

ERN-RND Scientific Symposium 2026

REGISTRIES FOR RND

10th October 2026
Rome, Italy



**European
Reference
Network**

for rare or low prevalence
complex diseases

 **Network**
Neurological Diseases
(ERN-RND)

www.ern-rnd.eu | info@ern-rnd.eu



**European
Reference
Network**

for rare or low prevalence
complex diseases

 **Network**
Neurological Diseases
(ERN-RND)



PROGRAMME

Saturday 10 October

SESSION 1

Framework for RND Registries

TIME (CET)	TOPIC	SPEAKER
08:00	Welcome and overview of ERN-RND activities	Holm Graessner / Ludger Schöls / symposium chairs
08:05	----- KEYNOTE ----- Why Registries Matter for Rare Neurological Diseases: from Natural History to Trial Readiness	Thomas Klockgether , German Centre for Neurodegenerative Diseases (DZNE), University Bonn, Germany
08:35	Framework for Multistakeholder Patient Registries in the Field of Rare Neurological Diseases	Nicole Wolf , Amsterdam UMC - Amsterdam University Medical Center, Netherlands
08:55	Patient Perspective: What should registries deliver for patients and families?	Mary Kearney , FARA Ireland
09:05	Flash talks (5 min max): ERN-RND local registry initiatives	

SESSION 2

Registry Examples in ERN-RND

TIME (CET)	TOPIC	SPEAKER
09:50	ERN-RND use case	Christina Vossler-Wolf , University Hospital Tübingen, Germany
10:05	TreatHSP Natural History and Outcome Validation Platform	Rebecca Schüle , University Hospital Heidelberg, Germany
10:25	The French MSA registry	David Bendetowicz , CHU - Reference Center for Rare Multiple System Atrophy, University Hospital Bordeaux, France
10:45	NKX2-1 registry: Building an International Disease Registry in a Very Rare Disorder	Dario Ortigoza , Sant Joan de Déu Hospital, Barcelona, Spain
11:05	Panel Discussion	
11:30	Coffee/Lunch Break	

SESSION 3

Regulatory and Methodological Perspectives

TIME (CET)	TOPIC	SPEAKER
12:00	Registry Qualification and Regulatory Expectations for Rare Disease Evidence Generation	Kelly Plueschke , European Medicines Agency
12:25	Natural History Studies as Historical Control Data in Trials	Ralf Reilmann , George-Huntington-Institute, Technology-Park Münster, Germany
12:50	Q&A and Closing remarks	
13:00	End of event	





THOMAS KLOCKGETHER

German Center for Neurodegenerative Diseases (DZNE),
Bonn, Germany

Why Registries Matter for Rare Neurological Diseases: **from Natural History to Trial**

A registry is a database that collects structured data from patients with shared symptoms, clinical signs, or diseases. Clinical cohort studies are performed in specifically recruited groups of patients, who are studied according to a detailed protocol in order to address a specific research question. Cohorts may also include risk and healthy control persons. Boundaries between registries and cohort studies are blurred, e.g. cohort studies can be run within an existing registry, or cohort studies initially planned for a defined time can be extended as a registry. Registries and cohorts typically have a longitudinal design, which allows researchers to study the natural history study of diseases. Data from registries and clinical cohorts are essential for research in rare diseases. First and foremost, they make it possible to study the natural course of the disease under study. Data from such natural history studies are needed to design and plan interventional trials. Registries are particularly useful to recruit participants of interventional trials. In such a run-in design, knowledge of the individual natural history data helps to detect possible effects of the intervention. The data of longitudinal studies can also serve as real-world controls in interventional trials so that exposure of trial participants to placebo can be minimized. Furthermore, data from registries and clinical cohorts are indispensable for the development and validation of clinical outcome assessments, digital assessments, and fluid as well as imaging biomarkers.



Prof. Klockgether received his medical degree from the University of Göttingen. After a postdoctoral fellowship at the Max-Planck-Institute in Göttingen, he completed his neurology training in Tübingen, where he also began to focus on degenerative ataxias. In 1998, he was appointed as Professor and Chair of Neurology at the University of Bonn. Prof. Klockgether has been the Dean of the Medical Faculty of the University of Bonn from 2008 to 2011, and the Director of Clinical Research at the German Center for Neurodegenerative Diseases (DZNE) from 2011 to 2024. Prof. Klockgether led the team that developed the Scale for the Assessment and Rating of Ataxias (SARA). He has been the coordinator of the European EUROSCA, RISCA and ESMI cohorts and one of the principal investigators of the international READISCA cohort. Currently, he is Chair of the Ataxia Global Initiative (AGI) Steering Committee.



