

# REPORT

## **IPOPI's 10<sup>th</sup> EU Primary Immunodeficiency Forum** **“Tackling diagnostic odyssey in rare diseases through ERNs: the case of PIDs”**



**22 November 2017**  
**European Parliament**  
**Brussels, Belgium**

## Introduction

On Wednesday 22 November 2017, IPOPI organised its 10th EU PID Forum “Tackling the diagnostic odyssey in rare diseases through ERNs: the case of PIDs” at the European Parliament in Brussels (Belgium). Chaired by the Member of the European Parliament Mr José Inácio Faria (EPP, Portugal), the meeting brought together representatives of the European Commission, Permanent Representations, PID patients, academics and healthcare professionals to discuss an issue of key importance across the rare disease field – that of diagnosis. For primary immunodeficiency (PID) conditions, diagnosis is still not optimised across the European Union and many patients do not receive an accurate and timely diagnosis which is crucial for successful PID management and care. The 10th PID Forum aimed to investigate how the newly launched European Reference Networks (ERNs) can be used to optimize PID diagnosis in the EU and identify other potential mechanisms to improve PID diagnosis.

## Opening remarks



**José Inácio Faria MEP** opened the 10<sup>th</sup> EU PID Forum by thanking IPOPI for co-organising an anniversary Forum and their continuous collaboration with the European Parliament. He emphasized that in the last years the European Union has significantly contributed to rare diseases policies across Europe: the establishment of ERNs sent out a strong message that information, diagnosis and treatment of rare diseases will now be undertaken in a much more strategic way than before. Taking into account that genetic diagnosis for PIDs is not available in some EU countries, international collaboration through ERNs is expected to provide patients with better opportunities to receive timely diagnosis and, as a result, better manage their condition. He expressed his interest in exploring

political actions needed to strengthen the ERNs to contribute to better rare disease diagnosis, as well as continuing his cooperation with IPOPI both at the European and national levels.

## EU added value in rare disease diagnosis

**Rory Palmer MEP** underlined the importance of European collaboration through the ERNs to provide better services to patients, as well as to enhance knowledge on rare diseases. As a British MEP Mr Palmer expressed his concern that a great potential of the ERNs can be undermined by the UK’s upcoming departure from the EU: currently 6 of the 24 ERNs are led by centres in the UK, and as currently ERN membership is restricted to EU and EEA member states, dependently on the outcome of negotiations the UK’s future involvement in the networks might be at risk. Mr Palmer noted that ensuring a continuous public health collaboration between the UK and the EU after the Brexit would be his top priority during the upcoming Brexit negotiations.



## PID diagnostic disparities across EU



**Dr Peter Jandus, ESID WP Development** highlighted that in the last years, diagnostic delay in PIDs has been decreasing, however there are still major differences and inequalities remaining in PID diagnosis between adults and children; urban and rural areas; and amongst EU regions. Despite some improvements, many PID patients face long delays in diagnosis and consequently do not receive appropriate and timely treatment that can result in severe complications and even death in some cases. Dr Jandus noted the following measures to reduce diagnostic delay: (1) increased awareness on PIDs on different levels of medical education; (2) inclusion of PIDs in the national newborn screening programmes; (3) ERN-RITA use for better PIDs detection and diagnosis, especially for less common PIDs which are more difficult to detect.

## Presenting ERN-RITA: goals & way forward

**Johan Prévot, IPOPI Executive Director and ERN-RITA Board patient representative** provided an overview of ERN-RITA, the European Reference Network dedicated to PID, autoinflammatory disorders and autoimmune diseases, uniting 24 healthcare providers in over 10 Member States. The mission of RITA is to bring together concerted efforts to improve patient care across Europe using complex diagnostic evaluation and highly specialised innovative therapies. Mr Prévot stressed that cross-border healthcare is not limited to treatments but also includes diagnostics, and ERN-RITA has a great potential to improving equal access to genetic diagnosis, which is currently one of the key challenges across Europe. Mr Prévot also highlighted the need for a European approach to harmonize access to newborn screening in all Member States, which is crucial for PIDs and particularly for Severe Combined Immunodeficiency (SCID).



