RSNN EXPERT MEETING REPORT – POTENTIAL OF THE EUROPEAN PLATFORM FOR NEURODEGENERATIVE DISEASES (EPND) TO AID BIOMARKER DISCOVERY AND VALIDATION

The meeting took place on Thursday 11 September, 2025, from 9.30 to 12.30 CEST, via Microsoft Teams.

Authors	Audrey Hermans	Dutch Medicines Evaluation Board, University Medical Centre Groningen, EPND
	Marjon Pasmooij	Dutch Medicines Evaluation Board, Utrecht University, Regulatory Science Network Netherlands, EPND
	Sjaak Bot	Lygature, Regulatory Science Network Netherlands
	Raj Long	Gates Ventures, EPND
	Visda Vaghayenegar	Sanofi, EPND
	Maike Tauchert	BBMRI-ERIC, EPND
	Ilse Custers	Lygature, Regulatory Science Network Netherlands
	Yvette Schipper	Lygature, Regulatory Science Network Netherlands

ABSTRACT

On Thursday 11 September 2025, a Regulatory Science Network Netherlands (RSNN) Expert Meeting was held with a total of twenty-six participants with diverse expertise from nine different European countries. Participants included regulators, clinicians/researchers, industry, and a patient representative, amongst others. At the current stage of the European Platform for Neurodegenerative Diseases (EPND) there has not been identified a complement biomarker from the EPND Hub. Therefore, the meeting aimed to discuss the potential of EPND to aid biomarker discovery and validation and identify opportunities for regulatory advice on complement biomarkers for use in trials.

The meeting started with two short presentations; an introduction presenting two examples of biomarkers and a short overview of the EPND project, the development and deliveries to date. The meeting was designed as an interactive dialogue and took place under Chatham House Rule. The dialogue was structured around questions to guide discussion on (1) the usability of the EPND Hub as a metadata catalogue, (2) how EPND can be used for biomarker development, and (3) challenges and opportunities of aggregation of data in EPND as a metadata catalogue. During the meeting participants discussed the current use of the presented biomarkers, specificity and validation requirements for these biomarkers, and the potential need for a conceptual and cultural shift regarding biomarkers for neurodegenerative diseases. Furthermore, it was noted that biomarker qualification by the European Medicines Agency (EMA) could further stimulate adoption of emerging biomarkers. The discussion explored different options for a qualification procedure: presenting an entire metadata catalogue such as the EPND Hub, a pre-specification of methods or individual biomarkers.

Generally, the value of EPND was recognised. However, several suggestions were made for EPND, including ways to enhance the value and sustainability of EPND, possibilities to apply Artificial Intelligence (AI), and opportunities for collaboration. Ultimately, the meeting resulted in the following recommendations for EPND. It was advised to strengthen longitudinal and diverse datasets, including healthy controls and underrepresented groups. Furthermore, it was recommended to reduce assay variability and continue harmonisation efforts across datasets and platforms. Last, EPND could explore AI, and foster collaborations with other efforts such as Parkinson's Progression Markers Initiative, while also aligning with broader European frameworks like the European Health Data Space and European Reference Networks.

INTRODUCTION

The European Platform for Neurodegenerative Diseases (EPND) is a consortium of multidisciplinary public and private sector partners in neurodegenerative disease research. With support from the Innovative Medicines Initiative (IMI), the EPND consortium aims to accelerate research into the discovery and validation of biomarkers to ultimately support the development of diagnostics and disease-modifying therapies for neurodegenerative diseases, such as, for example, Alzheimer's disease (AD) and Parkinson's disease (PD). To do so, EPND aims to remove barriers to data and biosample sharing and foster collaboration. In November 2024 the EPND Hub was launched. This Hub is a single point of access for data sharing, discovery, and analysis for available studies, datasets and biosamples with an infrastructure and processes built to ensure long-term sustainability for data access and reuse. The EPND Hub is interoperable with the Alzheimer's Disease Data Initiative's AD Workbench, meaning that registered users can use a single set of login credentials to view and request available datasets across both the EPND Hub and AD Workbench and perform analyses within their secure, cloud-based workspaces. The EPND Hub has been designed in such a way that in the future it can also connect to other data catalogues. Additionally, the Hub has an option for users to contact study owners to request data and/or biosamples, and for study owners to share information about their research to increase discoverability and use. The EPND Hub, with its resources and operating procedures, will be a self-sustaining entity by the end of 2026. As of May 2025, the EPND Hub contains 102 studies (267.740 participants), 110 datasets (574.393 participants), and 33 biosample collections (46.896 participants).