MARY KEARNEY

FARA Ireland

Patient Perspective: What should registries deliver for patients and families?

Patients are central to patient registries, and understanding their perspectives is important to ensure that registries meet their needs. A European survey was conducted among participants of the ERN-RND Registry and the International Friedreich Ataxia Patient Registry. Fifteen people from five European countries participated, including 11 individuals with Friedreich ataxia and 4 carers. The results showed that participants were keen to contribute to patient registries and share information about their condition. However, they also expressed an interest in receiving information about how their disease progresses over time and how their progression compares with that of other registry participants. These findings highlight the importance of not only collecting patient data but also providing meaningful information and feedback to patients and carers.

Mary Kearney is medically qualified and is currently Neurology Research fellow at Tallaght University Hospital, Dublin. She is a Patient Advocate at the European Reference Network for Rare Neurological Diseases (ERN-RND); She is responsible for the International Friedreich's Ataxia registry in Dublin where she recruits and reviews participants. She took an active role at Tallaght University Hospital in consenting those with Ataxia for the ERN-RND at its inception there. She is also a member of the Cochrane Collaboration.



CHRISTINA VOSSLER-WOLF

ERN-RND Registry Manager,
Germany

From data collection to scientific analysis: **a cross-ERN registry use case on time to diagnosis**

Growing patient datasets, structured data collection and shared EU-defined common data elements now enable European Reference Network (ERN) registries to address scientific questions about rare diseases and their care. Their coverage of different disease groups and countries provides opportunities to investigate diagnostic pathways across Europe. A cross-ERN registry use case has therefore been established to demonstrate this scientific potential by examining time to diagnosis.

Although ERN registries differ in their overall structure, their common data elements provide a basis for joint analysis and comparison. This use case investigates how long patients wait for a clinical or genetic diagnosis and how these intervals vary between disease groups and countries. Time to diagnosis thus serves both as a research outcome and as a key indicator of the diagnostic situation of people living with rare diseases.

This talk will present 2025 data from the ERN-RND registry and compare findings with those from ERKReg (ERKNet) and EuRREB (Endo-ERN and ERN BOND). The analysis will explore similarities and differences between

cohorts, while considering data completeness, comparability and cohort composition. It will also identify opportunities to improve data collection and quality.

This use case illustrates how ERN registries can increasingly generate scientific evidence on diagnostic delays, identify questions for further investigation and inform efforts to improve rare disease diagnosis across Europe.

Christina Vossler-Wolf has been a project manager on various projects relating to rare diseases at Tübingen University Hospital since 2019. Since 2022, she has been part of the ERN-RND coordination office and is in charge of the registry at ERN-RND. In this role, she is responsible for all administrative tasks relating to the registry and, in particular, for the annual data submission. She manages the REDCap database, carries out annual analyses and coordinates the ERN-RND pilot project within JARDIN WP8 and the ERN-RND's internal working group, AuDaT, both of which focus on the implementation of automated data transfer.





DAVID BENDETOWICZ

CHU - Reference Center for Rare Multiple System Atrophy,
University Hospital Bordeaux, France

The French MSA registry

Multiple System Atrophy (MSA) is a rare and rapidly progressive neurodegenerative disease for which no neuroprotective treatment is currently available. To increase the likelihood of identifying effective therapies, a reliable understanding of the disease's natural history and longitudinal progression is essential. I present the current framework of the French MSA (FMSA) Registry (>750 patients). Patients undergo annual assessments using a standardized protocol that incorporates validated diagnostic criteria, clinical rating scales, and quality-of-life measures. A collection of biofluids (CSF and blood, 140 and 100 samples, respectively) and MRI data (n=240) with multiple measures is also integrated into the registry. Using dedicated statistical methods, we aim to characterize disease trajectories and patterns of heterogeneity across clinical, imaging, and biological data sources.



David Bendetowicz is an adult neurologist specializing in neurodegenerative diseases. He is currently the referent physician of the Multiple System Atrophy reference center at the University Hospital of Bordeaux.





