ERDERA
European Rare Diseases
Research Alliance

Extended Information Webinar
ERDERA Joint Transnational Call 2025

Pre-clinical therapy studies for rare diseases using small molecules and biologicals – development and validation

Ralph Schuster, DLR Projektträger
14 January 2025

Co-funded by
the European Union

ERDERA has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement N°101156595.
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Objectives of the webinar

The webinar aims to provide educational and preparatory support to you at the **pre-proposal stage**, focusing on key elements that enhance the quality of the submissions.

- **Inform** about lessons learned from the evaluation.
- **Guide** with key translational, regulatory, data managing, and methodological considerations for drafting strong pre-proposals.
- **Address** questions through dedicated Q&A sessions.

It will not address questions about consortium eligibility or other call procedure related topics – please refer to webinar of 17th December, materials (presentations, FAQ, video recording) to be found on ERDERA website

Agenda

14.00-14.10	Welcome and Introduction	(Ralph Schuster)
14.10-14.20	Lessons learned from previous calls	(Christine Kinnon)
14.20-14.30	Q&A Round 1	
14.30-14.45	Innovation Management Toolbox and Mentoring service	(Agustin Arasanz Duque, Rosan Kreeftmeijer-Vegter, Toni Andreu)
14.45-15.00	Regulatory Support Service	(Viviana Giannuzzi / David Morrow)
15.00-15.10	Q&A Round 2	
15.10-15.25	Methodological support	(Rima Nabbout, Ralf Dieter Hilgers)
15.25-15.40	Data standards and FAIRification	(Marco Roos)
15.40-15.50	Q&A Round 2	
15.50-16.00	Closing remarks	

Call topic: **Pre-clinical therapy studies for rare diseases using small molecules and biologicals – development and validation**

Research studies on therapies using small molecules, small non-coding chemically synthesized nucleic acid-based therapies, repurposed drugs or biologicals (e.g., antibodies or proteins such as enzymes, immune modulators or growth factors etc.). Proposals must cover **at least two** of the following areas**:**

1. development of novel therapies in a pre-clinical setting through cell, organoid and animal disease model studies, and/or use of *in silico* or artificial intelligence models to accelerate the success rate of the pre-clinical stage
2. development of predictive and pharmacodynamics biomarkers correlated to the efficiency of the therapy in a preclinical setting that could serve as surrogate endpoints
3. replication of pre-clinical studies in an independent lab to increase validity of exploratory findings
4. pre-clinical proof of concept studies for evidence of pharmacological activity *in vitro* and *in vivo*, pharmaco-kinetics and pharmaco-dynamics of the investigational drug (i.e., small molecule(s) and/or biologic) and first toxicology and safety data as well as studies to support readiness for initiating clinical trial authorization conforming to regulatory requirements

General considerations 1

- Projects should focus on rare diseases or disease groups with high unmet medical need, high disease burden, and no currently approved therapeutic options in Europe (European marketing authorisation). Preferably, they should address group(s) of rare diseases with commonalities such as, but not exclusively, shared molecular etiologies and/or clinical symptoms, such that the same drug and/or drug combinations could be used for clinical trials of multiple diseases
- Existing knowledge from multiple sources (natural history studies/registries, real-world data/evidence, multi-omics, medical imaging, etc.) should be used to underpin the therapeutic hypothesis and therapeutics development.
- Consortia **performing preclinical development of therapeutics** are strongly advised to engage or consult experts in the various stages of product development to ensure that the data generated is suitable for future regulatory filings such as for application of receiving orphan designation and/or clinical trial preparedness for regulatory advice and authorisation → establish one or more: **Target validation, Suitable formulation and route-of-administration, Right Tissue, Right safety profile, Right patient, Readiness for clinical trial application (CTA)-directed studies**

General considerations 2

- **For the development of novel therapies or pre-clinical proof-of-principle studies** → Orphan medicine designation (OD) planning, EMA Scientific Advice Working Party (SAWP) and/or Innovation Task Force (ITF) early engagement, target validation in relevant preclinical disease and/or models
- **Validation or development of predictive and pharmacodynamics biomarkers** → Robust analytical procedures, analytical validation using high quality samples from an independent collection, should follow a risk-based approach
- **Describe and justify the use of disease models** → how the model replicates the pathology or human condition as well as aspects of the therapy target, justification on use of animals, availability of the model, statistics for robust and well controlled pre-clinical efficiency studies, primary endpoints
- The **design of the study** (sample collection, statistical power, interpretation, relevant models for hypothesis validation) must be well justified and should be part of the proposal.
- Study design, preclinical models and reagents should be selected **to facilitate approval in human trials** and future clinical grade manufacturing.

General considerations 3

- Appropriate bioinformatics and statistical methods, whenever included and justified, should constitute, an integral part of the proposal, and the relevant personnel should be clearly specified. These personnel should either be an eligible partner of the consortium, part of the research group of an eligible partner or involved as direct contractors of an eligible partner. They cannot be external collaborators that participate with their own funding. **Their responsibilities must be clearly described and align with the requested resources and a CV must be provided.**
- Data generated or newly collected for the project must be made ready for reuse according to **FAIR principles**. This should be achieved by contributing to the creation of the ERDERA Data Hub, a collaborative responsibility of the ERDERA partnership. Effort and budget must be earmarked for FAIR data stewardship and a milestone should be included to mark the contribution.
- Risk management should be considered including the identification of possible bottlenecks and go/no go contingencies.
- The analysis of IP status, freedom to operate and access to therapeutic molecules for development should be clearly described.

Application Timeline

Call opens

December 10, 2024

Informational webinar

December 17, 2024

Add. Webinar Jan 14, 2025

Pre-proposal submission

February 13, 2025

Eligibility check

Early March 2025

Invitation full proposal

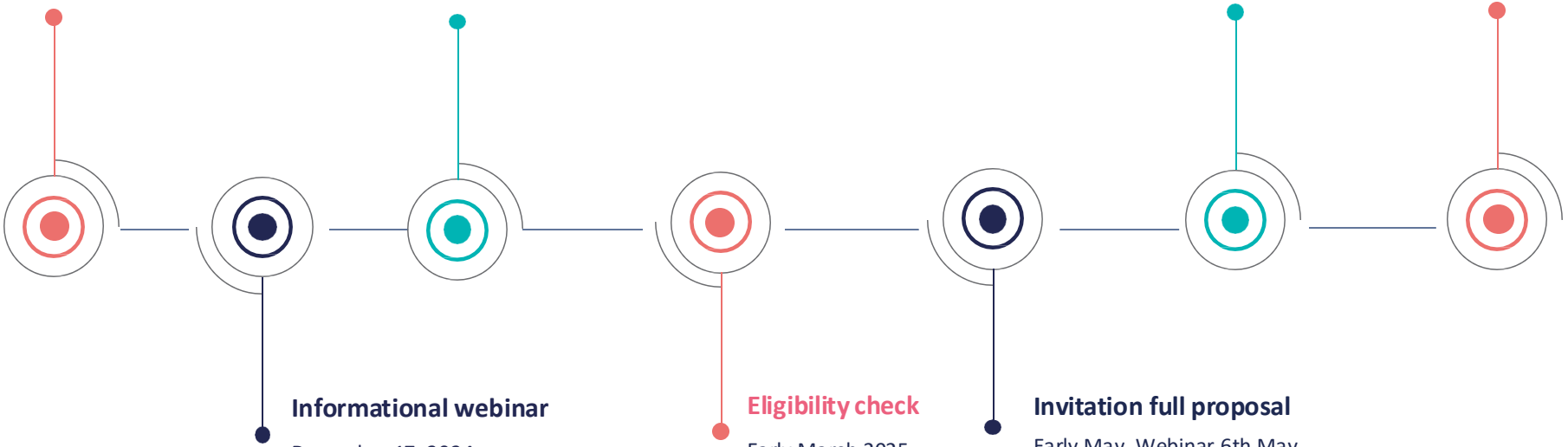
Early May, Webinar 6th May

Full proposal submission

July 9, 2025

Decision

Dec 2025



Description of the project

Introduction and background (max. 4.500 characters)

Project description (max.13.500 characters)

- **Objectives and hypothesis**
- **Soundness and pertinence**
- **Workplan and Methodology**

Impact (max. 1.500 characters)

Added value of the consortium (max. 1.500 characters)

Patient Advocacy Organisations (PAOs) engagement/involvement (max. 2.000 characters)

Results of previous EJP RD or E-Rare funded project, only if applicable (max. 4.500 characters)

Participant information

Narrative CVs

European Rare Diseases Research Alliance

Contact Joint Call Secretariat

DLR Projektträger (DLR-PT, Germany)

Dr. Katarzyna Saedler, Dr. Michaela Fersch, Dr. Ralph Schuster

Tel: +49228-38212453

E-Mail: SelteneErkrankungen@dlr.de

Co-funded by the European Union

ERDERA has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement N°101156595.

Eligible countries/regions and budget

- **35 funding agencies from 27 EU, EU associated countries & Canada, co-funded by European commission**
- **Participating countries:** Austria, Belgium, Bulgaria, Canada, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Hungary, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Norway, Poland, Portugal, Slovakia, Spain, Sweden, Switzerland, The Netherlands, Türkiye
- **Each funder funds only their respective national/regional teams → check guidelines!! → contact your national/regional contact point!!**
- **Partners from other countries (e.g. UK, USA, China) can only participate as collaborators with own funding**
- **3 years projects**
- **Overall budget: 32,6 Mio €**
- **Expected number of funded projects: ~25**
- **Usual success rate: from pre-proposal stage → funding 10-15%, pre-proposal → full proposal 30%, full proposal → funding 40-50%**

ERDERA

European Rare Diseases
Research Alliance

IMT & Mentoring service

JTC 2025

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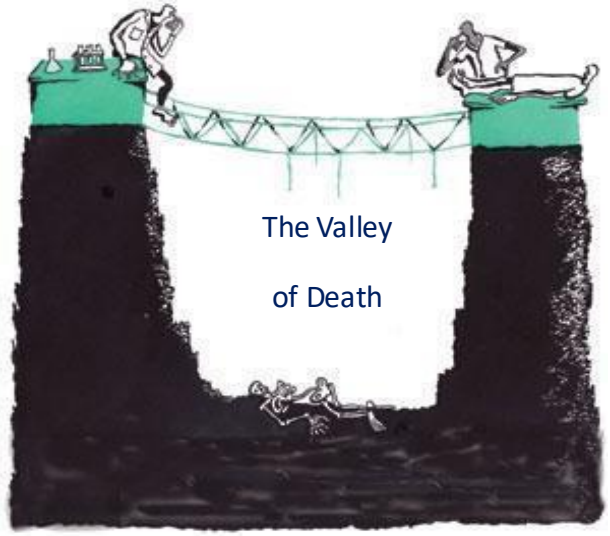
Challenges of translational projects

Improve the feasibility of translational and clinical research projects



Nature, 2008

- Poor predictive pre-clinical models
- Mode of action not fully validated
- Sub-optimal clinical trial design
- IP not secured – no freedom to operate
- Limited regulatory experience
- Limited data management knowledge

Innovation Management Toolbox
Mentoring Service

Innovation Management Toolbox

ERDERA European Rare Diseases Research Alliance

Innovation Management Toolbox (IMT)

- Launched in June 2022
- Library of translational medicine resources on rare diseases
  Currently 550 resources
- Mainly external open access resources addressed by categories: Research and drug development, Regulatory science, Intellectual property, Funding and Project management

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM
IRDiRC Recognized Resource

https://imt.ejprarediseases.org/

IMT features

Advanced browser

Filter the search by categories, tags, and geographical scope

Q&A List

Relevant questions on drug development steps

Use Cases

Short videos created by experts on different drug development topics

ERICA Catalogue

Catalogue of services for the Rare disease research community

Collections

Bookmark and download documents of interest

Highlight Mentoring packages

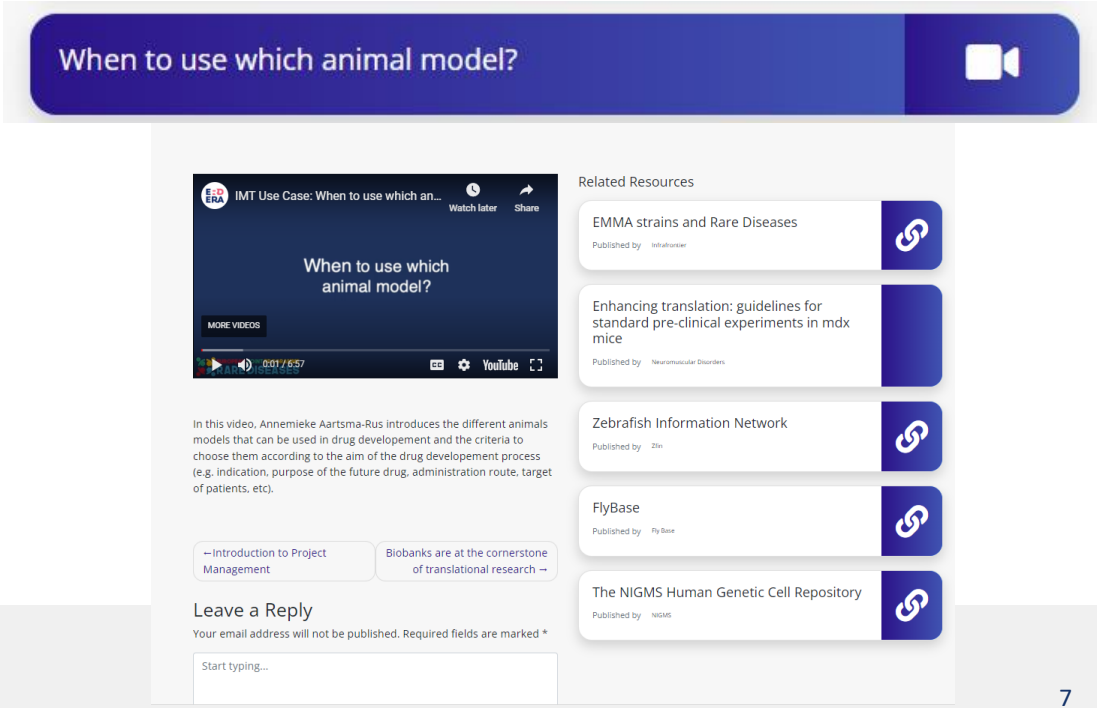
Covering key areas essential to translational research success

https://imt.ejprarediseases.org/collection/mentoring-packages/

- Introduction to Project Management
- Introduction to Innovation Management
- Introduction to the regulatory framework of medicinal products
- How to meaningfully engage with patients in your research
- Introduction to Data Management

