Conference on Rare diseases and the European Reference Networks

ERN ReCONNET Report

11th October 2023, Bilbao

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Session 1: Rare diseases: organisational models and good practices in health and social care

Link to recording: *https://www.youtube.com/watch?v=nI30UuADfIs)*
Report prepared by: Silvia Aguilera and Eva Collado

Enrique Terol García Health Counsellor, Permanent Representation of Spain to the EU, summarizes the topics of the introduction panel: what has been done so far, what the current challenges are and the importance of rare diseases, and introduces this panel, that will gather the view of 5 speakers from different perspectives, all of them with a long career path on rare diseases. It is crucial to reflect on the next steps at European level and how to integrate the efforts of all actors working for the quality of life of rare disease patients.

Alain Coheur, Member of the European Economic and Social Committee, talked about ensuring strong European solidarity for patients with rare diseases. The speaker emphasized their extensive experience in cross-border health projects, particularly in the region which spans Germany, the Netherlands and Belgium (including the French-speaking part), and proposed an interregional project focused on rare diseases. The aim was to secure cross-border funding for addressing specific health issues, rather than conducting research. To achieve this, collaboration was established with three regional hospitals, with a focus on understanding the challenges faced by individuals with rare diseases. The study involved over 100 patients and interviews with an equal number of individuals. The findings revealed the complexities in accessing healthcare, especially for those with rare diseases. The study focused on eight specific rare diseases and identified the extensive medical care required, involving various specialists and numerous medical procedures.
Coheur highlighted the administrative hurdles patients face, including securing funding for essential care beyond medical appointments and diagnosis. This financial burden falls on the patients and their families, often leading to significant personal and professional sacrifices. It was emphasized that this issue affects people of various ages, including older individuals.
The multidisciplinary approach to healthcare was stressed as crucial, along with the observation that medical professionals are often inadequately trained to deal with patients with rare diseases. The diagnostic journey can be lengthy, spanning two to seven years. Coheur expressed the need for political action to address these challenges and lamented the delay in publishing a report on rare diseases.
The report underlined the importance of coordination among healthcare professionals, as well as addressing the fragmentation and segmentation within the medical system. Coheur also highlighted the need to prevent rare diseases from exacerbating existing healthcare inequalities for individuals with multiple health conditions.
While acknowledging positive steps taken by the European Commission, Coheur argued that current political actions remain insufficient. He called for the establishment of a dedicated health authority for non-transmittable diseases and advocated for the creation of a European solidarity fund to cover expenses not covered by Social Security.

Yann Le Cam, CEO of EURORDIS, highlighted the pressing issue of unmet medical needs for rare disease patients, estimating a minimum of 20 million affected individuals in the EU. He emphasized the prolonged delays in diagnosis, with 50% of patients experiencing waits of over a year, and sometimes more than a decade. Le Cam noted the progress made over the past 20 years, proving the feasibility of common solutions to shared challenges. He emphasized the need to move beyond pilot programs and scale up efforts.
Le Cam called for a shift towards a genuine Public Health strategy, aligned with sustainable development goals. This would entail reducing child mortality, lessening the social and economic impact on families, and implementing outcome measurements. He emphasized that this approach must be cohesive, rejecting fragmented efforts. Le Cam stressed the importance of listening to member states and citizens, emphasizing that the drive for change comes from the ground up, from the families, the citizens.
He commended the current European strategy on rare diseases as a model of innovation and efficiency, blending healthcare and research with integrated data systems. Le Cam emphasized the need for early diagnosis, particularly

through expanded newborn screening. He called for increased investment in clinical research to position Europe as an attractive destination for rare disease studies.
Le Cam underscored the collective efforts already underway and urged the Commission to heed the recommendations of experts, citizens, and organizations. He highlighted widespread support for a new policy framework, including calls from the European Parliament, member states, and key stakeholders. Le Cam emphasized the urgency of action, calling for the European action plan for rare diseases to be a priority for the next Commission. He acknowledged the challenges faced by the Commission but stressed that the time for this critical plan is now.

