# From Small Populations to Robust Evidence: EU Methodologies for Paediatric and Rare Disease Drug Development

# Insights from IHI RealiseD

Dr Solange Corriol-Rohou, MD, PhD

RealiseD
compRehensive mEthodological and operational Approach to cLinical trIalS in ultra-rarE Diseases

## TEDDY General Assembly & Scientific Meeting

18 - 20 September, 2026, University of Bari Aldo Moro, Bari, Italy

# Establishing novel methodological approaches to improve clinical trials for rare and ultra-rare diseases

## IHI Call 4/Topic 4

Ref. Ares(2023)7602356 - 09/11/2023

**Realise D**

compRehensive mEthodological and operational Approach to cLinical trIalS in ultra-rarE Diseases

**5 Year project**

**Kick off January 2025**

Coordinator: Prof. Ralf-Dieter Hilgers; Sigmund Freud University, Austria

Project Leader: Dr Solange CORRIOL-ROHOU, MD, PhD

https://realised-ihi.eu/

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# Public-Private Partnerships (PPPs)

- In 2022, a PPP was drafted and proposed to IHI on behalf of EFPIA, as part of the RD Moonshot Initiative ➔ IHI RealiseD
- In June 2022, EFPIA and EURORDIS call for a Moonshot for basic and translational research for adult and paediatric rare diseases.
- The RD Moonshot initiative was officially launched in Dec. 2022.

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RARE DISEASE MOONSHOT
SCALING UP PUBLIC-PRIVATE PARTNERSHIPS TO ACCELERATE RESEARCH IN RARE DISEASES




Do you want to know more about the Moonshot coalition?

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# IHI RealiseD Consortium

**29 Public Partners**
**11 Private Partners**

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

IQWiG




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# IHI RealiseD - Mission



RealiseD will implement a collaborative and comp**R**ehensive m**E**thodological and operational
**A**pproach to c**L**inical tr**I**al**S** in ultra-rar**E** **D**iseases

## Key Elements

- Focus on ultra-rare diseases ((U)RD)
- Establish Tools for Drug Development
- Develop design and analysis tools for (U)RD clinical trials • Strong Cocreation of the work and results (EMA & IQWIG & Academia & Industry & Patients)
- Cocreate tools for clinical trial with 6 stakeholders
- Deliver findings in playbooks

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# IHI RealiseD Objectives

## Objectives & 1st approaches

1. To enable patient **referral strategies** to minimize risk of enrolment failure for trials in (U)RD.
2. To **address the main hurdles of CT conception in (U)RD** and to articulate the need for innovation in CT methodology based on 4 use cases.
3. To provide a framework for **centre certification**.
4. To **evaluate and optimise various aspects of CT designs** for (U)RD, allowing comparative assessment; to enable quantitative comparison of various designs by developing models and assessment functions.
5. To **develop methodology to maximally extract information** from the available patients, on multiple and longitudinal outcomes; to enrich this knowledge base with relevant additional sources, including from natural history studies, related indications, real-word data, and multiple sources; to develop user-friendly, stable, and precise inference methods for sparse data.

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# IHI RealiseD Objectives

## Objectives & 1st approaches

6. To build a **dialogue with regulatory and HTA authorities on acceptance of evidence** generated by innovative designs and data sources, accommodating the role of qualification pathways and need for new pathways.
7. To **ensure and maximize the alignment between RealiseD work, output, and outcomes, and the overall RD ecosystem** including ERDERA) as well as other relevant initiatives, infrastructures, or projects.
8. To **ensure patient-centricity and enable co creation throughout the workflow**, with input of all stakeholders, thus maximising relevance and subsequent buy in to methodological and operational innovative approaches.
9. To **create and make accessible to the RD community playbooks that contain tools, methodological products, and other resources** for facilitating efficient design and adoption of innovative methodological approaches for CT in (U)RD, using a co-creation approach that will foster active engagement of project partners.

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# Expected Outcomes

**Playbooks for novel CTs for rare diseases /clusters of diseases**, to be also used for education/ training; co-created with and validated by regulators, HTA bodies and patients, including:

- Good practice recommendations and expert advice for multinational innovative studies, study protocols, EHRs driven registries and longitudinal natural history studies;
- Standardized processes across all disease areas, countries and sites for fast and reliable feasibility processes, allowing for example for early feasibility assessment to support design of feasible development programmes. Effectiveness assessment of optimised CT designs as compared to the 'gold-standard' CT design for rare diseases.
- Information to support clinical research network set up to conduct innovative trials including e.g., RWE, remote elements …