Use cases

https://imt.ejprarediseases.org/use_case/



Functionalities integrated in the IMT

Collections

Integration of new resources with IMT

Orphan drug Guideline ODDG (IRDiRC): Is an interactive tool to guide researchers through the whole process of the rare disease therapies development

Rare Disease Clinical trial Toolbox (ECRIN): Resources organized in a way to guide and help clinical trialists and R&D managers understand the regulations and requirements for conducting trials

Mentoring service execution

European Rare Diseases Research Alliance

Execution of the Mentoring service

- **To Whom**: Shortlisted JTC's proposals and also projects from other funding schemes.
- **Format**: Webinar and 1-on1 meetings with expert mentors who provide advise on specific areas
- **Cost**: Free of charge, full confidentiality (signed Letter of engagement/CDA)
- **When**: During 2nd stage to prepare the final proposal , through full project lifetime

CureMILS: Mitochondrial DNA-associated Leigh syndrome (MILS)

Testimonial

Goal: enabling MILS drug discovery with reprogramming technologies

Coordinator: Prof. Alessandro Prigione (HHU Düsseldorf, Germany)

- The most severe form of mitochondrial disease in children → 1:36,000 births
- Caused by mitochondrial DNA (mtDNA) mutations
- Lack of model systems due to challenging in mtDNA engineering
- No treatments available

EATRIS mentoring was instrumental in several aspects:

- Identify strengths of our project
- Contacted experts that provided additional feedback with respect to methodologies and practical aspects
- Suggested an effective path for engaging with regulators to achieve the ODD

These advices and suggestions significantly improve the impact and translational potential of our proposal

testimonial video

Pre-clinical development of ManNAc-6P Phosphoramidate, a potential treatment for GNE Myopathy

Testimonial

GNE myopathy (GNEM): 1-9: 1,000,000

- Progressive skeletal muscle weakness in young adults (18-40 years old)
- No approved therapy, no biomarkers. Limited animal models.

EATRIS mentoring service included:
Analysis of the proposed study to assess the potential of the concept:

- Translational feasibility
- End-product definition, regulatory compliance & pathway
- Suitability of models, assays and bio-resources
- Future development and technology transfer strategy

Benefits for the consortium

- Easy access to support (before proposal submission and during project timeline)
- Strengthened consortium expertise in pre-clinical drug development
- Prompt feedback from the team

European Rare Diseases Research Alliance

Thank you!

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Testimonial

EpiThe4SHD project: Safety and efficacy of a possible epigenetic therapy for FSHD muscular dystrophy

Goal: use cellular and animal models of the disease to investigate a novel pharmacological approach

Davide Gabellini
Group Leader Division of Genetics and Cell Biology
San Raffaele Scientific Institute

EJPRD JTC 2020 participant

During a period of about one month, I interacted with various professionals collaborating with EATRIS to discuss issues related to ***preclinical models; medical statistics; technology transfer, industrialisation and intellectual property; regulatory affairs****.*

The support has been ***professional, timely, creative, flexible and accurate.*** *Always ready to accommodate any request for the benefit of the project. All of this while maintaining a friendly and positive attitude.*
Thanks also to the mentoring support, ***my application was funded.***
In summary, the ***mentoring professionals are well trained, honest, patient and meticulous****. I believe they are an ideal choice for mentoring service provider."*

Worked Example 2

To be completed

Alessandro PRIGIONE

- Unmet need identified
- The support received
- Benefit of mentoring

Mentoring and application Timeline

Call opens

December 10, 2024

Informational webinar

December 17, 2024

January 14, 2025

Pre-proposal submission

February 13, 2025

Kick off Webinar

May 2025

1-on-1 meetings

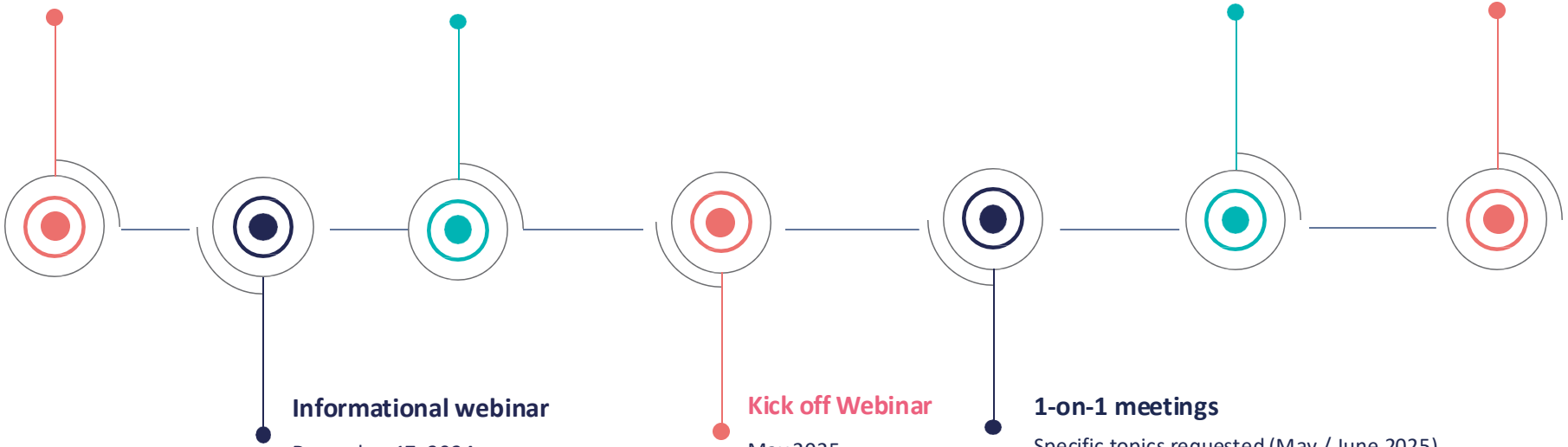
Specific topics requested (May / June 2025)

Full proposal submission

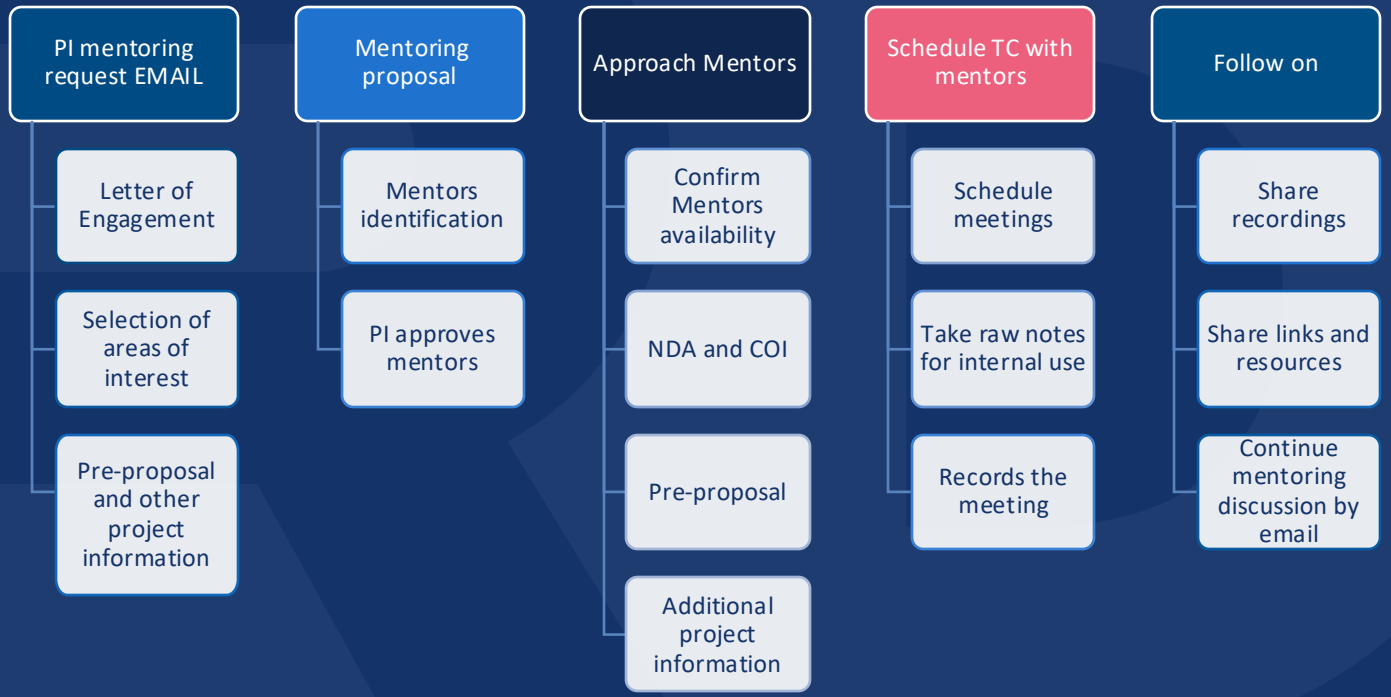
July 9, 2025

Decision

Dec 2025



One on one mentoring meetings



European Rare Diseases Research Alliance

Regulatory Support Service

Viviana Giannuzzi

JTC 2025 – 14 January 2025

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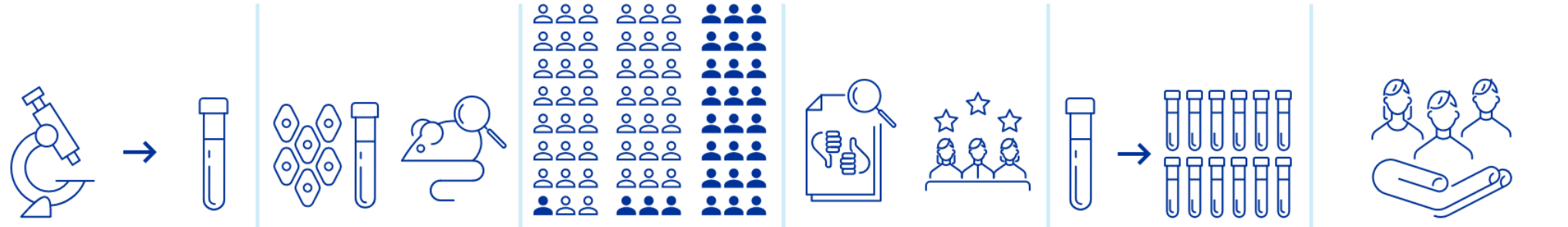
Developing medicines



- QUALITY
- SAFETY
- EFFICACY

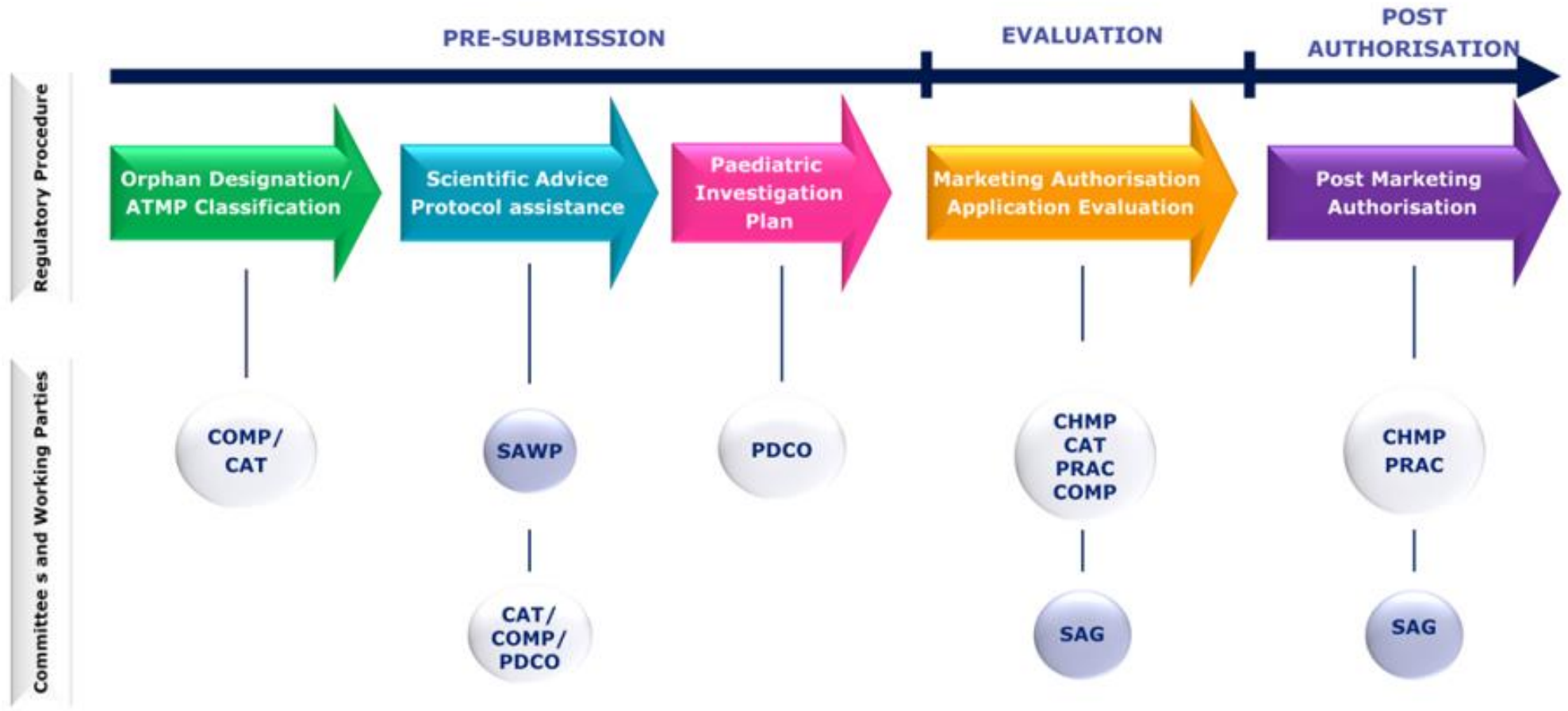
marketing authorisation
(centralised/non-centralised procedures*)