To understand what EPND and its Hub can contribute to unlocking the potential of existing biomarkers and developing new biomarkers, an expert meeting was organized in collaboration with Regulatory Science Network Netherlands (RSNN). The goal of this meeting was to receive input on the EPND Hub as a metadata catalogue and the types of data variables in the databases, biosamples and studies accessible through the EPND Hub. Specifically, the meeting aimed to discuss which variables are considered important for the regulatory qualification of biomarkers in neurodegenerative diseases, and how these data could support a qualification procedure with regulatory authorities. This could inform the consortium on what should be added to the catalogue to strengthen its position in aiding the development of biomarkers for neurodegenerative diseases.

A variety of stakeholders were invited, and the discussions generated input from multiple perspectives. From a developmental perspective, participants discussed what kind of research can be performed using the EPND Hub and which variables and biosamples are essential. From a regulatory perspective, discussions included the requirements for, and acceptability of, biomarkers developed using data from the EPND Hub.

MEETING STRUCTURE AND METHODOLOGY

The expert meeting was organized in collaboration with RSNN. This network of experts from government bodies, patient organisations, academia, industry and the broader regulatory science field offers a unique platform to meet with stakeholders from different backgrounds as equal partners. RSNN organizes expert meetings and workshops on different topics related to regulatory science. These usually result in meeting reports and recommendations to support development, marketing authorization, access and appropriate use of medicines. The RSNN already exists for 10 years, and is a unique platform in Europe for discussing regulatory science topics (Pasmooij et al., 2024).

All participants received pre-read materials with information (Appendix 1). These consisted of a briefing document describing RSNN, EPND, and the EPND Hub. The briefing document included an overview of the metadata variables in the studies, datasets and biosample collections accessible through the EPND Hub, and the quality requirements and standard operating procedures (SOPs) developed for EPND. Additionally, two case examples were shared with participants. One case example was on AD and plasma-measured tau phosphorylated at threonine 217 (plasma p-tau217) and included a screenshot of the Amsterdam Dementia Cohort in the EPND Hub. The other case example was on PD and α-synuclein seed amplification assay (αSyn-SAA) and included a study performed within EPND that compared cerebrospinal fluid (CSF) markers of amyloid, tau and neurodegeneration and αSyn-SAA between AD, PD, dementia with Lewy bodies and healthy controls.

The meeting was framed by two short presentations. First, an introduction given by an academic EPND-partner presenting two examples of biomarkers: plasma p-tau217 and CSF α-Syn, which can both potentially play an important role in diagnosing neurodegenerative diseases, including AD and PD. Second, a short overview of the EPND project, the development and deliveries to date to provide context for the following discussion (Figure 1).

The meeting was designed as an interactive dialogue and took place under Chatham House Rule. Names and affiliations of participants therefore remain confidential. The dialogue was structured around guiding questions that participants had received with the briefing document. The guiding questions were intended to guide discussion on (1) the usability of the EPND Hub as a metadata catalogue, (2) how EPND can be used for biomarker development, and (3) challenges and opportunities of aggregation of data in EPND as a metadata catalogue.