Luis Varona Franco, a clinical neurologist with 27 years of experience in ALS patient care, discussed the success of their care model at the Basurto University Hospital. He emphasized the transformation from a bleak outlook for ALS patients to a comprehensive and compassionate approach. The ALS clinic's coordinated care has become a gold standard for treating not only ALS but also other diseases. The clinic's impact is evident in extended patient survival and improved quality of life. Dr. Varona highlighted the importance of personalized information and respect for patient autonomy. He credited the active involvement of patients and their families in shaping this model of care. The ALS clinic's success is attributed to a dedicated team, combining clinical expertise with advanced technology and empathy. Dr. Varona expressed gratitude to the patients and their families for their crucial role in this transformative approach to ALS care.

Anne-Sophie Lapointe, Project Manager for Rare Diseases at the French Ministry of Health and Prevention, focused on patients, families, and caregivers as the driving force behind the French strategy for low prevalence diseases. She highlighted the pivotal role of patient associations in advocating for rare diseases, emphasizing the importance of visibility for experience centers. Over the years, France has developed rare disease plans, with the latest one focusing on health data sharing to better assist patients in their diagnostic journey and clinical trials. Lapointe stressed the need for a robust national plan for rare diseases, laying the foundation for organized care. She also emphasized the significance of European collaboration, citing the role of Health Agencies and the importance of data collection at a European level. Lapointe called for a holistic approach that integrates the human and social dimensions, aligning with sustainable development goals. She expressed gratitude to the European Commission for their support and underlined the necessity of restructuring and creating a European plan for rare diseases.

Milan Macek, the Czech Republic representative on the ERN Board of Member States, and chairman of the National Coordination Center for Rare Diseases in Czech Republic, highlighted the success of a major conference organized one year ago with the title: “Towards a new European policy framework: building the future together for rare diseases”, which was a huge success. The call to action received unambiguous political support from 22 EU member states (representing over 82% of the EU population). Macek emphasized the need for a new European action plan to coordinate, harmonize and standardize approaches to rare diseases, citing the success of the EU Council recommendation in 2008 drafted along with France. He stressed the importance of early diagnosis, particularly through standardized newborn screening. Macek called for attention to diagnostics, highlighting obstacles in the in vitro diagnostics regulation that need revision. He emphasized the need for a Europe-wide approach to improving access, including collaboration in pricing and negotiation. Finally, Macek discussed the importance of holistic care pathways, involving European Reference Networks, and the need for sustainability and attractiveness in the field of rare diseases.
He mentioned that there are more than 1500 specialized teams in the ERNs, based on the voluntary work of enthusiastic people, but the next generation will not accept this. Therefore, the ERNs need to be made more attractive, not only about financing but also reducing the bureaucracy.

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Session 2 - European Reference Networks for rare diseases: Consolidation, future and integration into EU health systems

Link to recording: https://youtu.be/oZLYSGDI-PU
Report prepared by: Eleonora Passeri

Moderator: Enrique Terol García, Health Counsellor, Permanent Representation of Spain to the EU **-Session 2 was opened by Donata Meroni** from DG SANTE, European Commission, which presented the *Implementation and evaluation of the ERNs five years since their creation: future and sustainability.* The presentation provided an overview on the legislations and evaluation criteria as well as results obtained by the ERNs. The AMEQUIS (Assessment – Monitoring – Evaluation – Quality – Improvement – System) approach and the specific objectives (e.g., identification of best practices and areas of improvements) as well as the criteria currently used for the external and scientific evaluations were recalled. In particular, the scientific evaluation was based on 7 different areas, 20 operational criteria, and 52 measurable elements, while the HCPs saw 24 operative criteria and 64 measurable elements. Preliminary results from the ERNs evaluation done by IEB were reported, specifically: 87% obtained all satisfactory results, 10% need improvements, while 3% deny sharing their results. Overall, the ERNs evaluation showed positive results. Regarding the next steps, on 24/10 the evaluation results were presented to the Board of Member States representatives during the plenary meeting, then the Board of Member States will decide whether to grant one year implementation period followed the re-evaluation to those members that submitted the improvement plan, the Board of Member States will decide on termination for those Members that do not fulfill the evaluation criteria. All the 626 members that joined the ERNs in 2022 will be evaluated latest in 2027, the aim is to look at what has been done and support the ERNs strengths.