Academia more and more involved in R&D

European Rare Diseases Research Alliance

Source: EMA website

The European regulatory framework



Source: https://www.ema.europa.eu/en/documents/presentation/presentation-centralised-procedure-european-medicines-agency_en.pdf

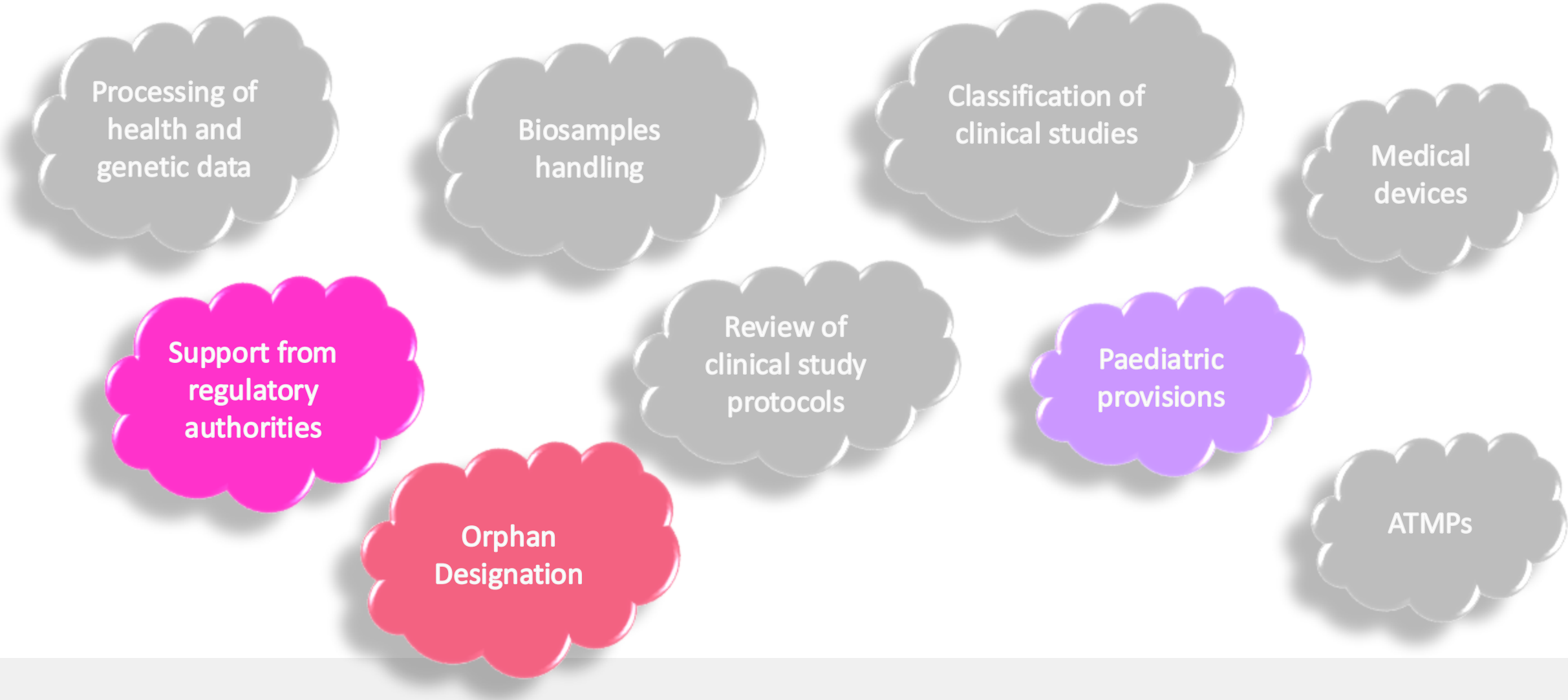
ERDERA Regulatory support service

Facilitate the engagement with regulatory agencies

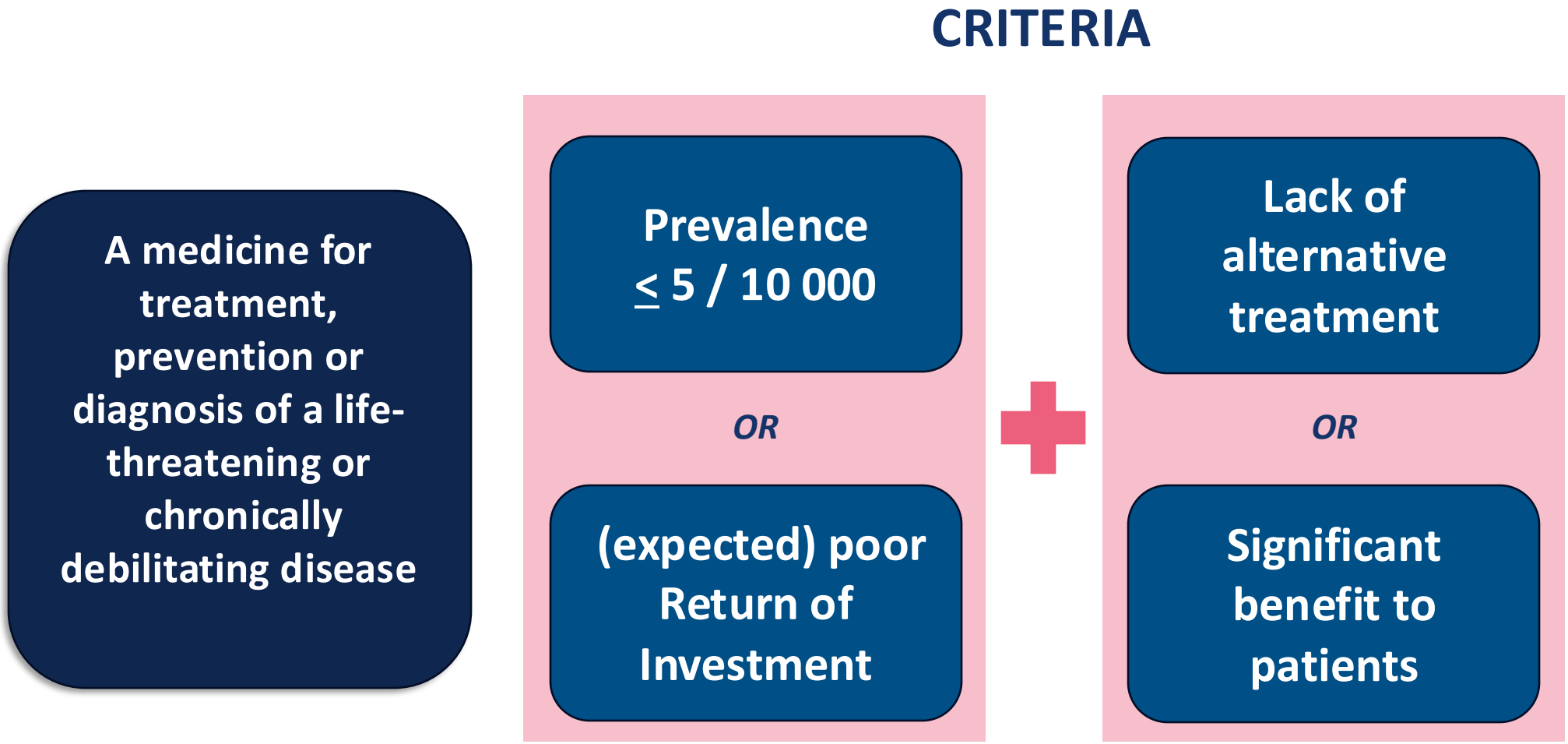
Preparatory activities to help identify the most suitable regulatory procedures

Regulatory support can be provided to produce **high-quality (non-clinical) data**

Regulatory issues relevant for RD community

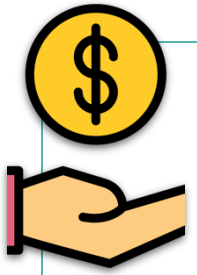


1- Orphan designation

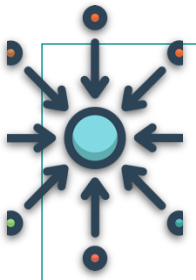


1- Orphan designation

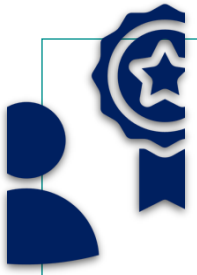
INCENTIVES & ADVNTAGES



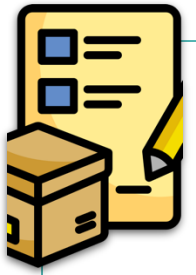
R&D financing through the EU or national fundings



Centralised EU MA



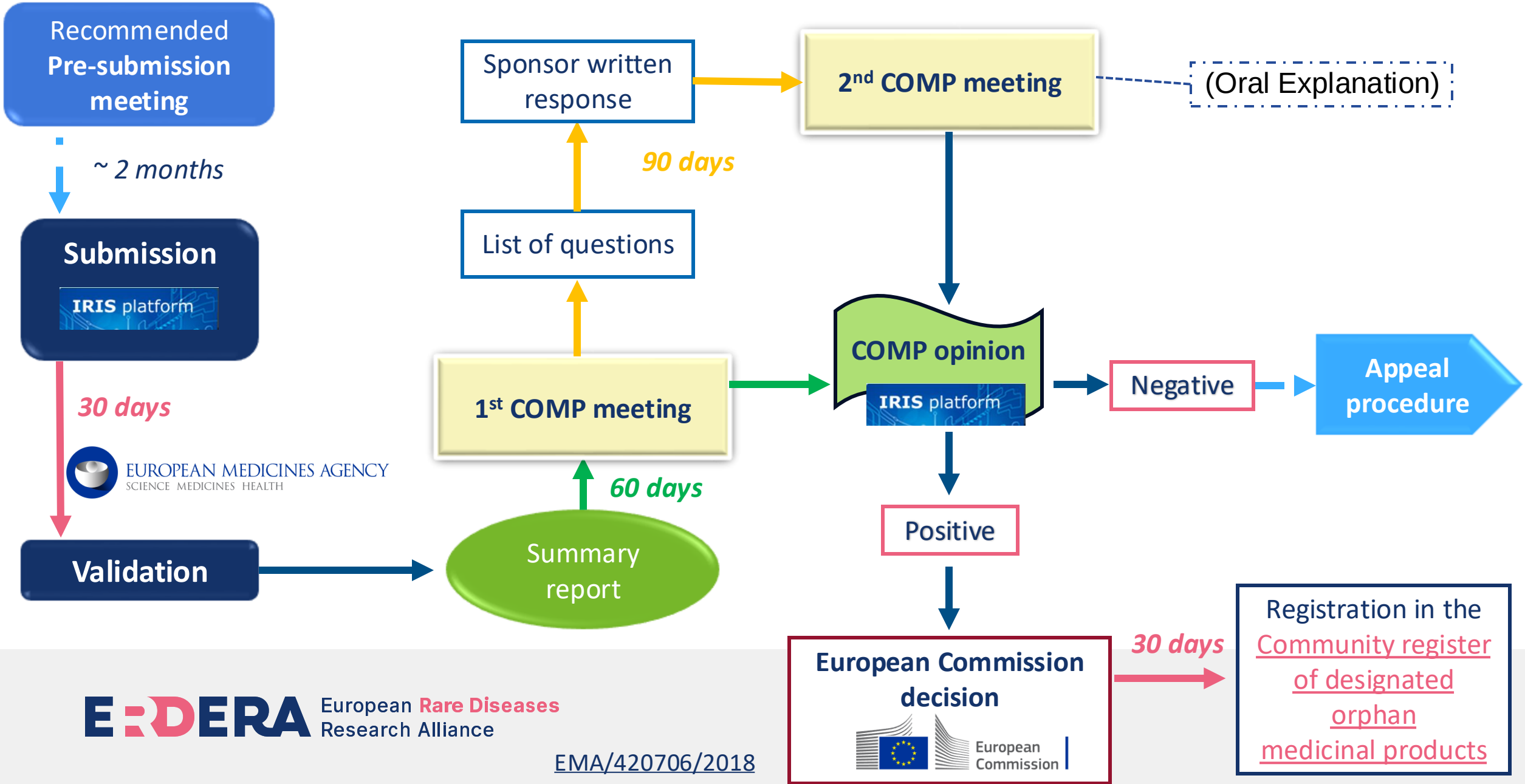
A monopoly period of 10 years market exclusivity