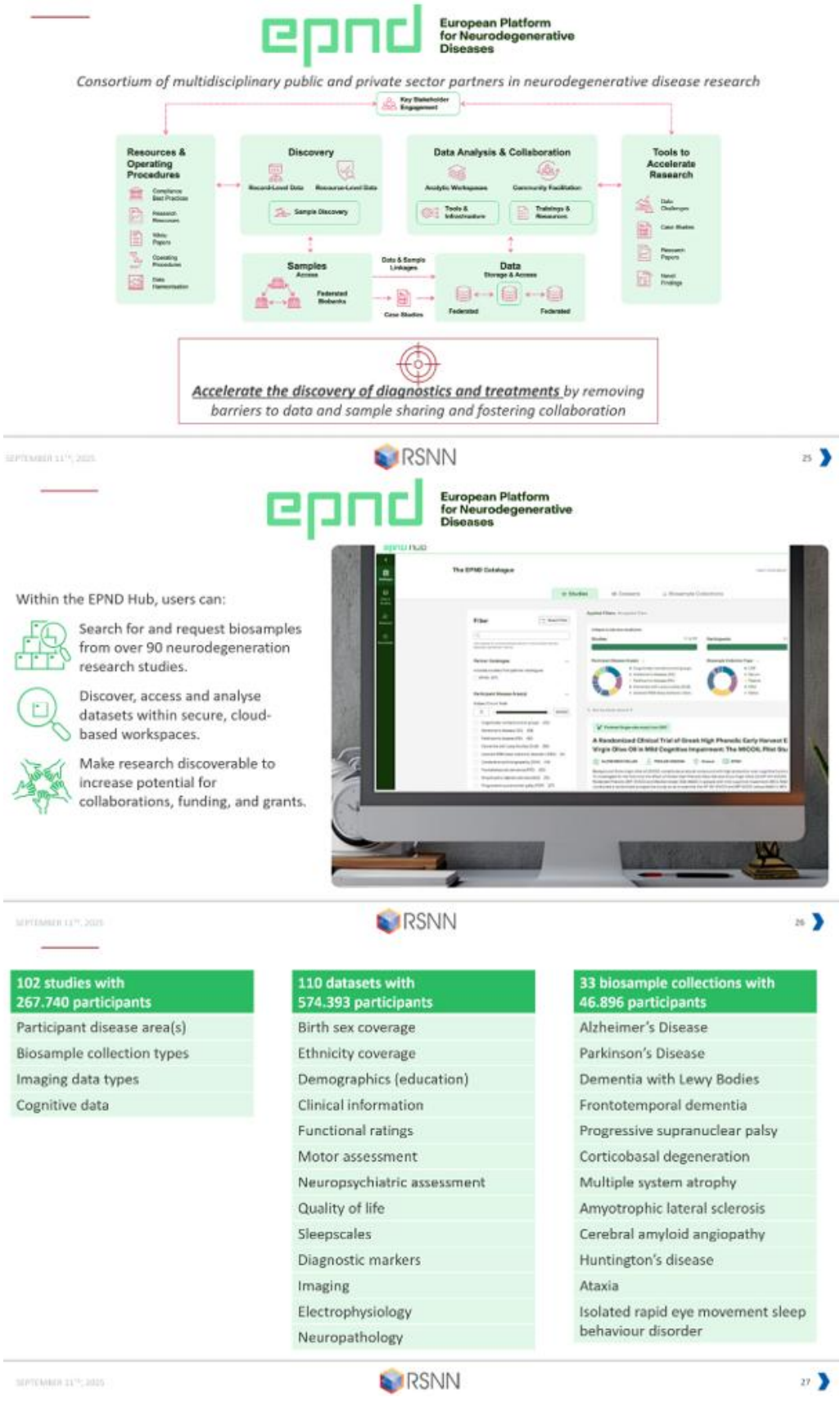

Figure 1: Slides of the introductory presentation on EPND given at the start of the expert meeting.

MEETING OUTCOMES

The expert meeting took place on Thursday 11 September 2025, from 9.30 to 12.30 CEST, via Microsoft Teams. A total of twenty-six participants attended the meeting and actively took part in the discussion (Figure 2). Unique to this meeting is that, besides their diverse backgrounds and specialisations, the participants are from nine different European countries. Additionally, three of the regulators are members of committees or working parties at the European Medicines Agency. All participants have a background related to the use and assessment of data for biomarkers and neurodegenerative diseases.