- **Till Voigtländer,** Coordinator of the future Joint Action JARDIN talked about the *Integrating the ERNs into the EU's health systems: joint action under the EU4HEALTH health programme*. He focused his presentation on the JARDIN Joint Action that is a huge project, constituted by 60 partner institutions from 29 Member States (MS), Ukraine included, specifically: 28 competent authorities, 31 affiliated entities, and 1 associated partner. Regarding the funding, JARDIN is under the so called "exceptional utility rule" so 80% of the budget comes from the EU (15.000.000 euro), 20% from the MS (3.750.000 euro) for a total of 18.750.000 euro. Additional funding should come from some MS that will put a bit more money as it has been told. The call will start in March 2024 and will end in February 2027. JARDIN promotes the ENRs integration in the NHS, this can not be ensured thou since JARDIN has not any legal competence, however JARDIN will provide documents and all the tools to support the Member States and help them in the dialogue with the different stakeholders. The Joint Action is organized in 9 different WPs: WP1. Coordination and Management; WP2. JARDIN dissemination and ERNs dissemination; WP3. Evaluation; WP4. Sustainability and national plan capacity; WP5. National governance and Quality assurance; WP6. National care pathways and ERNs referral system; WP7. National reference networks and Undiagnosed disease programs; WP8. Data management; WP9. National support options for ERNs-HCPs. Specifically, the promotion of ERNs integration in the NHS will be pursued by the development of several approaches based on each WP: WP2) full scale and professional information ERNs campaigns where primary target groups are patients, medical doctors, and staff members such as primary care level, WP3) national governance models for ERN-HCP and care pathways adapted to different types of health systems, indicators for national monitoring of rare and complex diseases primarily focusing on care pathways as well as for national ERN integration, WP6) a sign-posting tool for national expertise and multidisciplinary team access, linkages to ERNs of exemplary national care and ERN referral pathways, WP7) national reference networks linked to related ERNs that should bridge the gap between more general national health structures and ENRs, a European undiagnosed disease program, WP8) improving interoperability of health data and facilitate the data sharing, WP9) recommendations for national health structures and hospitals to support of ERN-HCP and for reimbursement model of CPMS activities. He underlined the fact that JARDIN won't be able to solve all the problems in 3 years, but the idea

is to integrate the actions and plans to make the system sustainable in the future where the care pathway will be also seen as medical but also social.
- **César Hernández García,** DG Services Portfolio, Spanish Ministry of Health – *Spain's model for integrating reference centres, services and units with the national health system centres and the ERNs.* The ERNs are extremely important for us due to their positive impact in our society. The ERNs are triggering a more equal society where fundings are provided also for rare diseases. Thanks to the ERNs, rare disease patients have been recognized as a crucial stakeholder for the definition of appropriate care and treatments. However, there is still a need for patients to have a proper and early diagnosis as well as integrated treatments. Reference centers for rare and complex diseases should comprehend all the different expertise needed to take care of patients in a holistic and multidisciplinary approach. In addition, he stated that the healthcare professionals should organize the supports and care around the needs of patients and not the other way around. There is a huge need, a must he said, when it comes about planning the help and support to be provided to patients. The system should be kind and generous with patients and put them at the center of its attention and actions. The health system should be plastic enough to be tailored on each patient and provide them the best care possible; also, it should be integrated in order to provide a real multidisciplinary assistance to patients and their families. Based on his consideration, the health system should integrate the care with the research, it should also seek practical collaborations between public and private sectors. Lately, the health system has been under a lot of changes due to digitalization, he continued, and the rare disease models can be translated and adapted to other diseases; these processes are leading to new integrated health multidisciplinary systems based on strong collaborations among the different stakeholders.