Protocol assistance

Fee reductions

1- Orphan designation



EURORDIS European Rare Diseases Research Alliance

1- Orphan designation

For more information about this

Innovation Management Toolbox

2- Support from regulatory authorities

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

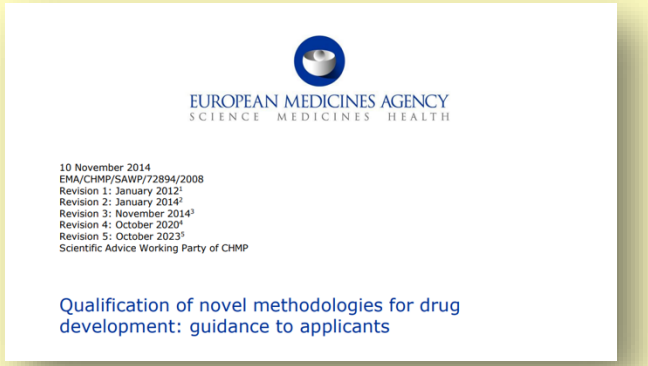
- Scientific Advice
- Innovation Task Force (ITF) Briefing Meeting with the EU-Innovation Network for innovative products
- PRIME

EMA website

2- Support from regulatory authorities

SCIENTIFIC ADVICE/PROTOCOL ASSISTANCE

- Guidance on methods and study designs (clinical and non-clinical aspects, methodology)
- Responding to specific questions
- At any stage of a medicine's development
- For orphan medicines ⇨ protocol assistance
- Free of charge for paediatric-related issues


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 November 2014
EMA/CHMP/SAWP/72894/2008
Revision 1: January 2012[1]
Revision 2: January 2014[2]
Revision 3: November 2014[3]
Revision 4: October 2020[4]
Revision 5: October 2023[5]
Scientific Advice Working Party of CHMP

Qualification of novel methodologies for drug development: guidance to applicants

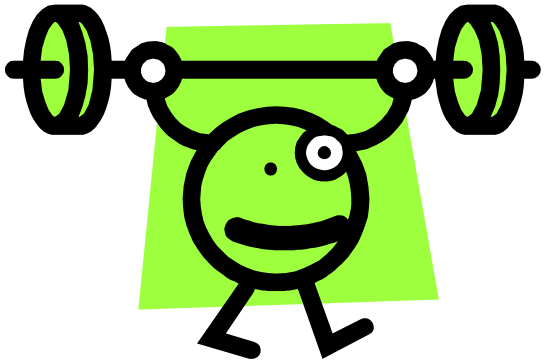
Acceptability of specific use of proposed innovative methods/tools not yet integrated in medicines R&D and clinical management, based on assessment of submitted data

EMA website

2- Support from regulatory authorities

EMA applications for innovative medicines & unmet needs

Innovation Task Force (ITF) briefing meetings: early dialogue with applicants (SMEs, academics, researchers) on innovative aspects in medicines development ⇨ informal exchange of information and guidance



PRIME: priority medicines designation for early and proactive support to SMEs and academia to develop medicines targeting conditions with unmet medical needs

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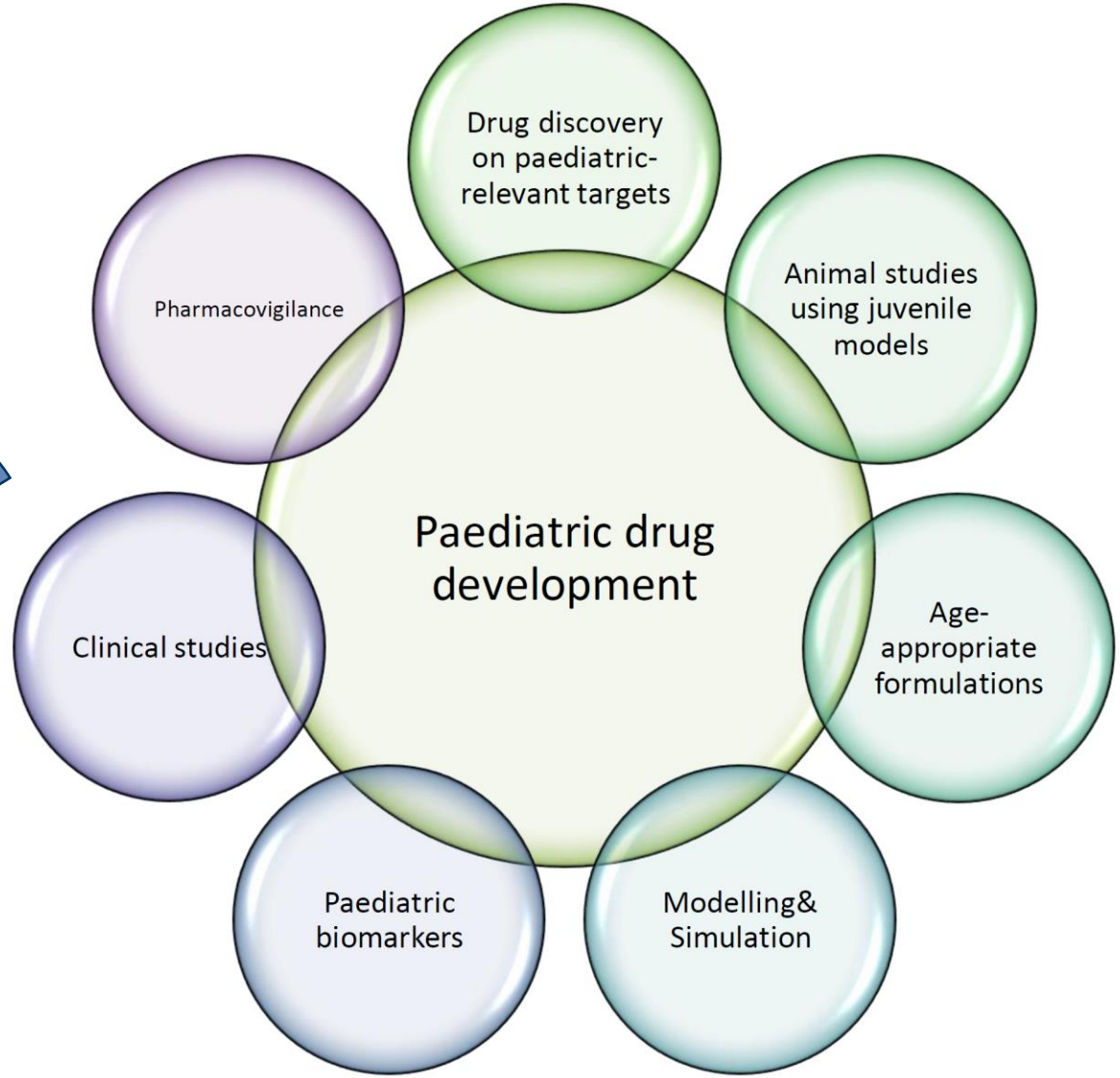
SCIENCE MEDICINES HEALTH

3- Paediatric provisions



All these data are intended to be included in documents for regulatory agencies

Paediatric Investigation Plan (PIP)

What is

- **A research & development** programme **focused on the development** and **authorisation** of medicines for children
- Details to demonstrate **quality, efficacy and safety** of the medicinal product for a therapeutic indication in the paediatric population

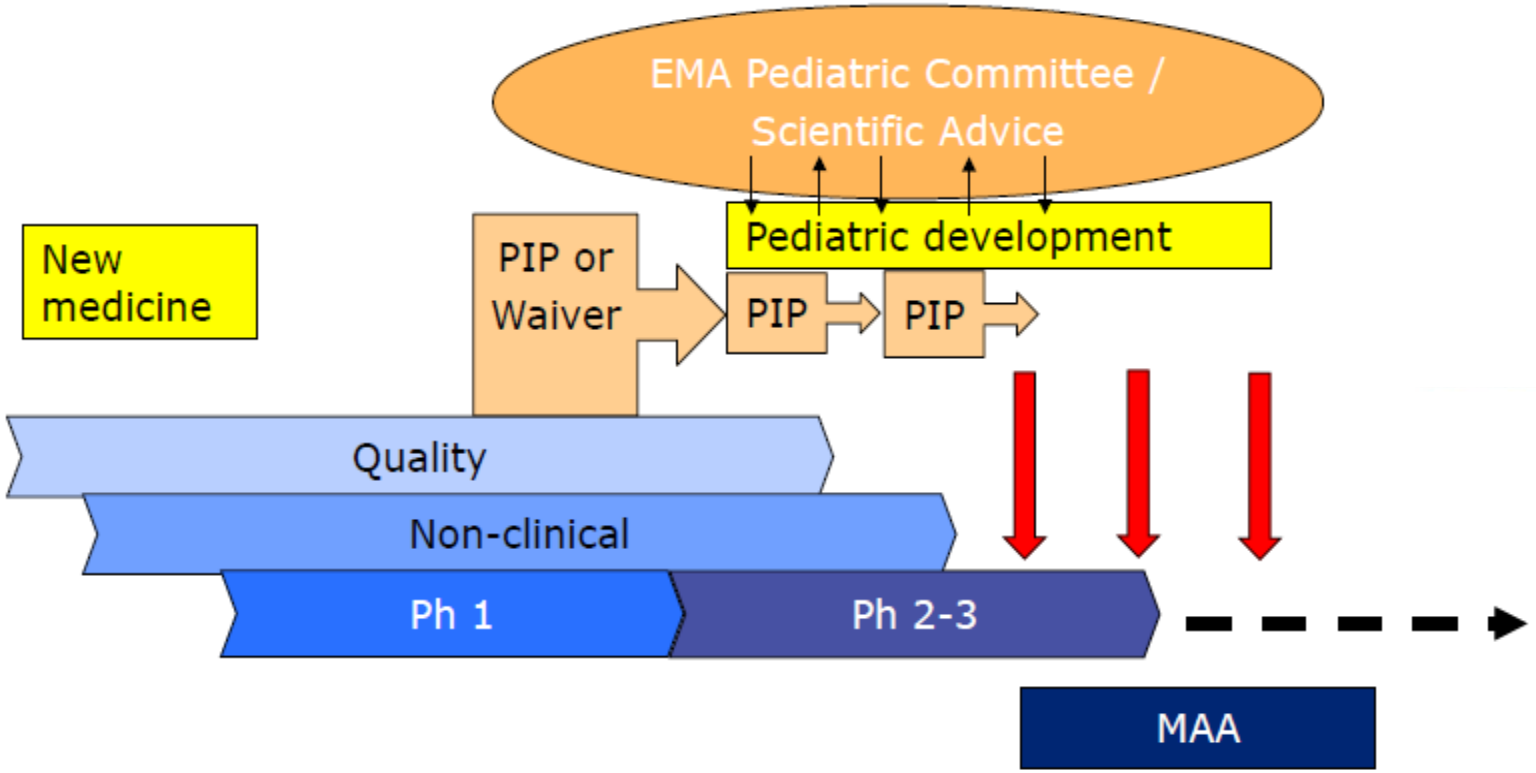
Aim

- Ensure availability of paediatric data and results
- Cover the needs of all age groups of children

Content

- which (sub)populations need to be studied
- proposed **timing** and **measures**
- measures to **adapt the formulation** of the medicinal product
- how to ensure the **long-term follow-up** of possible adverse reactions and efficacy

3- Paediatric provisions



Need for juvenile animal studies?

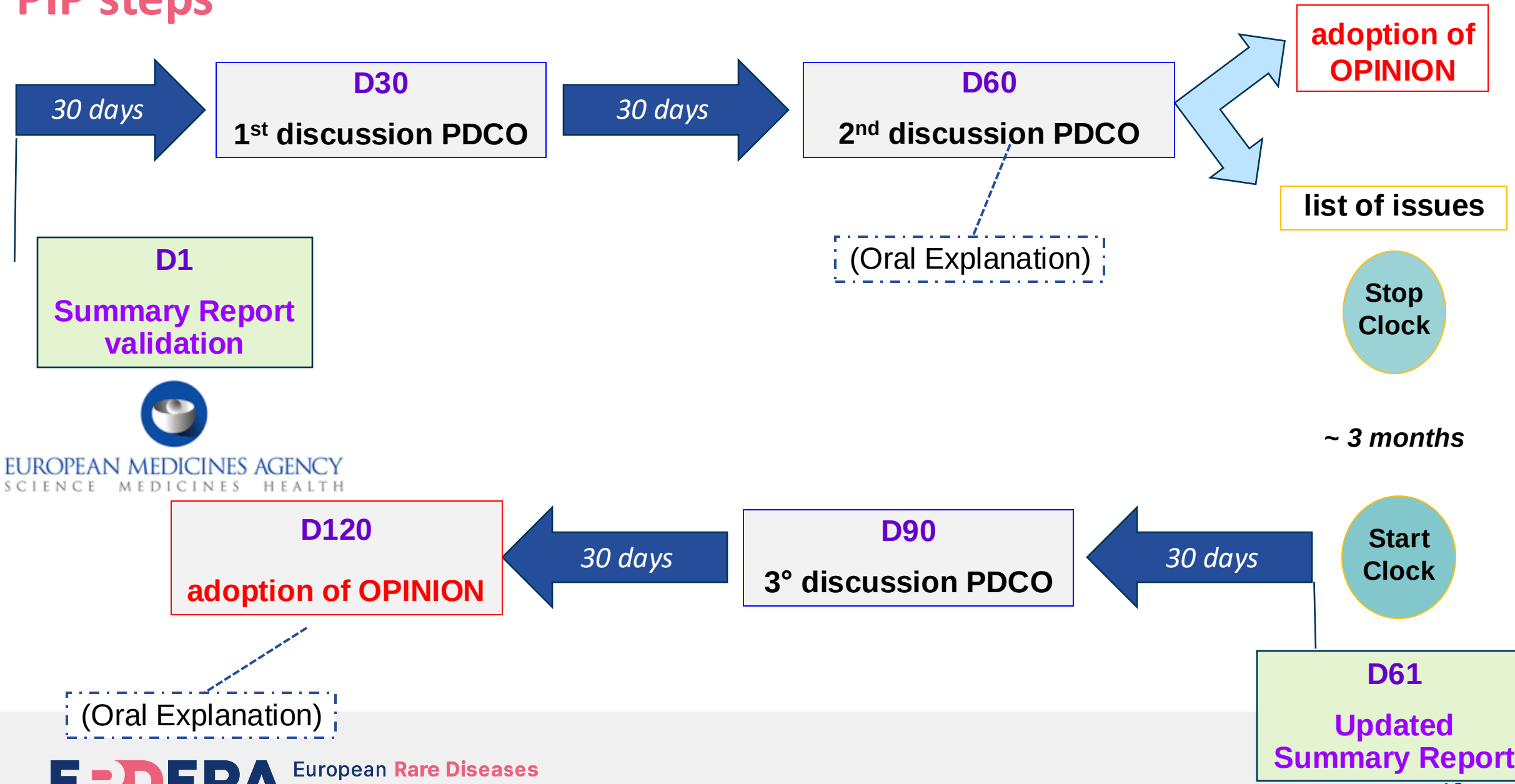
European Medicines Agency

London, 24 January 2008
Doc. Ref. EMEA/CHMP/SWP/169215/2005

COMMITTEE FOR HUMAN MEDICINAL PRODUCTS (CHMP)

