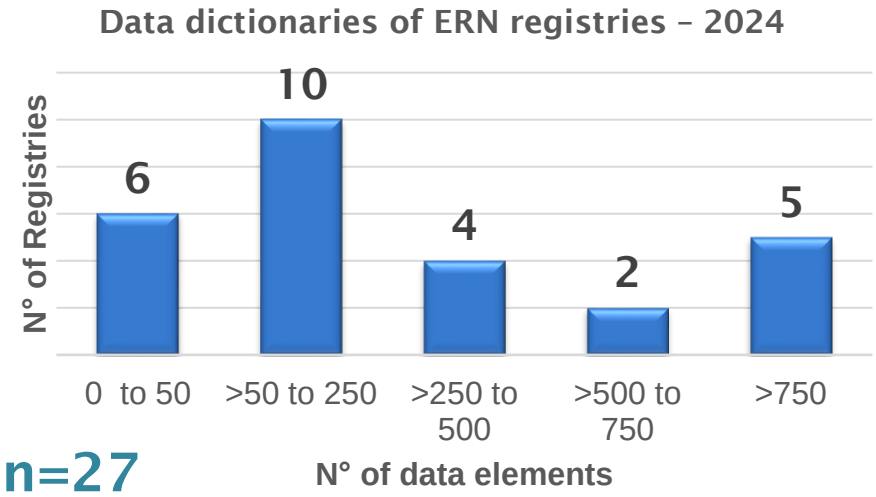
- Modularly integrated within the same infrastructure as subregistries (e.g. ERKNet)

Choice of implementation

	Molgenis	Castor	RedCap	Other provider	Own system
Number of ERNs	5	7	6	5	6


Data dictionaries of ERN registries – 2023
N° of Registries
7
7
4
4
3
0 to 50
>50 to 250
>250 to 500
>500 to 750
>750
N° of data elements