- **Holm Graessner,** Coordinator of ERN-RND – *Challenges for the sustainability of the ERNs.* He opened his talk by mentioning the reasons why it is important to make the ERNs sustainable, the ERNs are permanent infrastructures for knowledge generation and sharing. In particular, the ERNs demonstrated their capacities in terms of knowledge and data sharing, building collaborations and partnerships as well as in networking experts with rare disease patients across Europe. In addition, the ERNs proved to be able to trigger innovation in the health ecosystems and research. The ERNs core activities can be summarized in the development of CPMS, of training and educational programs and initiatives, of patient journeys, patient registry, and on the publication of important guidelines in the rare disease field. The ERNs were able to keep, maintain, and improve high level of standards delivering important results for the benefits of rare patients. The management of the ERNs can be seen as one of the large European networks among HCPs and one of the biggest European healthcare infrastructures so far. The ERNs are a solid network built among national experts in rare diseases and the reference centers belonging to the national health systems.
- **Javier Cobas Gamallo**, Deputy CEO University Hospital La Paz (Madrid) – *The key role of the hospital managers in the integration of the ERNs into the healthcare systems.* The ERNs have built a model in the health system that allows hospitals to use the generated knowledge, methodology, and strategies to deliver better cares and support to their patients. This is an important aspect to be taken into consideration by the hospital managers who can seek and get logistical support and help for their own hospitals and for the governance and administrative personnels from the ERNs. He continued mentioning that it is crucial then to inform people involved in the hospital governance and in administrative offices about the ERNs by providing them the proper information about the kind of support the ERNs can provide them. He said that by doing so, the hospital personnels will see the ERNs as a resource and not as a burden as often still happen. On the other hand, it is important to disseminate proper contents and knowledge about ERNs among the hospital personnel to increase the awareness of the Networks, their existence, their role in the health system, and how they can support the hospitals. He mentioned the importance of motivating hospital staff members by identifying strategies aimed at engaging with them and get them involved in the ERNs initiatives and actions so they will feel as part of the Networks. Moreover, he stressed the need of increasing awareness of ERNs among hospital staff employees at any level.

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Session 3 - Generating, exchanging and applying knowledge

Link to recording: *https://youtu.be/jc3qRoWOGZk?si=TYA8RfXSPlaK2mHb)*
Report prepared by: Diana Marinello

- Session 3 was opened by **Marta Mosca**, Coordinator of the European Reference Network on Rare and Hereditary Connective and Musculoskeletal Diseases (ERN ReCONNET) with a presentation on Clinical practice guidelines on rare diseases. The presentation focused on the role that the ERNs play in the development of new Clinical practice guidelines (CPGs) and other Clinical Decision-Making Tools (CDMTs) for rare diseases, as they can actively promote the active implementation of the existing CPGs into the clinical care, while ensuring a patient driven approach. Examples towards this statement were brought by the activities performed by ERN ReCONNET, such as the creation of Points to Consider for the care of rare and complex connective tissue diseases, the adaptation of existing CPGs, the development of red flags for the early detection of rare diseases, co-design of lay versions as well as the dissemination and educational activities delivered on the existing CPGs.

- The second presentation was focused on "Training on rare diseases for professionals", in which **Maurizio Scarpa**, Coordinator of the European Reference Network for Hereditary Metabolic Diseases (MetabERN) presented a wide range od educational and training activities already delivered by the ERNs. A transversal Working Group among ERN Coordinators, the ERN Board of Member Representatives and DG SANTE is currently active on the topic of Knowledge Generation and a decalogue was designed in order to define a possible plan for the future of rare disease education and training. An ERN Academy is being developed transversally for all ERNs and all the 24 ERNs are highly committed to delivering exchange programmes, online courses and webinars, summer schools, handbooks, formal courses (e.g. post-graduate courses), workshops, symposia and much more. In conclusion, the ERNs have created a model that could facilitate the set-up of a European Education Programme in the area of rare diseases and complex conditions.