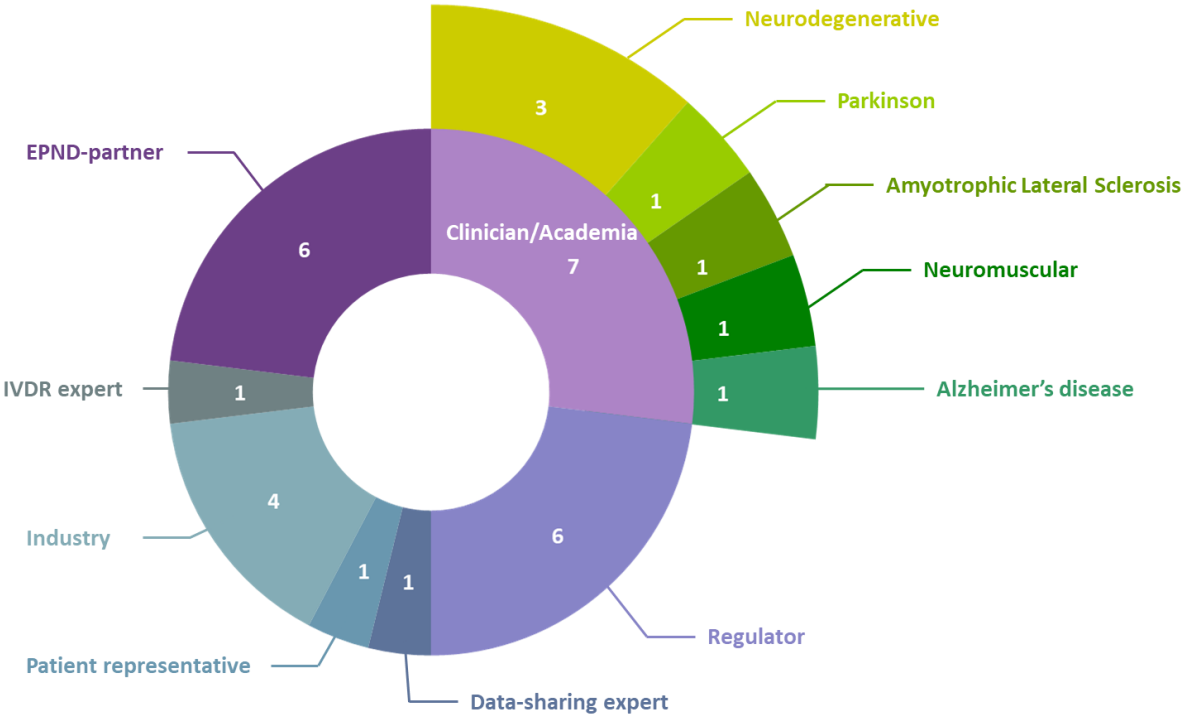

Figure 2: Backgrounds of the experts attending the meeting, including the specialisation of the clinicians/academia.

During the discussion, participants were invited to share their thoughts on the guiding questions. The main themes that emerged in the dialogue included: diagnosing neurodegenerative diseases, qualification procedure at the European Medicines Agency (EMA), requirements for biomarker development, perceived value of EPND, and recommendations for EPND. Each of these themes are summarised in the following sections.

DIAGNOSING NEURODEGENERATIVE DISEASES

Three main topics were identified in the dialogue regarding diagnosing neurodegenerative diseases: the current use of the presented biomarkers, specificity and validation requirements for these biomarkers, and the potential need for a conceptual and cultural shift regarding biomarkers for neurodegenerative diseases.

CURRENT USE OF PLASMA P-TAU217 AND ASYN-SAA

Participants agreed that both biomarkers are still relatively *young* and not yet fully validated for broad clinical use. Their novelty limits implementation in clinical practice, with most current applications restricted to lab-developed tests used for diagnostic purposes in specialised settings. At present, testing for plasma p-tau217 is recommended only in cognitively impaired individuals, due to the high risk of false positives within a healthy population.

SENSITIVITY, SPECIFICITY AND VALIDATION REQUIREMENTS

A clinician/academia expert emphasised that for testing in healthy individuals, specificity needs to be extremely high — around 99% rather than the 90% currently described in the criteria for analysing plasma p-tau217. To better inform individual prognostic decisions, further studies and data and biosamples from healthy controls with longitudinal follow-up as reference are considered essential. Amyloid positron emission tomography (PET) remains the most widely recognised method for diagnosing amyloid pathologies. From a regulatory standpoint, participants noted that validating a plasma-based proxy for amyloid PET could be relatively straightforward once findings are replicated across cohorts. However, a crucial question for the acceptability of diagnostic biomarkers for disease staging remains their association with cognitive decline and disease progression.