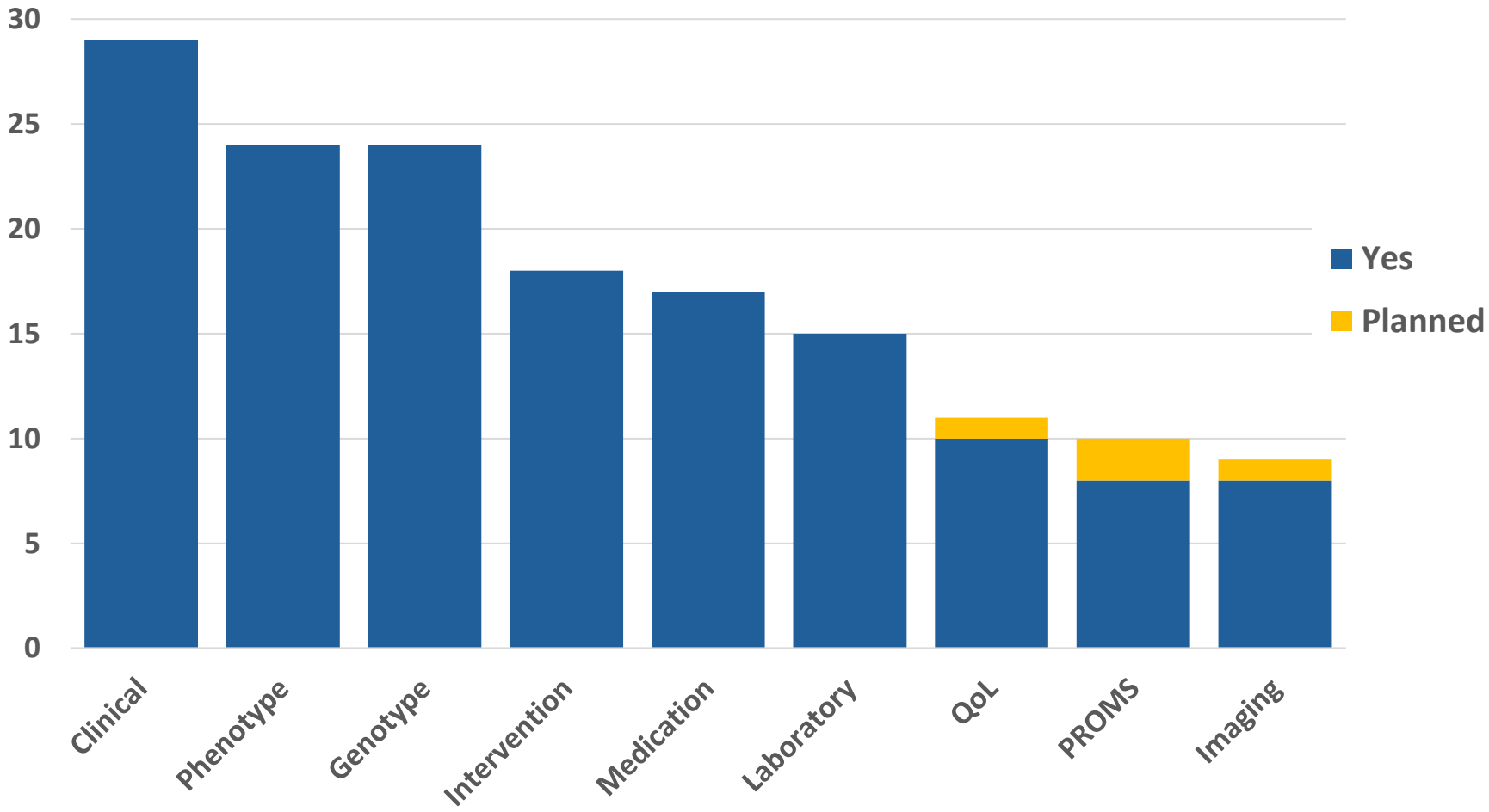
n=25


Data dictionaries of ERN registries – 2024
N° of Registries
6
10
4
2
5
0 to 50
>50 to 250
>250 to 500
>500 to 750
>750
N° of data elements