DARIO ORTIGOZA

Sant Joan de Déu Hospital, Barcelona, Spain

NKX2-1 Registry: Building an International Disease Registry in a Very Rare Disorder

International registries are essential for defining the natural history of very rare disorders, but their development requires coordinated recruitment, standardized phenotyping, secure data capture, and sustained international collaboration. We established the International NKX2-1 Registry using a REDCap database hosted at Hospital Sant Joan de Déu, recruiting through ERN-RND, professional societies, patient communities, scientific meetings, and direct clinician referrals. Forty specialists from 29 centers in 17 countries contributed standardized clinical, genetic, imaging, neurological, respiratory, and endocrine data. The initial cohort comprised 68 genetically confirmed individuals aged 2–60 years. Motor delay was the most frequent early manifestation, chorea affected more than 90%, and only approximately half displayed the complete brain–lung–thyroid triad. The registry identified clinically relevant associations: neonatal respiratory distress predicted later respiratory morbidity; deletions were associated with better gross motor function; and frameshift or nonsense variants showed greater respiratory involvement. The registry remains active and has now enrolled more than 80 individuals. This experience demonstrates how a collaborative registry can overcome fragmented case-based knowledge, generate genotype-informed clinical insights, and establish a platform for longitudinal follow-up, harmonized outcome measures, clinical guidelines, and future therapeutic studies in NKX2-1-related disorders.



Juan Darío Ortigoza-Escobar, MD, PhD, is a pediatric neurologist and Head of the Movement Disorders Unit at Hospital Sant Joan de Déu Barcelona. His work focuses on pediatric movement disorders, rare neurogenetic diseases, GPCR signaling-related disorders, deep brain stimulation, and natural-history studies. He coordinates international research programs in GNAO1- and NKX2-1-related disorders and the Chorea and Huntington's Disease Group of the ERN-RND. He contributes regularly to national and international scientific meetings and has co-authored more than 110 indexed publications through collaborative multidisciplinary work. He is a Board Member of the European Paediatric Neurology Society.



KELLY PLUESCHKE

Senior scientific officer Data Analytics and Methods
Task Force, Real-World Evidence workstream

Registry Qualification and Regulatory Expectations for Rare Disease Evidence Generation

Registry data may be used for a range of regulatory purposes throughout the lifecycle of a medicinal product, including in pre-authorisation activities by providing information on disease natural history, patient populations, unmet medical need, but also in post-authorisation safety studies (PASS) and post-authorisation efficacy studies (PAES), including long-term monitoring of effectiveness and safety in routine clinical practice. Such data are particularly valuable for rare diseases and advanced therapy medicinal products (ATMPs), where conventional clinical trials may involve limited patient numbers and long-term follow-up is needed.

To support regulatory decisions, registries should be fit for purpose, meaning they must contain relevant, well-defined, and sufficiently complete data to answer specific research questions. The talk will focus on existing and upcoming guidances to help registry holders collect reliable data that can be used to generate relevant evidence on medicines. Through its Qualification of Novel Methodologies procedure, EMA offers a voluntary scientific tool that allows registry holders and sponsors to obtain regulatory feedback and, where appropriate, formal qualification of a registry's methodology and fitness for regulatory use.



Kelly Plueschke is a pharmacist with a master's degree in medicines regulatory affairs who joined EMA in 2008. Before that, she worked in the pharmaceutical industry, mostly in pharmacovigilance. At EMA, she has been involved in many different projects for the implementation of Pharmacovigilance legislation, in signal management and in RWE activities. She coordinates the EMA/HMA Patient-registries initiative.



RALF REILMANN

George-Huntington-Institute, Technology-Park Münster, Germany

Natural History Studies as Historical Control Data in Trials –

Problems and possible Solutions

Conducting well designed clinical trials in rare neurodegenerative diseases remains a significant challenge on the path to urgently needed novel effective therapies. Proof of concept for novel therapeutic approaches in clinical trials is burdened by the lack of sensitivity and reproducibility of clinical rating scales. In some diseases low subject numbers challenge the feasibility of clinical trials. Also the nature of the therapeutic interventions may limit recruitment in trials. Disease dynamics may challenge the readiness to employ placebo groups in clinical trials. Hence there are scenarios in which the use of natural history control data has been considered in the clinical development programs. The opportunities and challenges around these considerations will be discussed. Examples will be provided, e.g., the first gene therapy trials conducted in HD with low subject numbers and long durations. The behavior of rating scales will be discussed including the problem of placebo effects and the challenges remaining when using natural history controls. Novel observations and opportunities around digital objective endpoints that seem to lack placebo responses will be presented. Possible solution for future proof of concept studies and clinical developments in rare disease will be discussed also considering regulatory perspectives.



Dr. Reilmann is Founding Director of the George-Huntington-Institute (www.ghi-muenster.de) in Muenster, Germany, where he follows one of the largest groups of Huntington's disease (HD) families globally. He also holds appointments at the Universities of Tuebingen and Muenster. His main interests is the conduct of innovative clinical trials in HD, several of which he leads as global coordinating principle-investigator, including the first gene therapy trials for HD HDGeneTRX1&2. He is specifically committed to the advancement of objective endpoints for clinical trials and developed the "Q-Motor" system, which is meanwhile widely applied in multiple global clinical trials in HD and beyond.