- **Juan Carrión Tudela**, President of the Spanish Federation of Rare Diseases (FEDER) talked about the access to knowledge and evidence for patients and highlighted the need to empower and educate patients in order to allow them to be at the centre of the care and to actively participate in the different decision-making processes. To this end, a joint effort among rare disease experts, patient organisations and administrators is required in order to ensure that the rare diseases remain in the public agenda of the EU Member States and promote the improvement of the quality of life of those patients. The ERNs have demonstrated to be the best practice on this topic as they enable this joint effort with their multi-stakeholder approach and that they can respond to the needs of the rare disease community. It is also important to ensure the sustainability of the ERNs by allocating appropriate resources to the experts as well as to the patient representatives that are involved in the ERNs. The talk was concluded by requesting an EU Action Plan on rare diseases.

- The presentation of **Alberto Pereira**, Coordinator of Endo-ERN "Strengthen research and innovation capacity by the integration of ERN research activities", presented the results of the ERICA project, in which all ERNs are participating and that is aimed to strengthen ERN's research and innovation capacity, through facilitating collaboration between ERNs, increase the visibility and impact of ERNs, optimal integration of the results into the new European Rare Disease Alliance (ERDERA) 2024-2030. ERNs demonstrated that they are unique infrastructures that have innovation and translation capacity with real world data in rare diseases and it is now crucial to set up a further development to ensure the future of rare diseases also through the research that can be developed by and with the ERNs.

- **Leire Solis**, from the International Patient Organisation for Primary Immunodeficiencies (IPOPI) presented the Evidence based newborn screening strategy (NBS) and the Screen4Rare project, developed in collaboration with partnership between European Society for Immunodeficiencies, IPOPI and the International Society for neonatal screening, with the objectives of working to ensure that all babies have equitable access to newborn screening, to

exchange knowledge and best practices on NBS for treatable rare diseases, unbiased information and evidence, so as to help ensuring the best decisions are made. Two ERNs have contributed with a partnership in this project, namely ERN RITA and MetabERN, confirming that the ERNs have the expertise available and are key to foster equity on NBS for rare diseases in the EU and highlighting the need for a continued support from EU Presidencies & European Commission to make of NBS a key component of future EU rare disease policy.

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Session 4: Remaining challenges linked to research into rare diseases

Link to recording: https://www.youtube.com/watch?v=IoL1Y5NgMg0&t=3s
Report prepared by: Silvia Aguilera and Eva Collado

Simone Boselli, Director, Public Affairs Director at EURORDIS mentions that historically research in rare diseases has been fragmented mainly due to the low number of patients, the limited funding for research and the lack of effort. Due to the multisystemic nature of many rare diseases, coordination between basic, clinical, transitional and social research is key to advance in the challenges that we face in rare diseases. This panel will focus on how Europe faces the key challenges for research: genomic advancement, precision medicines, collaboration research networks, data sharing and patient registries and repurposing of medicines.

Irene Norstedt, Director for People at DG RTD, European Commission, emphasized her strong belief in collective efforts to address rare diseases. She highlighted the European Reference Networks (ERNs) established in 2017 as a prime example of collaborative knowledge-sharing. Norstedt proudly noted that the European Commission and the US National Institute for Health were the founders of the International Rare Diseases Research Consortium (IRDiRC) in 2011. IRDiRC, a multi-stakeholder network, aims to advance global research on rare diseases and ensure timely diagnosis and care for patients. The inclusion of ERN researchers and clinicians in IRDiRC's scientific committees, along with patient representation through Orphanet, demonstrates progress. Norstedt commended the practice of European solidarity in addressing research challenges on rare diseases through successive research programs. She highlighted the ERA project, initiated under Horizon 2020, to support ERNs in enhancing clinical research. ERNs are key partners in co-funded partnerships with member states and associated countries, as well as in the European Joint Programme on Rare Diseases (EJP-RD). Norstedt looked forward to the future European Partnership on Rare Diseases, set to begin after EJP-RD, aiming to further elevate rare disease research and innovation. She praised initiatives like the Solve-RD project for significantly advancing rare disease diagnosis. Norstedt mentioned individual researchers receiving grants for rare disease research and highlighted public-private initiatives like the Innovative Health Initiative (IHI) supporting projects such as Connect for Children and Screen for Care. She emphasized the importance of seeking synergies with EU member states and other funding programs. Norstedt also highlighted the potential for global collaboration through Horizon Europe. She emphasized the shared responsibility to deliver impactful research integrated into healthcare settings for the betterment of rare disease patients' quality of life and their caregivers.