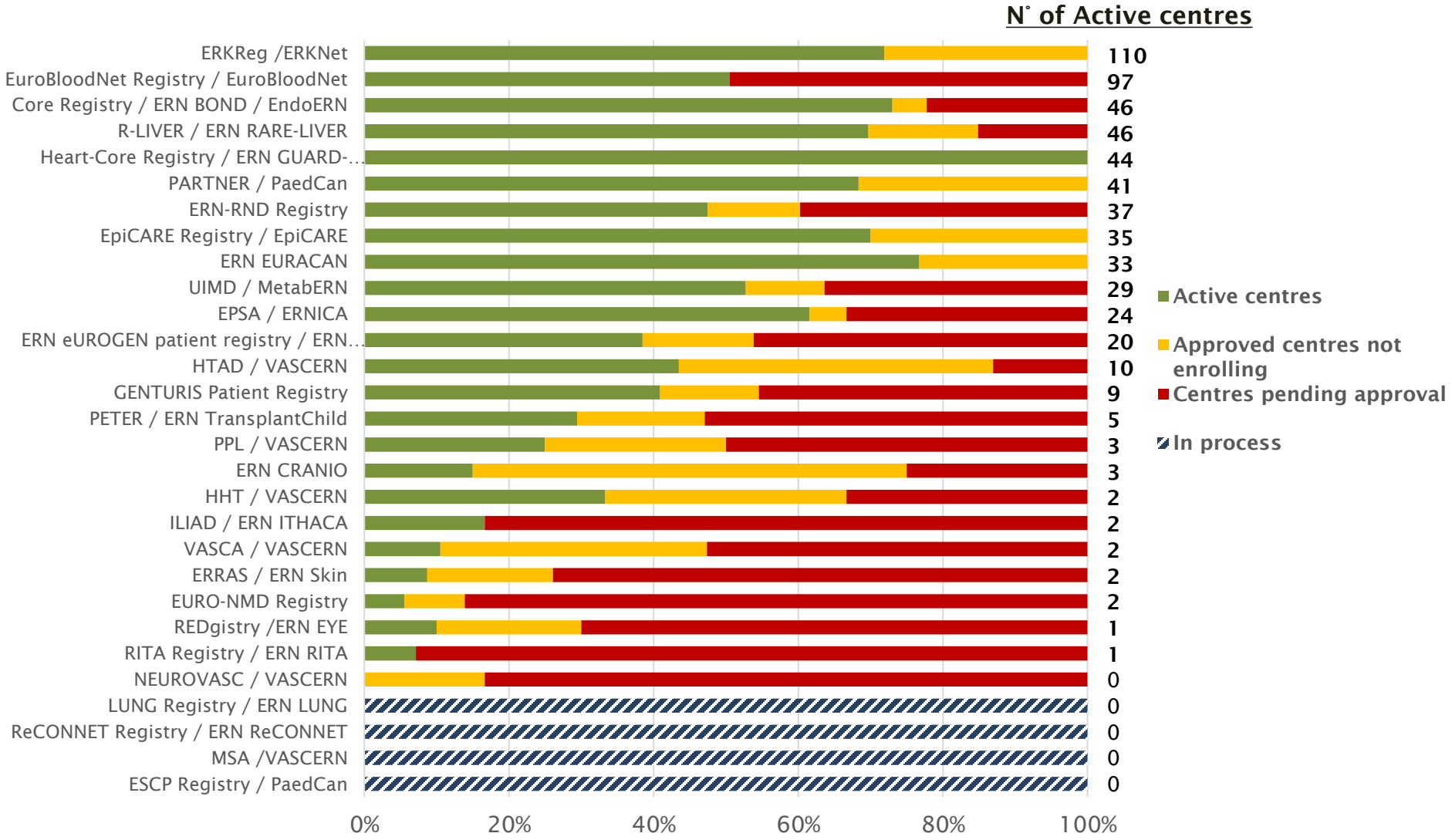
n=27

Types of Data Elements Captured in ERN Registries

N=29

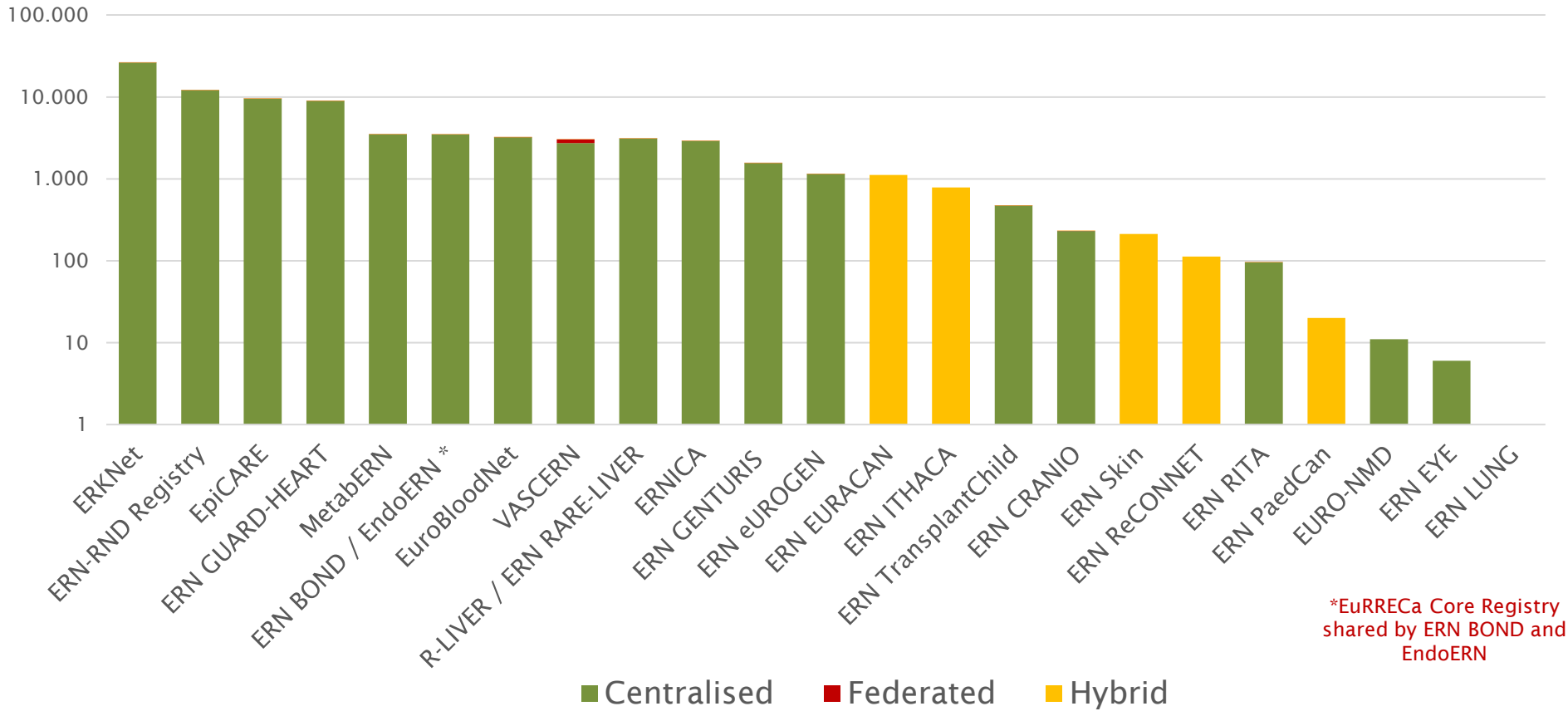


ERN Registries – Center enrollment



ERN Registries – Patient enrollment

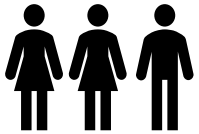
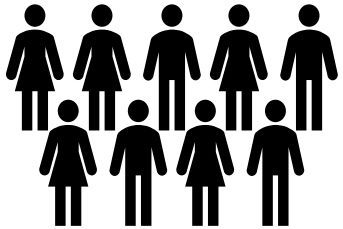
~81.000 patient records by Oct. 2024



*EuRRECa Core Registry shared by ERN BOND and EndoERN

Number of accessible patient records through the registries managed by each ERNs, depicted against a logarithmic scale

Progression of Patient Enrollment

Number of patients records	Number of ERN Registries				