GUIDELINE ON THE NEED FOR NON-CLINICAL TESTING IN JUVENILE ANIMALS OF PHARMACEUTICALS FOR PAEDIATRIC INDICATIONS

PIP steps


30 days
D30
1st discussion PDCO
30 days
D60
2nd discussion PDCO
adoption of OPINION
list of issues
(Oral Explanation)
D1
Summary Report validation
Stop Clock
~ 3 months
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
D120
adoption of OPINION
30 days
D90
3° discussion PDCO
30 days
Start Clock
(Oral Explanation)
D61
Updated Summary Report

PIP outcomes

PIP completed

verification that measures (studies) and timelines agreed in a PIP have been conducted in accordance with the decision **('compliance check')**

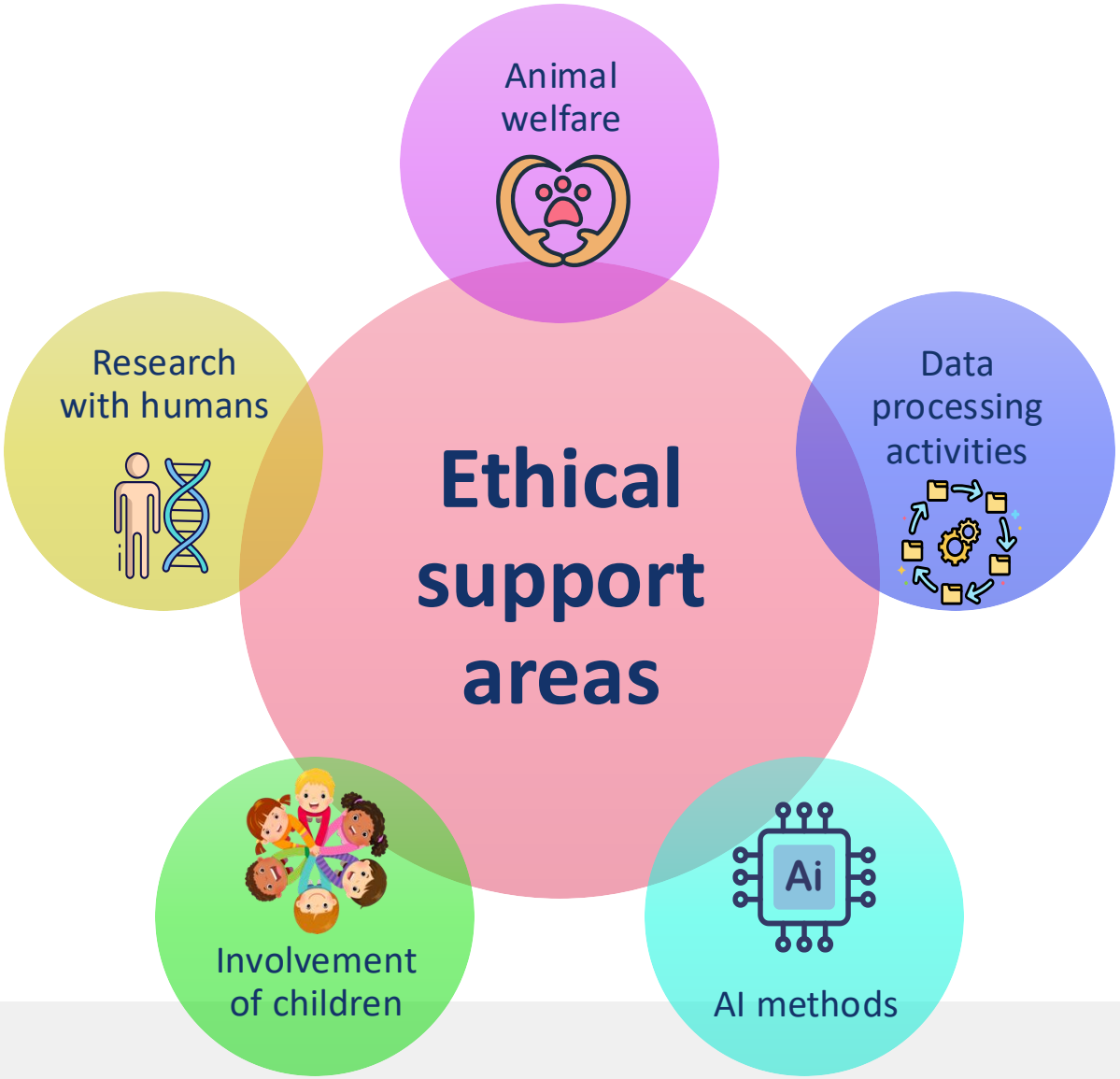
all information submitted to regulatory authorities

the medicinal product is authorised for paediatric use

Ethics support: from ERDERA Ethics Advisory Group

To **guarantee and support ethical compliance in all project activities** during the implementation and throughout their research phases

Through the ethics follow up



European **Rare Diseases** Research Alliance

Thank you!

Viviana Giannuzzi, Fondazione per la Ricerca Farmacologica Gianni Benzi onlus

vg@benzifoundation.org

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Methodological validity of the proposals Quality of research and data

Ralf-Dieter Hilgers / Rima Nabbout

JTC Call 2025

"Pre-clinical therapy studies for rare diseases using small molecules and biologicals – development and validation."

Methodological Support, WP19

Pre-clinical therapy studies for rare diseases using small molecules and biologicals – development and validation.

Projects should address at least two of the following

- Development of **novel therapies in a pre-clinical setting.**
- Creation and **validation** of predictive and pharmacodynamic biomarkers.
- **Replication of pre-clinical findings** to enhance reliability.
- **Pre-clinical proof-of-concept studies** for therapy readiness.

General Situation Preclinical Settings

Animal Studies Do Not Reliably Predict Human Outcomes

Nine Out of Ten Drugs That Appear Promising in Animal Studies Go on to Fail in Human Clinical Trials

Reliance On Animal Experimentation Can Impede and Delay Discovery

Animal Studies are Flawed by Design

Begley, C., Ellis, L. Raise standards for preclinical cancer research. *Nature* **483**, 531–533 (2012).

van der Worp HB, Howells DW, Sena ES, Porritt MJ, Rewell S, O'Collins V, et al. (2010) Can Animal Models of Disease Reliably Inform Human Studies? PLoS Med 7(3): e1000245.

https://aavs.org/animals-science/problems-animal-research/

Biostatistical Support in Design and Analysis is mandatory (Provided by WP19)

Novel therapies in a pre-clinical setting

Translational aim:

Animal Experiment should be informative for trials in humans

Establish the No Adverse Effect Level (NOAEL) in various animal models as a basis for the starting dose for first in human trials.

Support:

- Develop a research question and operationalization is statistical methodology
- Sample Size Justification
- Layout, e.g. Bias reduction
- Statistical Analysis
- Interpretation of Data

Begley, C., Ellis, L. Raise standards for preclinical cancer research. *Nature* **483**, 531–533 (2012).

van der Worp HB, Howells DW, Sena ES, Porritt MJ, Rewell S, O'Collins V, et al. (2010) Can Animal Models of Disease Reliably Inform Human Studies? PLoS Med 7(3): e1000245.

Shen, J., Swift, B., Mamelok, R., Pine, S., Sinclair, J. and Attar, M. (2019), Design and Conduct Considerations for First-in-Human Trials. Clin Transl Sci, 12: 6-19. https://doi.org/10.1111/cts.12582

validation of biomarkers

Translational aim:

validation of predictive and pharmacodynamic biomarkers

Consultation in Design and Analysis of Animal Experiments reflecting 3R principle specifically with respect to

Support:

- Develop a research question and operationalization is statistical methodology
- Sample Size Justification
- Layout, e.g. Bias reduction
- Statistical Analysis
- Interpretation of Data

https://www.bfr.bund.de/en/3r_principle-194147.html

Pre-clinical proof-of-concept studies

Consultation in Design and Analysis of Animal Experiments reflecting 3R principle specifically with respect to

Support:

- Develop a research question (**feasibility, or potential efficacy**) and operationalization is statistical methodology
- Sample Size Justification
- Layout, e.g. Bias reduction
- Statistical Analysis
- Interpretation of Data

Methodological Support, WP19

Contact R Nabbout, G Molenberghs

Mentoring in Cooperation with EATRIS WP with respect to design and analysis of preclinical trials

ERDERA
European Rare Diseases
Research Alliance

Making Europe a world-leader in rare diseases research and innovation

Data Standards and FAIRification

ERDERA Data Services Hub (DSH)
Marco Roos (presenter, FAIRification advisor)
Ana Rath, Ronald Cornet, Dimitrios Athanasiou (DSH co-leaders)
Heena Lad (DSH coordination support, ERDERA Coordination)

JTC 2025 webinar 14th of January 2025

Co-funded by
the European Union

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Outline

Joint Transnational Contributions to the Data Ecosystem of ERDERA

- **Recommendation on the lines on Data Management to include in your JTC project preproposal**
- **Why a Data Management Plan to contribute to the European Rare Disease Research Alliance?**
  - The **benefit** of data ready for automated use & reuse
  - The **problem** of data **not** ready for automated use & reuse
  - **Solutions** from engaging with the ERDERA Data Services Hub
- **Your questions**

Recommendations for your pre-proposal

If your project will collect or generate data…

- **Include some lines on Data Management** (e.g. 3-5)
  More possible, e.g. if your project is about Data or Data Reuse
- **Indicate your commitment to contributing data / data functions to the RD Data Ecosystem* of the European Rare Disease Research Alliance**

* encompassing the 'Data Hub' (origin: ERDERA) and 'Virtual Platform' (origin: EJP RD)

Recommendations for your pre-proposal

If your project will collect or generate data…

Consider to mention

- what data will be collected or produced (NB research results are data too)
- the use of ERDERA Data Hub Services
  (guidelines, data models, tools, federation infrastructure, repositories for sharing data/specimen)
- the role of 'FAIR Data Steward' (assigned to consortium members)
- FAIR competence in the consortium, if present (not an *a priori* requirement)
- if your commitment will be
  - **'Do It Yourself':** consortium is competent and chooses to contribute without help
  - **'Do It Together':** you commit time and effort to co-create your contribution
- uses of the RD Data Ecosystem after adding your data / new functions

Additional consideration for the full proposal (heads-up):

- processes for making data secure, accurate, available under which conditions

* encompassing the 'Data Hub' (origin: ERDERA) and 'Virtual Platform' (origin: EJP RD)

Why contribute to the Rare Disease Data Ecosystem ?

Benefits for rare disease research

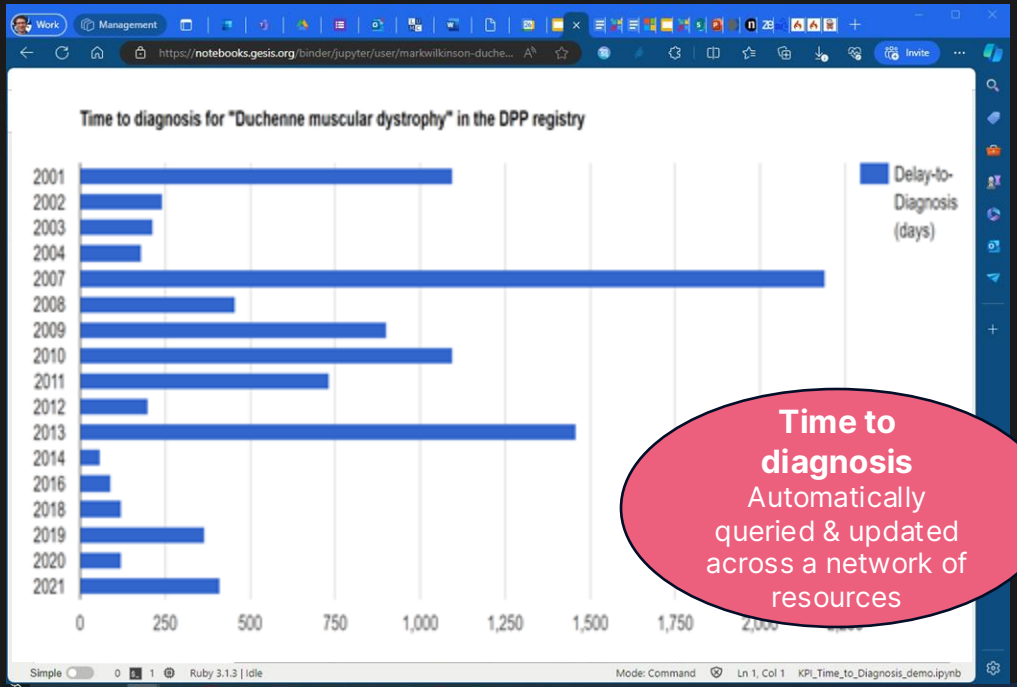
on behalf of People Living With a Rare Disease (PLWRD)

Reusing **FAIRified** data sources that implemented the guidelines for the EJP RD Data Ecosystem

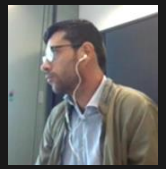
As a patient, I am happy to see that the RD data ecosystem can do automated calculations for our benefit!