## Improving PID diagnosis, through raising awareness on:

### The diagnostic odyssey from a patient perspective



**Ricardo Pereira, President of the Portuguese PID patient organisation (APDIP)** noted that in Portugal, the average delay for patients getting a PID diagnosis is seven years. Such a delay in diagnosis results in severe consequences for patients from both physical and psychological perspectives, as absence of treatment often leads to health deterioration, antibiotic abuse, work-related discrimination, psychological problems, and family conflicts. Mr Pereira highlighted that APDIP is actively involved in raising awareness on PIDs among healthcare professionals and that it is important to start working towards newborn screening for severe combined immunodeficiencies (SCID) in Portugal. He also expressed his hope that ERNs would provide PID patients with timely and accurate diagnosis in Portugal and across Europe.

## Newborn screening in the EU as a way to improve PID diagnosis and patient outcome



**Dr Nizar Mahlaoui, Necker Enfants Malades Hospital, Chairman of the IPOPI Medical Advisory Panel,** outlined that PIDs include over 350 known genes, and SCID is the only screenable PID condition that can be cured with treatments such as Hematopoietic Stem Cell Transplantation or gene therapy. There is strong evidence and arguments that SCID fulfils internationally established criteria for the newborn screening: SCID is an important health problem; there is an accepted treatment for patients; there is a recognizable latent stage; there is a suitable and acceptable test for SCID; there can be agreed policies on whom to treat; and it is cost-efficient. Based on the mentioned criteria, SCID newborn screening

should be widely available and ERN-RITA can greatly contribute to SCID newborn screening promotion across the EU through sharing best practices on PID diagnosis, research and developing clinical guidelines.

## When to consider PID diagnosis and how to use ERNs

**Dr Siobhan Burns, Royal Free Hospital London and Chair of RITA's Transition of Care Working Party,** emphasised that ERNs as virtual networks involving healthcare professionals (HCPs) across Europe have a great potential to improve quality, safety and access to specialised healthcare to patients affected by a rare disease. ERNs foresee a clinical patient management system which aims to enable sharing of patient data, provide advice on diagnosis and treatment and archive patient data. To fully benefit from the ERNs there is a need to recruit more HCPs in the countries which are currently not represented; ensure use of advanced cross-border information technologies; and raise awareness on PID for better patient referral.



## Molecular testing inequalities and how ERNs can address them



**Dr Marielle van Gijn, University medical centre Utrecht and Chair of RITA's Molecular Testing Working Party,** outlined that the majority of PIDs are monogenic autoimmune diseases (controlled by a single gene), however they are heterogeneous in terms of onset and clinical manifestation, thus the diagnosis is very complex. Genetic molecular diagnosis is the standard of care for most patients with PIDs however there are major inequalities in access to such diagnosis across the EU. Dr van Gijn emphasised that it is important to aim for a standardized and uniform European-wide approach for molecular diagnosis of monogenic immune-mediated diseases such as PIDs and to

ensure access for genetic diagnosis for all patients. These goals can be achieved through ERNs which will enable data and results sharing and would result in development of common guidelines and quality standards for PIDs.

## Future of ERNs



**Enrique Terol, European Commission**, revealed the timeline foreseen by the European Commission in relation to ERNs progress: for 2017-2018 ERNs will continue their deployment stage to conclude all initial organisational processes and provide initial services; following ERNs full implementation in 2019-2020, the networks and their initial outcome will be continuously monitored; in 2021 ERNs will undergo full evaluation and will be updated based on the assessment results. While noting the continuous commitment by the European Commission to support ERN development, Mr Terol pointed out that Member States are the owners of ERNs and their role is crucial for successful ERN implementation and their integration to the national healthcare

systems. Mr Terol noted that once implemented, ERNs are expected to increase the likelihood of early and accurate diagnosis and effective treatment for rare diseases, including PIDs. This may also result in the development of new care models, innovative medical solutions, and overall change of the way in which treatment is delivered.

## Discussion

**Nessa Childers MEP** emphasized the significant progress over the last years in the approach to rare diseases and PIDs. Ms Childers highlighted the success of the Cross-Border Healthcare Directive for rare disease patients, and she expressed her hope that the importance of international cooperation in cross-border healthcare will be a top priority during the Brexit process. She noted that many Irish rare disease patients go to the UK to receive the service, thus the benefits of EU collaboration for Ireland are critical.