	2020	2021	2022	2023	2024
 **<100**	17	13	10	14	6
 **100-1.000**	4	5	5	3	5
 **>1.000**	3	4	9	7	13

1.000-5.000
9 Reg.

5.000-10.000
2 Reg.

>10.000
2 Reg.

ERN Registries – Data Recording

Data is recorded following different approaches:

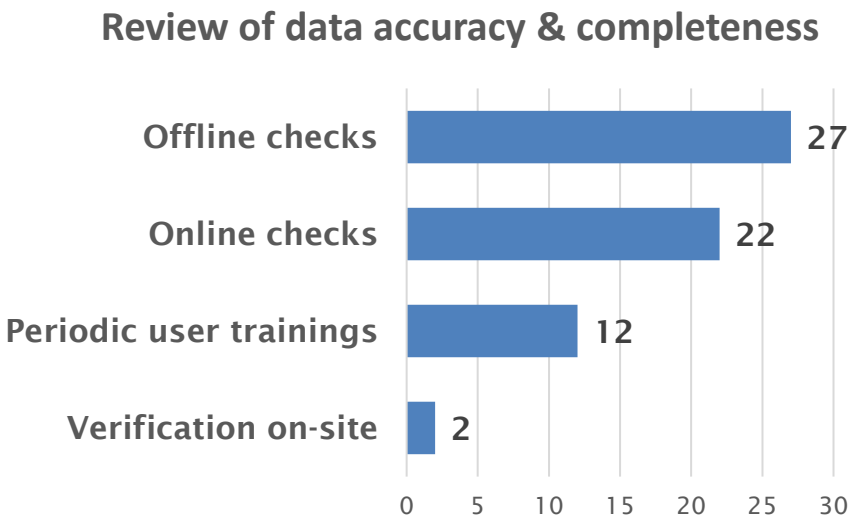
- For **27 registries**, data can be entered **manually** by clinicians.
- For **7 registries**, data can be transferred **automatically from other relevant registries or databases**.
- For **1 registry**, data is currently entered **manually by personnel at the coordination office**.