WP7 knowledge map

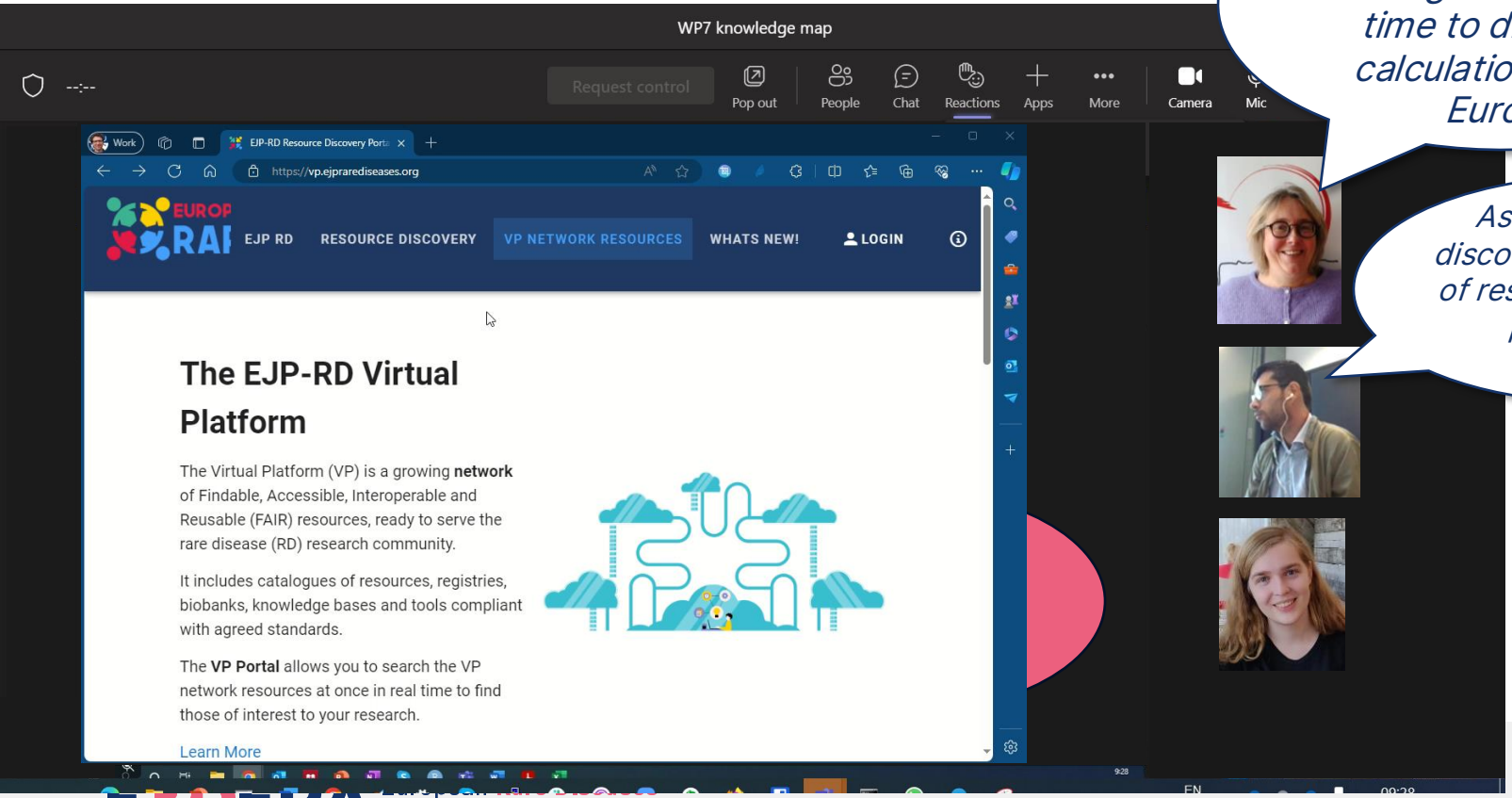
Request control | Pop out | People | Chat | Reactions | Apps | More | Camera | Mic



Time to diagnosis
Automatically queried & updated across a network of resources



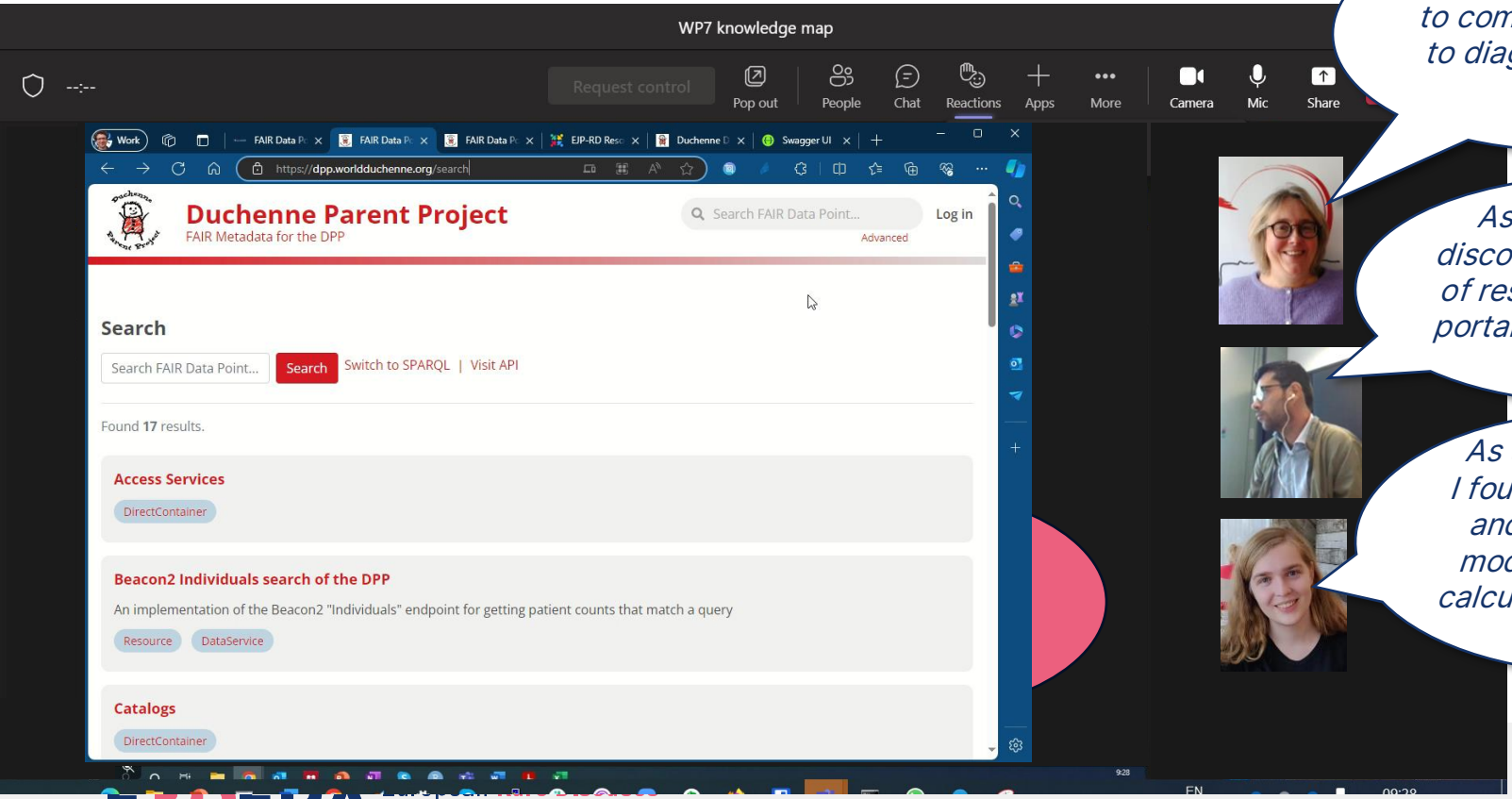
Reusing **FAIRified** data sources that implemented the guidelines for the EJP RD Data Ecosystem



As a patient representative, I asked for a regular up-to-date time to diagnosis calculation across Europe

As a researcher, I discovered many types of resources via a user portal on the ecosystem

Reusing **FAIRified** data sources that implemented the guidelines for the EJP RD Data Ecosystem



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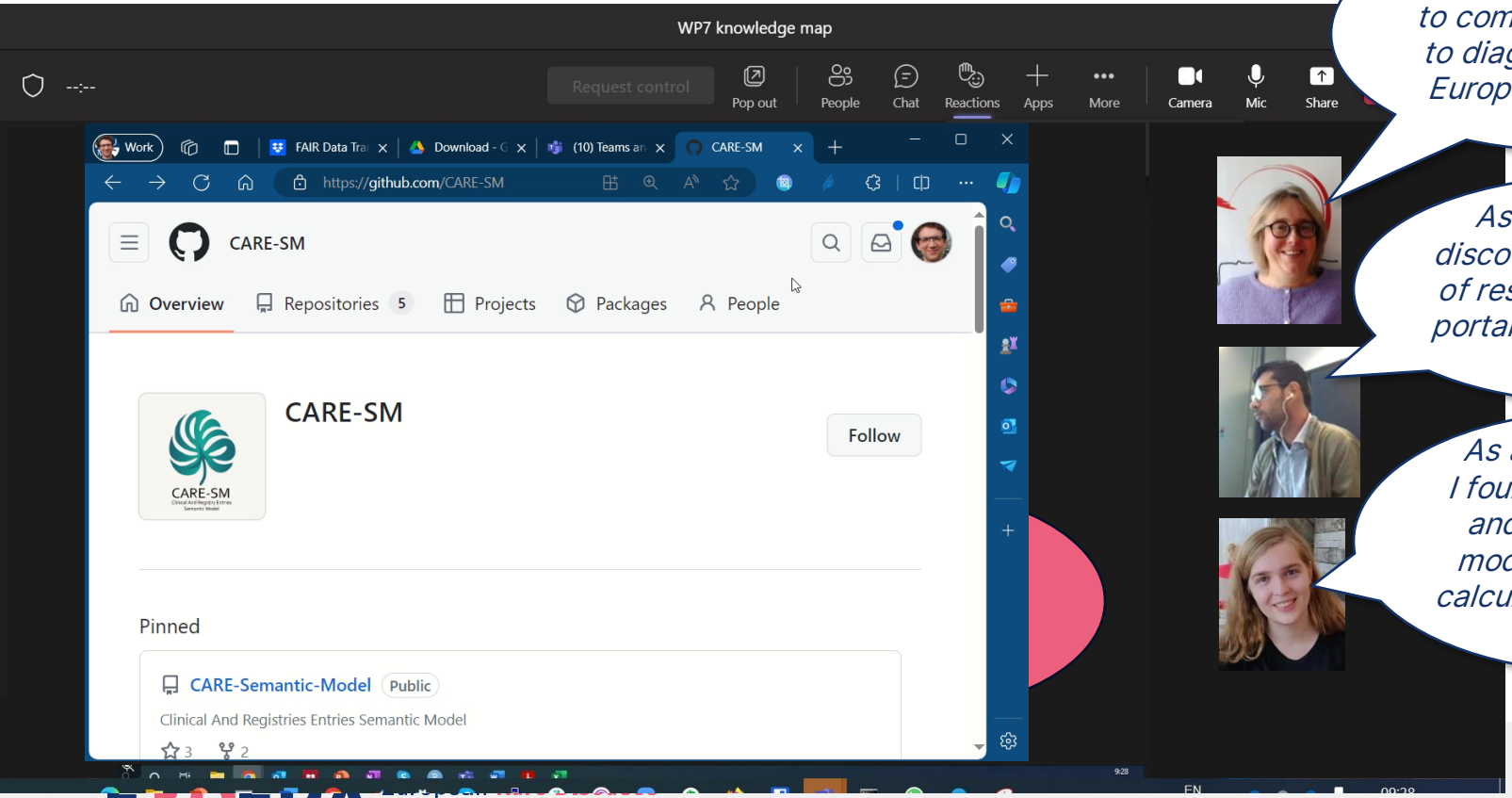
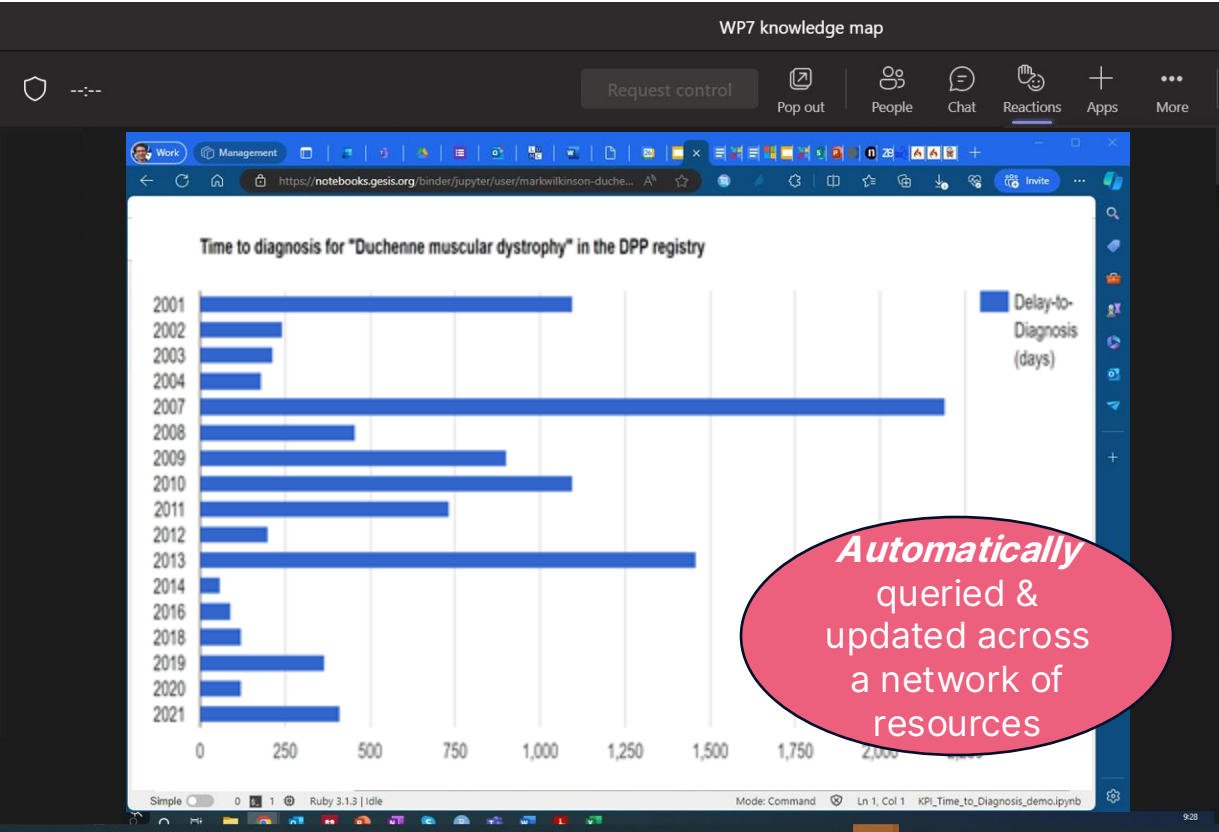