CONCEPTUAL AND CULTURAL SHIFTS

The discussion also highlighted a broader conceptual challenge. A participant suggested that acceptance of blood-based biomarkers may require a shift in how amyloid pathologies themselves are viewed — seeing them as *measurable alterations* in the blood that reflect a probabilistic risk of clinical consequences. From the patient community, concerns were raised about the potential binary interpretation and use of amyloid biomarkers, especially in asymptomatic individuals. It was emphasised that a cultural, ethical, and educational shift will be needed before such biomarkers can be responsibly applied beyond symptomatic populations.

QUALIFICATION PROCEDURE AT THE EMA

A regulator noted that there is a clear urgency within the field of neurodegenerative diseases to stimulate developments regarding biomarkers, with the aim to become surrogate endpoints in the future and contribute to the development of novel treatments. It was noted that certification of diagnostic assays by notified bodies and biomarker qualification by the EMA could further stimulate adoption of emerging biomarkers such as plasma p-tau217. The discussion explored how qualification procedures might be approached and what would be required to support, e.g., **the qualification of individual biomarkers or a metadata catalogue such as the EPND Hub**.

QUALIFICATION OF THE EPND HUB

Regulators and industry experts emphasized that assessing datasets issued from a platform like the EPND Hub presents challenges in the context of a qualification procedure. The EPND Hub is extensive and contains a heterogeneous set of data variables collected across different neurodegenerative diseases, settings and using different standards. The Hub's diversity and size are recognized as strengths, as agreed by all participants, but also make preparation for and assessment within a qualification procedure challenging. While the diversity and size increase the platform's scientific value, they complicate data preparation, contextual definition, and quality assurance required for qualification. Regulators evaluate both the context of use and the available data. A **qualification procedure for the EPND Hub** would therefore need to:

- Describe the context of use—either for the Hub as a whole or for each distinct, applicable context.
- Define the contribution of each type of data to the broad context of use of the Hub.
- Address missing data, ensuring transparent documentation of gaps.
- Demonstrate how quality across all relevant variables is ensured, considering the broad scope of the EPND Hub.
- Minimise heterogeneity between assays while maintaining sensitivity to detect changes, when researchers/developers want to merge datasets.
- Aspire to incorporate long-term follow-up data.

QUALIFICATION OF PRE-SPECIFIED METHODS

Another suggested option for a qualification procedure is to present a pre-specification of methods, to not only register methods in a protocol registry but also present them for qualification before conducting the analyses. This would include specifying:

- Dataset splitting approaches between replication cores.
- Boundaries and thresholds for analyses.
- Statistical methods to be applied.

Participants noted that another initiative has previously received a qualification opinion for its framework to address gaps in approaches to incorporate patients' views into decision-making and to select methods fit for application to future patient preference studies: Qualification Opinion of IMI PREFER.

QUALIFICATION OF INDIVIDUAL BIOMARKERS

In contrast, a **qualification procedure for an individual biomarker** with a more narrowly defined context of use was seen as less complex. Requirements regarding missing data, validation, and data quality can be confined to that biomarker. A regulator noted that when focusing on a single biomarker, it is more likely that all data needed to establish the specific context of use of that biomarker are available. The conversation also touched on biomarkers with strong evidence for use in multiple contexts, such as neurofilament light chain (NfL). The IVDR-expert made a comparison with the marketing authorisation process for medicines, where a product approved for a strict indication can lead to off-label use, subsequently generating additional data.

It was highlighted by a regulator that to qualify a biomarker as supportive to functional and cognitive scales that are currently accepted as primary endpoints—such as the Clinical Dementia Rating Scale Sum of Boxes (CDR-SB) in AD—three aspects are essential:

1. Addressing all limitations of the biomarker.
2. Showing a relationship between the biomarker and clinical outcomes for patients.
3. Clarifying how the biomarker, when used as an endpoint, aligns with other endpoints.