**José Inácio Faria MEP** stressed that the situation in Portugal is similar, especially in the Northern part, where patients are looking for care outside of the country, mostly in Spain, as the Portuguese healthcare



system is not yet ready to address the specific needs of rare disease patients, therefore it is crucial to use the international expertise. Mr Faria has noted that it is important to analyse and control the implementation of the Cross-Border Healthcare Directive in the Member States. **Stephen Mifsud, Maltese Health Attaché**, noted that the Maltese Presidency has been contributing to further ERNs development. He is optimistically looking forward to future developments in international health and research collaboration that could be beneficial to a small country like Malta. **Mr Johan Prevot** stressed that the challenge of integrating EU countries that do not yet have an ERN centre needs to be addressed since these countries would have a huge added value from the ERNs.

**Industry representatives** highlighted that their expectations towards ERNs are optimistic, however, there are still financial issues to be addressed. **Mr Enrique Terol** agreed and noted that even though

the industry and the member states have common approaches to ERNs, there are still a lot of differences between them and therefore these should be addressed carefully before exploring the possibility of industry funding to the ERNs. **José Inácio Faria MEP** noted that he welcomes a close collaboration with all stakeholders, including industry, to further develop ERNs and benefit from an improved rare disease knowledge, diagnosis and treatment.

## Conclusions

- **Many PIDs are complex and require genetic testing** to ensure the best diagnosis possible. Genetic diagnosis for PIDs is not available in some EU countries. In other cases, the specific PID is not so complex and can be diagnosed by an immunologist. The problems arise when GPs and other healthcare professionals do not suspect a PID and patients are confronted with many tests and visits to specialists before getting the right diagnosis.
- **SCID is the only screenable PID condition** that can be cured with treatments such as Hematopoietic Stem Cell Transplantation (HSCT) or gene therapy. SCID newborn screening fulfils all the internationally recognised criteria for a clinical condition to be screened at birth. SCID newborn screening is a cost-effective method of diagnosing patients and saving lives. SCID newborn screening is considered to be a paediatric emergency.
- **ERNs have a great potential to improve the speed and accuracy of diagnosis**, harmonise the management of patients in the EU, and support health professionals in sharing information and data. ERNs have the potential of being beneficial especially for member states with less diagnostic means and expertise. However, insufficient knowledge on how to use ERNs, upcoming UK's departure from the EU, potential issues with reimbursement and lack of continuous funding might significantly impair ERNs' benefits for rare disease patients.

## Recommendations

### *EU*

- The EU should develop a common approach on harmonized access to a newborn screening in all Member States, which is crucial for all PIDs but particularly for the Severe Combined Immunodeficiency (SCID), as well as for many other rare diseases.
- A standardized and uniform European-wide approach for genetic molecular diagnosis of PIDs is needed to ensure access for genetic diagnosis for all patients.
- Based on the ERNs' performance and identified need, the EU should continue funding ERNs to improve diagnosis and outcomes of rare disease patients', including those of PID patients.

### *Member States*

- ERN Coordinators should consider, where relevant, organising a working group on newborn screening within relevant ERNs, to provide the Commission with scientific proof from the Member States.
- Member States should ensure the use of advanced cross-border information technologies and raise further awareness on PID for better patient referral.

## List of participants

### *European Parliament*

- José Inácio Faria (EPP, Portugal)
- Rory Palmer (S&D, UK)
- Nessa Childers (S&D, Ireland)
- Maria Teresa Goulao, Office of José Inácio Faria MEP
- Catarina Martins, Office of José Inácio Faria MEP
- Elena Walden, Office of Rory Palmer MEP

### *Permanent Representations*

- Stephen Mifsud, Permanent Representation of Malta to the EU
- Stefan Staicu, Permanent Representation of Romania to the EU

### *European Commission*

- Enrique Terol, European Commission's DG Health and Food Safety
- Joanna Drogowska, European Commission's DG Health and Food Safety

### *External Participants*

- Frank Willersinn, Alpha-1 Global
- Francoise Rossi, IPFA
- Jelena Malinina, RPP Healthcare
- Jose Drabwell, IPOPI
- Karl Petrovsky, PPTA
- Kit Greenop, RPP Healthcare
- Laura Ciglot, Health First Europe
- Dr Marielle van Gijn, University Medical Centre Utrecht
- Dr Nizar Mahlaoui, the Necker-Enfants Malades University Hospital, Paris
- Paul Strengers, IPFA
- Peter Jandus, University Hospital Geneva
- Ricardo Pereira, APDIP
- Ruediger Gatermann, CSL Behring
- Saara Kiema, IPOPI
- Siobhan Burns, University College London
- Toon Digneffe, Shire
- Yordan Aleksandrov, RPP Healthcare