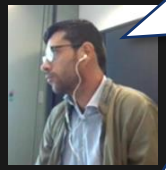
Reusing **FAIRified** data sources that implemented the guidelines for the EJP RD Data Ecosystem



Automatically queried & updated across a network of resources

As a patient, I am happy to see that RD registries enabled automating calculations for our benefit!

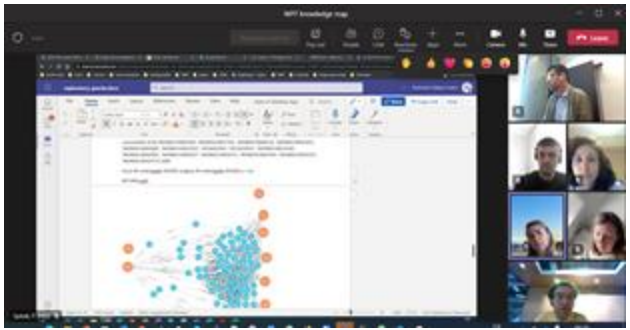
As a researcher, I discovered many types of resources via a user portal, including patient registries



As a data scientist, I used a common API and semantic data models to automatically find & use data across the ecosystem

... automatically filtering on data use conditions that allow my purpose

Other examples of potential automated use of the RD data ecosystem (non-exhaustive list)

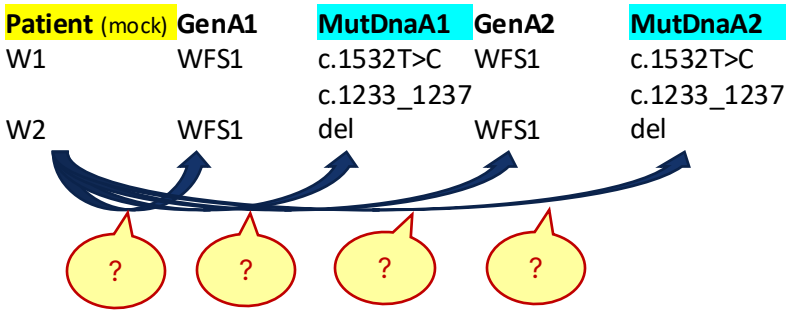


- Generate bio/clinical hypotheses *in real time*
- Machine learning across the ecosystem
- Collect evidence for the regulatory process
- Suggest possible diagnoses, genes, pathways, treatments, repurposable drugs, with evidence
- Collaborative scenarios with industry
- **What is your scenario!**

Why contribute? Problem of data unprepared for reuse

Example of data brought to a workshop

MutDnaA1	Finding_molecular genetic	nucleotide	c.
c.1532T>C	UBE3Adel	631+1 G>T	386dupC
c.1233_1237del	PAH deletion		2314G>A



Data ≠ (Re)Usable data

Once valuable data loses its value

Recommended for projects

to drive forward research questions to fruition and complement research outcomes

Standardise your data generation/collection approach

Engage with the ERDERA Data Services Hub to contribute conform to shared guidelines and specifications

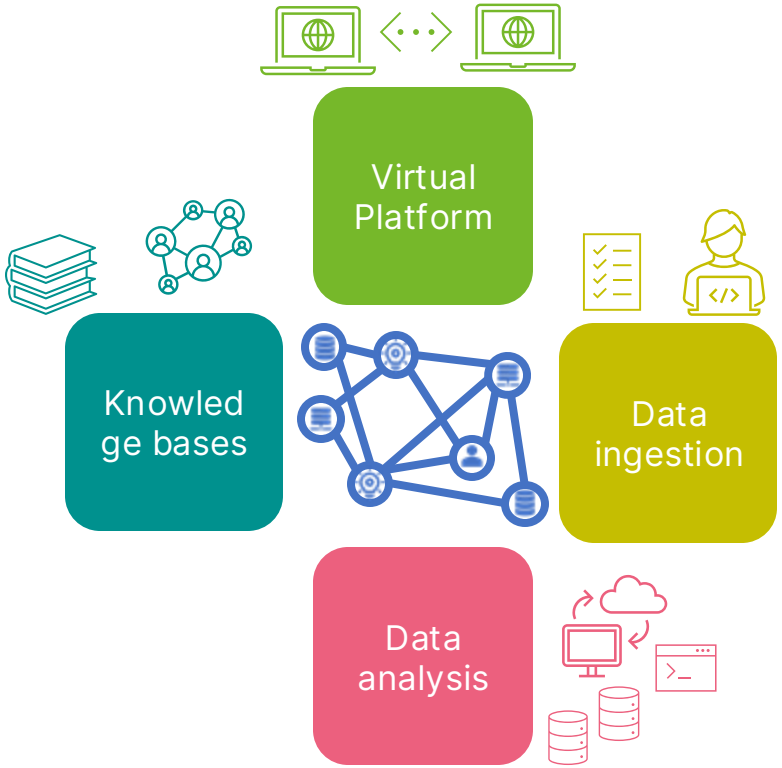
Access training and other support resources available in the ERDERA RD ecosystem

Data Services Hub offers **solutions** for

"Now! *That* should clear up a few things around here!"

- Standardising the descriptions of
  - F data sets **to automate finding resources**
  - A access protocols **to automate communication with data sources**
  - I data records (values, what they mean, how they relate to one another) **to automate query and analysis across the network**
  - R data use and access conditions **to automate filtering on resources that are safe to use**
- Federated Data and Analysis Infrastructure **to send questions, and receive and combine answers across the network** (under defined conditions)
- Guiding data producers to conform to shared standards and contribute to the ecosystem
- Collaboration to co-create new data and functionalities to the Data and Analysis ecosystem **for the benefit of PLWRD**

Data Services Hub support for building the ecosystem



- **RD Virtual Platform (RD-VP)** federated ecosystem to access and find data
- **Data readiness** standards ensuring data are F+A+I+R for automated use
- **Data sharing and federated analysis** of genome-phenome data
- **RD knowledge bases and ontologies** adding value to data in the RD ecosystem

Recommendations for your pre-proposal

If your project will collect or generate data…

- **Include some lines on Data Management** (e.g. 3-5)
  More possible, e.g. if your project is about Data or Data Reuse
- **Mention what data will be collected or produced**
  (NB research results are data too)
- **Indicate your commitment to contributing data / data functions to the RD Data Ecosystem* of the European Rare Disease Research Alliance**

* encompassing the 'Data Hub' (origin: ERDERA) and 'Virtual Platform' (origin: EJP RD)

European Rare Diseases Research Alliance

Thank you!

Recommendations for pre-proposal

- **Include 3-5 lines on Data Management**
- **Indicate your commitment to contributing data / data functions to the Data Ecosystem of the European Rare Disease Research Alliance**

Co-funded by the European Union

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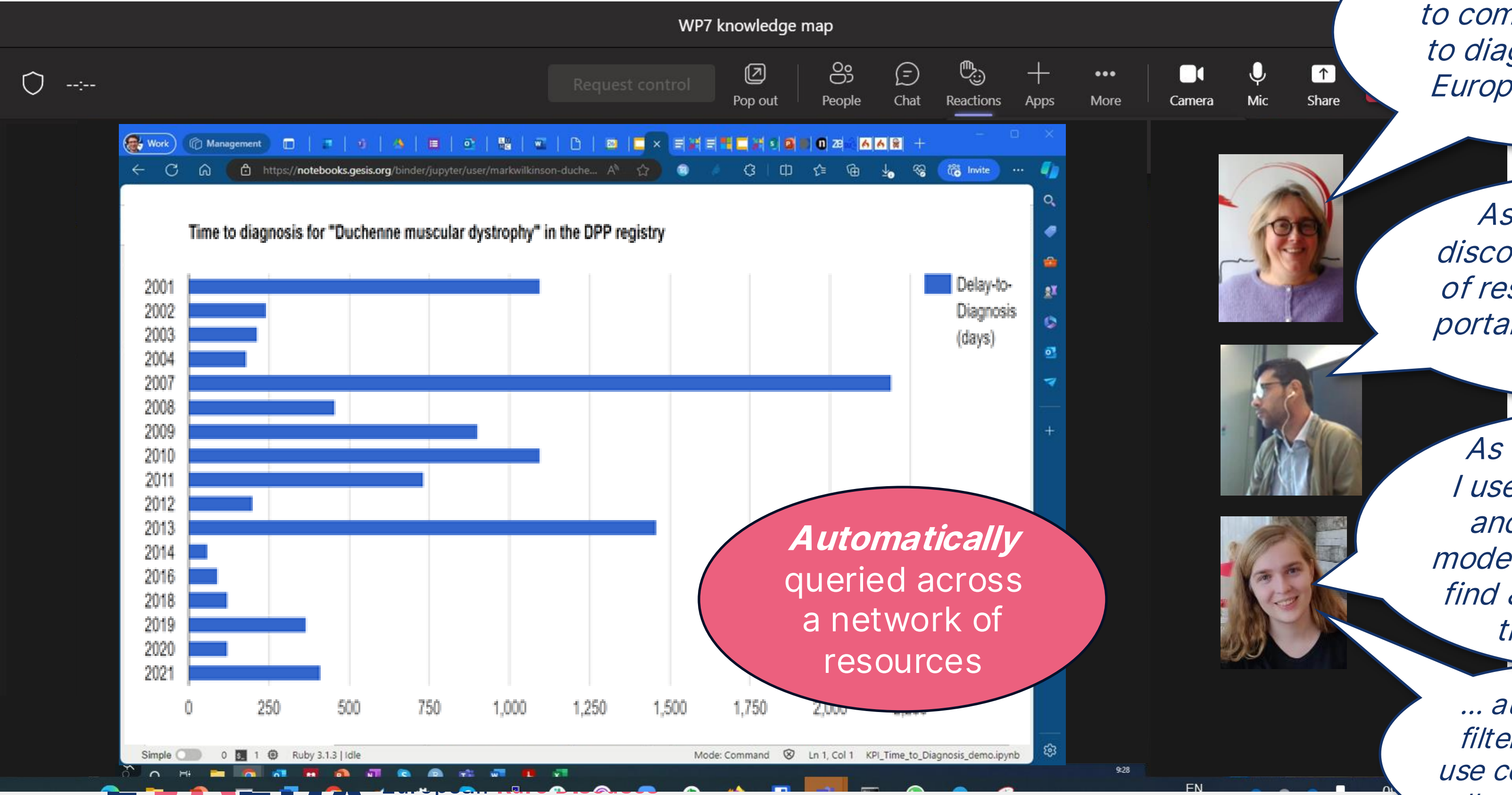
Services to use (and contribute to)

- Guidelines to help contribute data functions to the RD Data ecosystem
  - Standardised approach to data generation/collection
  - Common nomenclature, ontologies, and ontology-based data models ‘for machines’
  - Tools to deliver accessible and comprehensive metadata
    (machine actionable descriptions of what you share)
  - Federated analysis infrastructure for computational and automated applications to scale
- A platform to connect your stakeholders to a growing set of interconnected resources
  - Registries, genome-phenome databases, curated knowledge bases, molecular pathways, disease maps
- A platform for collaboration to add new capabilities for the benefit of PLWRD

Recap

- An example of the use of resources that contribute to a standards-based network of interconnected data resources
- Introduction to the ERDERA RD Data Services ecosystem

Reuse example of **RD registries collecting 'Common Data Elements' FAIRly**, including diagnosis & first hospital visit



Automatically queried across a network of resources

As a patient, I asked to compute the time to diagnosis across Europe in real time

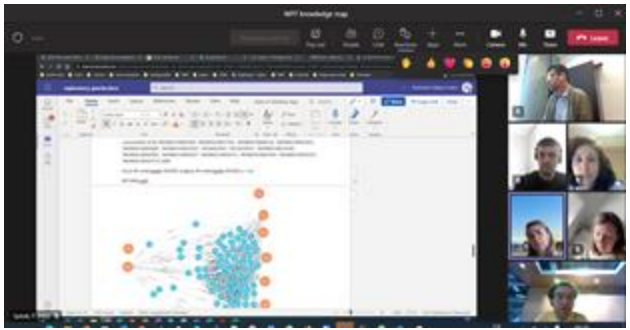
As a researcher, I discovered many types of resources via a user portal, including patient registries

As a data scientist, I used a common API and semantic data models to automatically find & use data across the ecosystem

... automatically filtering on data use conditions that allow my purpose

Research Alliance

Other examples of potential automated use of the RD ecosystem (*non-exhaustive list*)



- **Think of *your* scenario!**
- Real time hypothesis generation/evidence finding
- Continuous machine learning across the ecosystem
- Continuously update incidence statistics
- Suggest possible diagnoses, genes, pathways, treatments, repurposable drugs, with evidence
- Find clinical trials for patients & patients for trials
- Find and use authoritative mappings between codes
- Collaborative scenarios with industry

Opportunity to contribute to an **RD ecosystem**

It is vital that data collected for one goal are reused for other goals...