REQUIREMENTS FOR BIOMARKER DEVELOPMENT

Overall, participants agreed that multiple components are essential—not only for biomarker qualification, but also to unlock the full potential of currently used biomarkers and to enable discovery of new biomarkers for neurodegenerative diseases:

- High-quality assays, reference material and data.
- Longitudinal follow-up data of healthy controls.
- Inclusion of minority ethnic groups to improve representativeness.
- Minimising selection bias in data sources.
- Reducing heterogeneity across assays and laboratories.
- Using digital biomarkers and wearables as complementary data variables for biomarker assays.

Especially data-sharing is considered fundamental for further advancement of biomarker research in neurodegenerative diseases, and EPND and its Hub could be the host to provide a boost to this advancement. Furthermore, all participants agreed that harmonisation of data and protocols for biosample collection, processing and storage is critical, both within and across platforms such as the EPND Hub, to make the discovery of qualifiable biomarkers possible.

PERCEIVED VALUE OF EPND

When reflecting on the potential use of the EPND Hub, participants noted that it could aid biomarker development. Key strengths of EPND were highlighted:

- Transcends disease areas.
- Provides centralised access to data and biosamples within a single collaborative environment.
- Developed SOPs, including quality and biobanking protocols, which users can reference to verify adherence by dataset and cohort owners.
- Systematically documents cohort metadata.
- Performed case studies to harmonise datasets. While most datasets remain independent, some have been harmonised through these case studies.

RECOMMENDATIONS FOR EPND

Several recommendations were made for EPND, including ways to enhance the value and sustainability of EPND, possibilities to apply Artificial Intelligence (AI), and opportunities for collaboration.

Enhancing the Value and Sustainability of EPND

Participants discussed several ways to ensure the long-term sustainability and continued relevance of EPND. Suggestions were made to enhance the EPND Hub by incorporating:

- Data collected with wearables or other digital health technologies.
- Data from interventional studies.
- Longitudinal follow-up data from healthy controls.
- Data from minority ethnic groups.

It was noted that, over time, data will gradually become outdated, requiring ongoing maintenance and curation to keep the Hub up to date. A clinician/academia expert also emphasised the importance of specifying and communicating the value exchange for contributors, regarding advantages, recognition, and potential costs associated with sharing data and biosamples in the EPND Hub.

APPLICATION OF ARTIFICIAL INTELLIGENCE

Several participants suggested that AI could be applied to datasets within the EPND Hub. While regulators and industry experts recognised AI as a potential driver of further development, regulators and the IVDR-expert cautioned that if AI is used multiple European legislations regarding AI must be taken into account. Additionally, since AI models can lack interpretability, exploratory findings would need to be independently confirmed using conventional analytical methods before being considered reliable.

OPPORTUNITIES FOR COLLABORATION

Collaboration with other frameworks and initiatives—such as European Reference Networks (ERNs), the European Health Data Space (EHDS), the Parkinson's Progression Markers Initiative (PPMI), and other projects setting up e.g., platform trials—was identified as an important opportunity to increase the value and sustainability of EPND. Participants agreed that the value of EPND could be further reinforced if a biomarker were to achieve regulatory qualification based on data available through the EPND Hub.

SUMMARY

In the following table the key messages of the RSNN expert meeting are summarised.

PERCEIVED BENEFITS

- The European Platform for Neurodegenerative Diseases (EPND) provides access to diverse, well-documented datasets and biosamples, supported by standard operating procedures (to be used for biosample and data collection after completion of the EPND project) and harmonisation protocols.
- The platform fosters collaboration across disease areas and can accelerate biomarker discovery and qualification.
- Data sharing and harmonisation across cohorts were seen as essential for progress.

CHALLENGES

- The heterogeneity of EPND datasets makes preparation for and assessment within a qualification procedure complex, requiring clarity on context of use, data quality, and long-term follow-up.
- Qualification of a broad platform like the EPND Hub is more challenging than qualification of a single biomarker for a defined context of use.
- The use of AI offers opportunities but requires careful consideration.

RECOMMENDATIONS

- Strengthen longitudinal and diverse datasets, including healthy controls and underrepresented groups.
- Reduce assay variability and continue harmonisation efforts across datasets, biosamples and platforms.
- Explore applying AI cautiously.
- Foster collaborations with other efforts such as Parkinson's Progression Markers Initiative, while also aligning with broader European frameworks like the European Health Data Space and European Reference Networks.