**Certified/qualified CT sites**

**Structured and predictable system of referral of patient** (physically and virtually) to expert centres

**Alignment and complementarity with the EU Rare Diseases Partnership** to create synergies and avoid overlaps.

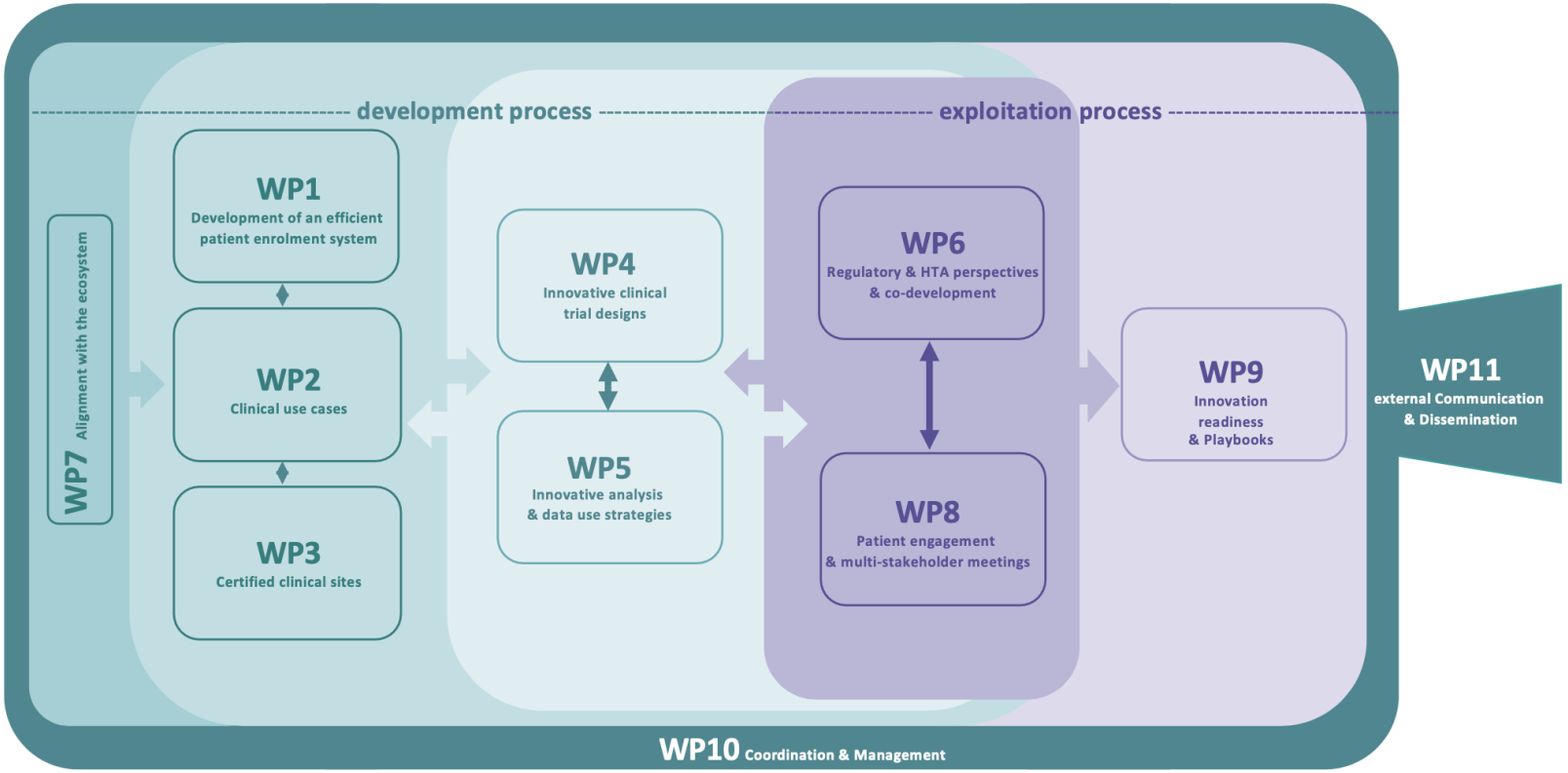
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# WorkPackage Structure




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# Alignment with the ecosystem – WP7 objectives

## 1 Ensure Ecosystem Alignment

Maximize alignment between RealiseD and the overall rare disease ecosystem, including ERDERA.

## 2 Structured Support

Implement processes for alignment and complementarity with relevant initiatives.

## 3 Capture Learnings

Maintain dialogue and accelerate dissemination through the Alignment Board and International Alignment Office.

## 4 Facilitate Adoption

Implement processes for open dialogue with public-private initiatives to ensure acceptance and uptake of results.

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# Multistakeholder collaboration

ERDERA
EUROPEAN RARE DISEASES RESEARCH ALLIANCE

**RealiseD WorkPackage 7**
**ECOSYSTEM ALIGNMENT**






# 11 projects funded under Horizon Europe







**Among these projects:**

•INVENTS is working on creating a comprehensive framework to improve the evaluation, assessment, and regulatory decision-making processes of new medicines targeting rare diseases, including paediatric rare diseases

•ERAMET aims to provide an integrated approach to support developers' and regulators' decision-making in the field of paediatric and orphan drug development

Horizon Europe EU funded projects: Rare Disease Day: discover 11 new projects funded under Horizon Europe - European Commission (europa.eu)

ACT EU: https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/accelerating-clinical-trials-eu-act-eu

# Insights from INVENTS



**Sarah Zohar,** PharmD, PhD
Director of Research at Inserm, Paris, FR
**INVENTS**

invents

https://invents-he.eu/

INVENTS is working on creating a comprehensive framework to improve the evaluation, assessment, and regulatory decision-making processes of new medicines targeting rare diseases, including paediatric rare diseases

The INVENTS program focuses on advancing the future evaluation of treatments and the regulatory decision-making for rare diseases (RD) including paediatric rare diseases.

https://invents-he.eu/

# Insights from ERAMET



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**ERAMET** Coordinator

https://www.erametproject.eu/

# ERAMET

Advancing Paediatric and Orphan Drug Development through Innovative Modelling and Simulation

The INVENTS program focuses on advancing the future evaluation of treatments and the regulatory decision-making for rare diseases (RD) including paediatric rare diseases.

https://www.erametproject.eu/

How innovative methodologies can support evidence generation in paediatric and other small populations, with particular attention to methodological maturity, regulatory qualification and practical implementation.

- Which evidence-generation challenges are shared across small populations?
- Which methodologies are already sufficiently mature for application?
- What is needed to support their qualification, regulatory acceptance and wider use?
- How can these approaches become more accessible to smaller paediatric projects and developers?






TEDDY - European Network of Excellence for Paediatric Clinical Research

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