Automated data transfers:

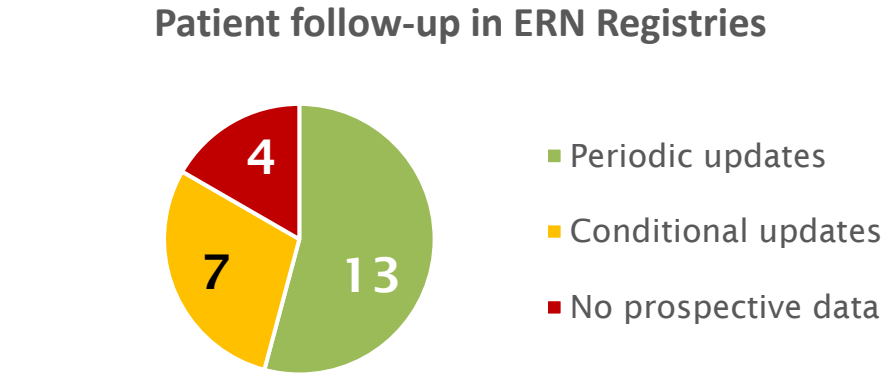
- Priority for ERNs at advanced stages of patient enrolment.
- **16 registries** have started to develop pipelines that facilitate automatic data transfers from other rare disease registries in Europe.
- **12** of these are working with the **BNDMR** in France, to receive/provide data from/to **BaMaRa**.

BNDMR
Banque Nationale de Données Maladies Rares

ERN Registries – Interactions with local HCPs



- **Offline sanity checks** are carried out periodically (mostly **yearly)**
- **23 registries** implement multiple strategies
- Complemented by **registry user manuals**
- **8 registries** periodically report centre performance through **KPIs**
- **12 registries** are developing KPI-based reporting

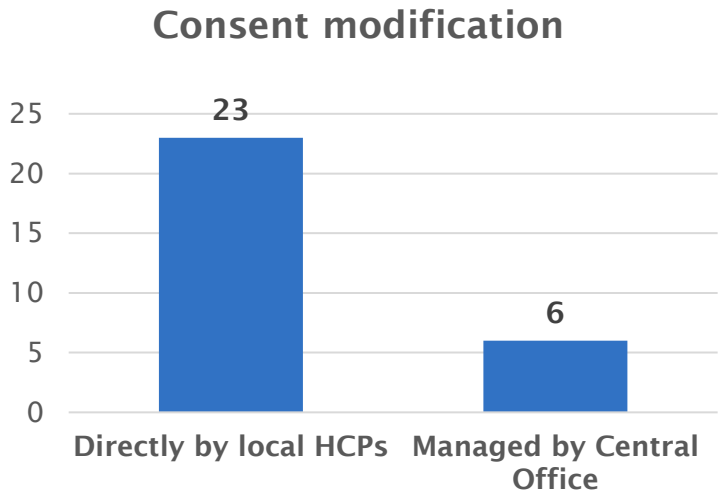


- Registries that collect **prospective data** tend to receive **updates** to their patient records **annually**.
- The exact frequency and data elements collected often depend on their cohort and disease progression.

ERN Registries – Modification of Consent

- **If a patient wishes to modify/withdraw consent:**
  - In **23 registries**, local HCPs can directly modify the consent items for each patient.
  - In **6 registries**, HCPs need to contact the registry management team.

  Note: in the EuRRECa Core Registry, patients themselves can modify their consent items too.



- **Timeline of consent modifications, according to previous experience:**
  - In **10 registries**, modification of consent takes full effect within a week.
  - In **9 registries**, it takes between a week and a month.
  - The remaining **9 registries** have no previous experience.

  The speed at which changes take effect depends on local HCPs.

	Within a week	1 week to 1 month	TBD
N° of registries	10	9	10

WP2 In-Person Events

ERN Data Collection Strategies (Heidelberg, Oct 2022)

- Patient representatives, policymakers, regulatory authorities, researchers

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

Joint ERICA-c4c Workshop:
Exploring and enhancing the potential for ERN registries to support paediatric research (Heidelberg, 4th-5th February 2025)

- ERN registry team members (2 per ERN), c4c partners, regulatory experts, industry experts, EC representatives
- **Agenda:**
  - Current status and aspirations of ERN registries
  - Promote research applications of ERN registry data
  - The c4c project
  - ERN registries as RWE generators
  - Interactions with industry

Contact: joseantonio.ramirezgarcia@med.uni-heidelberg.de

Q&A

Contact: joseantonio.ramirezgarcia@med.uni-heidelberg.de