Carmen Laplaza Santos, Head of Unit for Health Innovations at DG RTD, European Commission, acknowledged the remarkable progress achieved since the inception of European Reference Networks, emphasizing their uniqueness and the need for continued support. Rare disease research is a cornerstone of the European Commission's endeavors, representing a crucial area for collaboration. Over the past 25 years, nearly 3 billion EUR have been allocated, with 80% dedicated to collaborative research involving stakeholders from various European countries. This collaborative approach is deemed essential in this field.
Efforts have been consistently directed towards expanding the ecosystem for rare disease research. The main objective has been to involve more stakeholders, both in terms of countries and types of organizations. This approach is rooted in the necessity of efficiently utilizing research funds, given the critical nature of rare disease research. The International Rare Diseases Consortium (IRDiRC), launched in 2011, serves as a prime example of cross-sectoral collaboration, uniting research funders, including public and private entities, alongside active patient associations. The mission of IRDiRC is to promote global rare disease research, align priorities, identify funding gaps, and optimize funding models.
Laplaza highlighted various instruments, including the European Joint Program on Rare Diseases (EJP-RD), which has been active since 2019 with a budget of 100 million EUR, and involves a broad Consortium of partners across 35 countries. She emphasized the importance of registries and the platform on rare disease registration by the Joint

Research Center of the European Commission, stressing their potential for understanding natural history and prevalence, as well as identifying patients for clinical trials. The Solve-RD project, aimed at reducing diagnosis time for unsolved cases, was lauded for its significant contributions to the field.
Collaboration with the pharmaceutical industry has been fostered through initiatives like the Innovative Medicines Initiative (IMI) and Innovative Health Initiative (IHI). Projects like Connect for Children and Screen for Care have been instrumental in advancing clinical trials and diagnosis methods. Laplaza highlighted the ongoing commitment to rare disease research under the Horizon Europe framework program, with a recent call focusing on developing effective therapies for groups of rare diseases with commonalities. Additionally, efforts are underway to facilitate the uptake of therapies and address regulatory challenges associated with advanced therapies.
The upcoming ERA (European Rare Diseases Cofund) represents a major milestone, building on the achievements of previous instruments. With a budget exceeding 300 million EUR, it aims to strengthen the European research area, enhance clinical trial preparedness, support the diagnostic pipeline, implement multi-country clinical trials, and accelerate the development of advanced therapies. Industry collaboration will play a significant role in this endeavor. Laplaza emphasized the commitment to leave no one behind in the pursuit of rare disease research.

Alexis Arzimanoglou, Coordinator at the European Reference Network on Rare and Complex Epilepsies (ERN EpiCARE), emphasized the importance of member states supporting ERNs. Arzimanoglou emphasized that ERNs do not conduct research themselves, but rather facilitate it through their extensive networks of experts. He emphasized the significance of national health networks in providing accurate information for patient diagnosis and treatment. Arzimanoglou stressed that ERNs are no longer virtual entities, but existing consortia with specialized expertise. He pointed out that rare diseases are only considered rare once they are diagnosed, and highlighted the need for dedicated treatments. Arzimanoglou noted the challenges in rare disease research, including the complexity of the diseases themselves. He emphasized the importance of streamlining data sharing processes and urged collaboration between ERNs, the European Commission, and other stakeholders. Collaboration with the pharma industry is necessary. He highlighted the need for improved study designs and regulatory pathways in collaboration with ERNs to discover new therapies. Arzimanoglou concluded by calling for a legal framework that facilitates research and innovation in collaboration with ERNs.