...using multiple sources of data as if all are in one database (but distributed in reality)

...by multiple stakeholders (patients, clinicians, data scientists, regulatory experts, policy makers)

... computationally Findable, Accessible, Interoperable, Reusable to boost research

Contribute as ERDERA partner to collaborative automated data exploration and analysis *by and on behalf of people living with a rare disease* (PLWRD)

ERDERA Data Services Hub RD ecosystem

Developed to facilitate data capture, integration, analysis and sharing across the RD community

FAIR (Findable, Accessible, Interoperable, Reusable) data sources

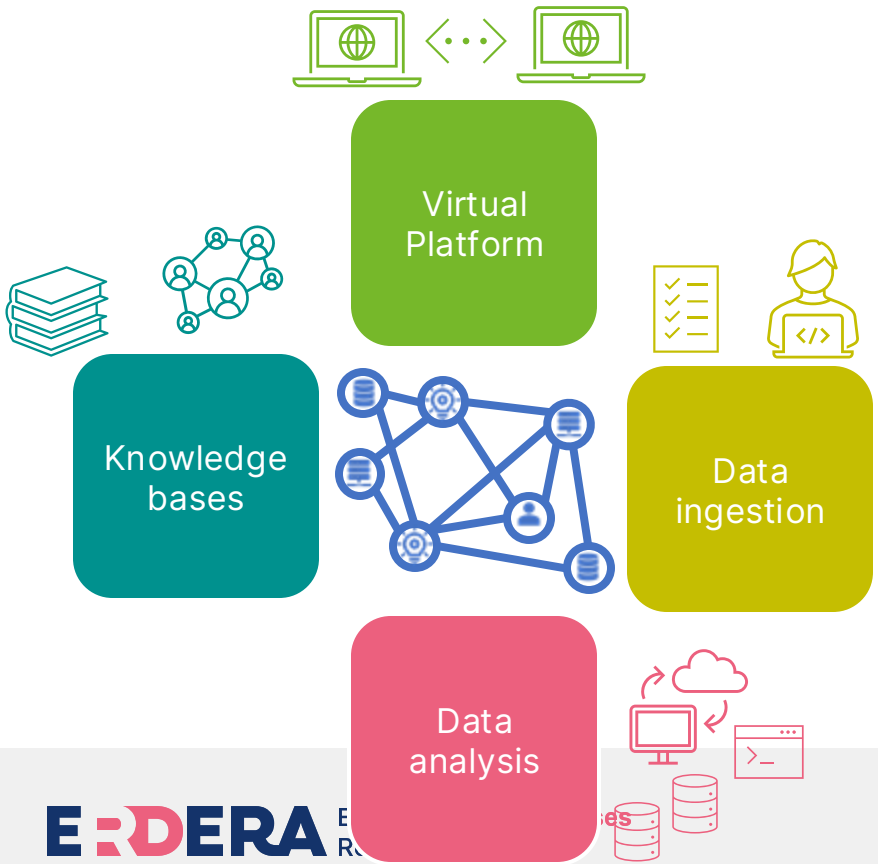
Data analysis pipelines

Knowledge bases

Federated data infrastructure - Virtual Platform

Towards enhancing the RD data and knowledge bases globally to benefit People Living With a Rare Disease (PLWRD)

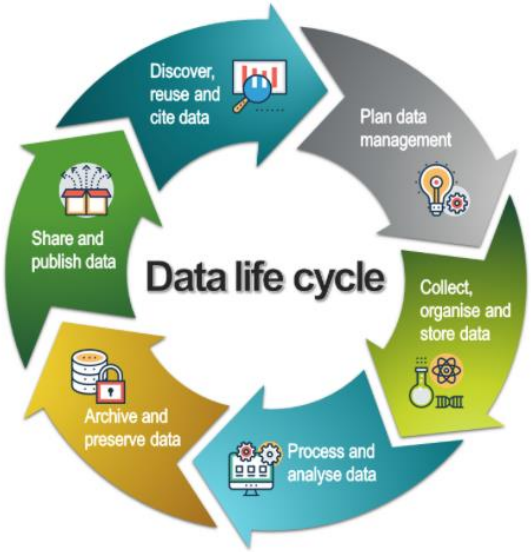
Data Services Hub RD ecosystem



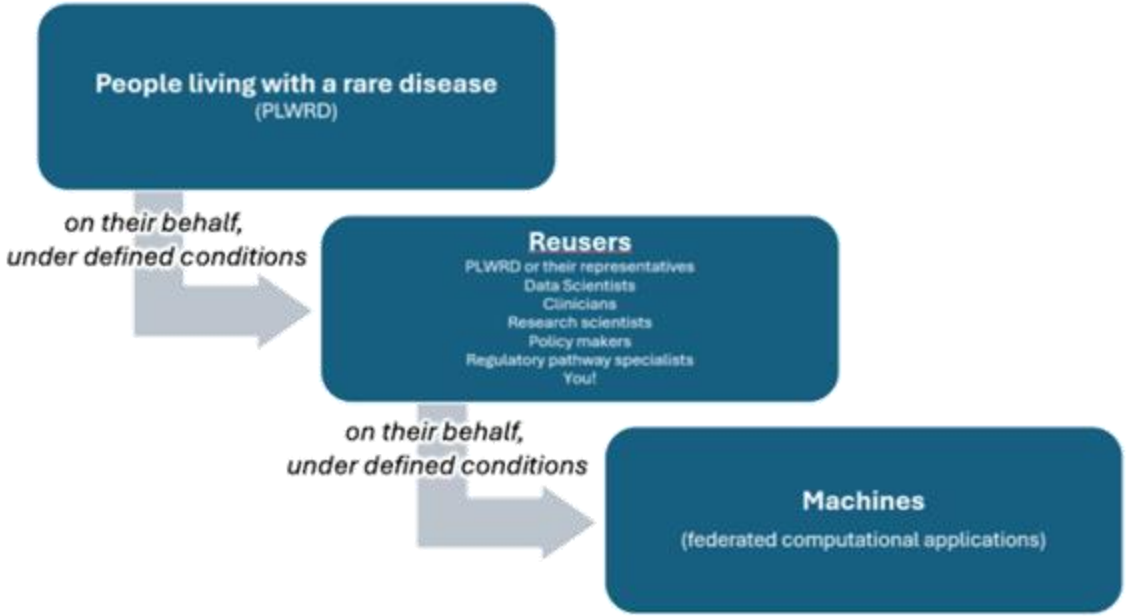
- **RD Virtual Platform (RD-VP)** federated ecosystem enabling to access and find RD data
- **Data readiness** adhering to standards and nomenclature ensuring data entering the RD-VP ecosystem are F+A+I+R for automated use
- **Data sharing and analysis** of genome-phenome data integrated into a federated infrastructure within the RD-VP
- **RD knowledge bases and ontologies** expanding and curating repositories, disease maps, semantic models and Patient-Centred Outcome Measures (PCOMs) across the RD ecosystem

Data Service Hub & RD-VP objectives

Facilitate data collection/generation by ERDERA partners that is sustainably standardised to enable automated finding, accessing, interoperating, and reusing for the benefit of PLWRD



Taken from www.slu.se/dms



Benefiting from the DSH RD ecosystem

- Minimal set of guidelines to facilitate FAIRification across the ERDERA RD ecosystem include:
  - Standardised approach to data generation/collection
  - Specified common nomenclature, ontologies, and ontology-based data models ‘for machines’
  - Tools to deliver accessible and comprehensive metadata (machine actionable descriptions of what you share)
  - Enabling computational and automated applications to scale
  - **Benefit to PLWRD and RD ecosystem sustainability**
- Enable multiple stakeholders to access a rich set of data services from the RD ecosystem to expand the utility of your service for PLWRD
- Access to a broad set of interconnected resources supporting your research in RD
  - Registries, genome-phenome databases, curated knowledge bases, molecular pathways, disease maps

Recommendations for proposals

JTC 2025: *"Pre-clinical therapy studies for rare diseases using small molecules and biologicals – development and validation"*

to improve the lives of People Living With a Rare Disease
contribute data that your project generates/collects to the RD data ecosystem by

Standardising your data generation/collection approach
Include the role of Data Steward

Engaging with the ERDERA Data Services Hub to implement guidelines and specifications for data ingested into the RD ecosystem and to exploit the results

Access training and resources available in the ERDERA RD ecosystem to drive forward research questions to fruition and complement research outcomes

Recommended activities to include

For data and functions that your project can contribute to the RD data ecosystem to increase the potential for improving the life of people living with a rare disease

Extending the RD data ecosystem with data and functionality.

Exploiting the results to drive new research and complement research outcomes.

Standardising your data generation / collection approach.

Applying international standards to make data and analysis functions Findable, Accessible, Interoperable, Reusable for automated federated analysis by you *and others.*

Engaging with the ERDERA Data Services Hub to conform to and extend the RD ecosystem's guidelines, specifications, and tools for ingesting data & analysis functions.

The role of Data Steward.

Designate responsibility and allocate effort and time to drive the contribution.

Applying Data Management training and policies available from ERDERA Expertise Services

Resources for implementation & training

Towards enhancing the RD data and knowledge bases globally to benefit PLWRD

Tools and guidelines for "Do It Yourself" contributions to the FAIR-based ecosystem
Recommended: always plan to engage with the ERDERA Expertise Hub to ensure a functional contribution

Online awareness training to advanced "Bring Your Own Data" workshops
Entry level webinars for FAIR project management; technical hackathon + training to learn, implement, exploit FAIR with experts

A platform for collaboratively adapting *YOUR TOOLS* and adopting *YOUR DOMAIN STANDARDs* to implement FAIR principles and evolve the ecosystem

Recommendation

Choose your mode of engagement

Do It Yourself (DIY)
Consortium includes proven experience with FAIR implementation conform to RD ecosystem guidelines.
Data Management plan elaborates on contribution to RD Data Ecosystem.

Do It Together (DIT) with ERDERA
Consortium designates data stewardship and project management roles.
Data Management Plan includes allocated effort & time for contributing to the RD Data Ecosystem.

You are unsure

Probably go for option 2

Let us know!
<e-mail address?>

References for contributing to the RD data ecosystem

Suggested reading, recommended to incorporate in Data Management Plan

DIY: describe their use in action plan; DIT: refer in general

Standardising your data generation / collection approach by FAIR standards.

Engaging with the ERDERA Data Services Hub to use and extend its services.

The role of Data Steward, include responsibility, effort and time to drive the contribution.

Applying Data Management training and policies available from ERDERA.

- RD Data Ecosystem vs 1.0 based on EJP RD Virtual Platform
  - VP Onboarding documentation
  - Deliverable 12.4 and the references therein <LINK?>
  - VP Specs <LINK?>
  - Stewardship information on EJP RD web site and VP Portal <LINKS>
- Anything from Solve-RD? <LINK>
- European Health Data Space framework <LINK>

Resources to consider for exploitation

Suggested to look at for inspiration

Optional: incorporate ideas in proposal (highly recommended by the DSH!)

Extending the RD data ecosystem with data and functionality.

Exploiting the results to drive new research and complement research outcomes.

- EJP RD VP Resource map, resources shown in the VP Portal, and FDP index
  - <LINKS>
  - Examples: WikiPathways, GPAP, ERN registries
- Resources that in ERDERA will be part of the RD data ecosystem too!
  - Other JTC projects
  - CRN projects
  - Clinical Trials conducted in ERDERA
- EU-funded FAIR projects

Optional, but highly recommended by the DSH!

Consider, especially for project data stewards

The role of Data Steward.

Designate responsibility and allocate effort and time to drive the contribution.

- Including data stewards joining
  - The ERDERA data steward network
  - The ERDERA reuser group to engage in and giving feedback on reusing other people's data

ERDERA

European **Rare Diseases** Research Alliance

Thank you!

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