Ángel María Carracedo Álvarez, Precision Medicine Infrastructure linked to Science and Technology (IMPaCT), CIBERER, introduced the PERTE Salud de Vanguardia branch, the IMPaCT GENOMICS project as an initiative by the Institute of Health Carlos III, focused on personalized medicine. The project aims to establish a high-capability sequencing infrastructure to support personalized medicine strategies in Spain. This includes a network of three sequencing centers with standardized procedures and a combined sequencing capacity of over 300 genomes per day. Additionally, a network of 110 hospitals across the country, with regional coordinators, ensures equal access to diagnosis for patients with undiagnosed diseases. The project covers rare diseases, inherited cancer, and cancers of unknown origin. It offers whole genome sequencing, transcriptome studies, and functional analyses beyond the standard of care. The project also prioritizes high-quality data for research and integration into the European data space. Carracedo emphasized the importance of standardized procedures, including clinical diagnosis, bioinformatic tools, and variant analysis. The project involves over 400 experts covering more than 1,500 genes and diseases. As of now, the project has achieved a diagnosis rate of 21% for patients with an average diagnostic journey of nine years. The project also addresses pharmacogenomics and population genomics, with patient associations playing a crucial role. Despite budget constraints, Carracedo expressed pride in the project's accomplishments and thanked the over 1,000 individuals involved in its implementation. He highlighted the project's contribution to improving access to diagnosis and generating valuable research data for the European Data Space.

Ana Rath, Director of Orphanet, discussed the role of Orphanet in the collaborative research ecosystem for rare diseases. Orphanet, with 27 years of service, provides information to patients, healthcare professionals, and the public about rare diseases and related expertise and initiatives. Over time, Orphanet has transformed from an

information portal to a research resource, known as a knowledge base, which holds reference data for interpreting research results and providing services to researchers and the community. Orphadata science, the scientific component of the Orphanet knowledge base, is recognized globally as a key bio-data resource for rare diseases. Orphanet's rich data, standardized, structured, and manually curated, supports interoperability and serves as an essential backbone in the rare disease ecosystem. The implementation of Orpha codes, a unique nomenclature, in health records across European countries further enhances data accessibility. Orphanet collaborates closely with European Reference Networks (ERNs) to improve nomenclature and information about rare diseases. They also offer services to ERNs, leveraging their clinical research capabilities. Orphanet's data model has the potential to be adapted for the HPRD virtual platform, facilitating accessibility to research infrastructures. Orphanet envisions a seamless data ecosystem for rare diseases, emphasizing the importance of embedding specific data sets in hospitals for structured and interpretable data collection. This data, collected at the source of care, should follow patients to enhance their care and contribute to real-world evidence, therapy development, and diagnostics. The key challenge lies in ensuring organizational and legal interoperability for effective data pathways.

Juan Fernando Muñoz Montalvo, Secretary-General for Digital Health, Information and Innovation at the Spanish Ministry of Health, highlighted the significance of European regulations on data spaces for research and the care of patients with rare diseases. He emphasized the importance of clinical implementations and outlined key possibilities offered by the regulations, such as extending access to health data for professionals across countries and enabling data transfer. This is especially crucial for patients seeking second opinions. Additionally, the inclusion of additional information in diseases with limited data can greatly benefit patients. Muñoz stressed the need for robust security measures and authentication to build trust and ensure data integrity. He emphasized the role of a digital health authority in overseeing structured data exchange. The speaker also discussed the potential of secondary use of data for rare disease patients, providing access without requiring prior consent. Muñoz emphasized the convergence of European regulations and digital transformation in healthcare, aiming to prioritize patient needs. He highlighted the use of Internet of Things (IoT) devices for data collection and the importance of integrating this data into healthcare processes. Muñoz introduced a project focusing on pediatric rare diseases, aiming to provide specialized care and support for patients and their families. Collaboration between the Ministry of Health and the Spanish regions, led by Catalonia and Madrid, was emphasized. Muñoz underlined the importance of terminology standardization and information exchange to facilitate comprehensive patient care. He expressed support for a federated model for data spaces, connecting healthcare professionals with other sectors and utilizing the European Health Data Space. In conclusion, Muñoz emphasized the urgency in taking action and building upon existing initiatives.