The European Reference Networks and newborn screening –
What has been achieved and what still needs to be done?

Meeting Report

Executive Summary:

Screen4Rare (S4R) and its founder organizations International Patient Organization for Primary Immunodeficiencies (IPOPI), International Society of Neonatal Screening (ISNS), and European Society for Immunodeficiencies (ESID), held a working meeting on 6 December 2023 in the European Parliament in Brussels to discuss the role of the European Reference Networks (ERNs) in newborn screening (NBS).

The meeting was hosted by MEPs Billy Kelleher (Renew, Ireland) and Stelios Kympouropoulos (EPP, Greece), supported by leading member of the industry and research Committee (ITRE) MEP Maria da Graça Carvalho (S&D, Portugal). The discussion occurred following the fruitful meeting that the SMA Alliance and other stakeholders present on 6 December organized with the Cabinet of Commissioner for Health and Food Safety, Stella Kyriakides, on 28 September 2023 to debate the importance of including NBS in the EU institution working program for 2024 and beyond.

The roundtable had the participation of a wide range of relevant stakeholders, such as Coordinators and Members of three European Reference Networks for rare diseases (ERNs) - MetabERN, ERN RITA, EURO-NMD, and organizations Eurordis, SMA Europe, SMA Screening Alliance.

All participants present agreed that the European Union can and must have a role in supporting the Member States to develop their own independent newborn screening programs, with a clear added value of offering advice and best practice. It is now time to act. This can only happen through a broad cooperation:

- Consolidate the intensity of the dialogue with EU policy makers considering the next European elections in 2024 and try and ensure it continues to be on the agenda under the next Parliament and Commission;
- Take advantage of the funds provided by EU4Health and Horizon Europe 2024 budget to build EU resources on NBS;
- Consider the establishment of an independent and advisory group on NBS made up of doctors and expert stakeholders based around the ERN infrastructure;
- Support the ERNs where NBS is relevant to integrate it into their work, including through funding for specific activities led by those ERN coordinators.

Detailed overview of interventions:

Hosting MEP Billy Kelleher, former Irish Minister for Trade and Commerce and spokesperson for the chief Health Officer from 2009 to 2011, introduced the event. The work of the ERNs in the development of advanced practices for the improvement of NBS programs has been and will be fundamental over the next few years, as is the need for the allocation of European funds in research for the development of orphan and innovative medicines. Currently, NBS programs in different EU countries differ too much: EU Member States like Ireland provide screening programs for 8 diseases, while Italy for 48. More screening does not mean better screening but nevertheless the divergence of approaches from country to country are stark. Data show that, however, EU is currently not investing enough in life sciences innovation, despite the declared commitment, and EU Countries are evaluating

NBS' potential harms in different ways. This is not enough: great results are only possible by working together in a continuous dialogue between civil society and policy makers.

The presentation by Leire Solis, Health Policy and Advocacy Senior Manager of IPOPI, gave a general and comprehensive overview of the main activities of S4R, mentioning the main principals of the 2019 Call to Action. A point was made also on the fact that NBS should not be considered as a simple test, but rather as an entire system at European level. Crucial is that in the development of a European program an assessment of both the harms and benefits of screening is considered to ensure benefits outweighing: screening can also cause harm.

Connecting to the previous final point, Prof. Peter Schielen, ISNS' Office Manager, highlighted how his organization supports the development of a quality rather than quantity NBS program that provides more benefit than harm at a more reasonable price. This is achievable by embracing the Wilson and Jungner criteria, as well as the updated WHO adaptation of these criteria considered a basis for decision making. The intervention then focused on an update and next steps of the collaboration between S4R and the ERNs on their three NBS-related workstreams. These have the triple aim of developing a blueprint of NBS in Europe, identifying case definitions of rare diseases, and the development of interoperable disease registries for screened conditions.

MEP Maria da Graça Carvalho, an MEP supporter of S4R working on research policy said that it is essential not to lose the focus on European research funds, which can be obtained from the Horizon Europe budget. In this sense, the importance of the Innovative Health Initiative (IHI), EU public-private partnership funding health research and innovation, was also reiterated.

Prof. Fabian Hauck, Head Pediatric Immunology of LMU Clinic in Munich, provided an overview of the work of ERN RITA of which he is a member. Fabian outlined compelling evidence for early identification of patients from his hospital's SCID NBS screening program. One of the most important findings as an output of his presentation is that a screening approach based on the identification of an index case in the family including prenatal siblings and NBS, can lead to a 90% survival probability benefit. This would outperform an approach based on the identification of symptoms and subsequent clinical attention (40% survival probability).

The work of ERN EURO NMD was presented by Coordinator Prof. Teresinha Evangelista. Building on the qualitative study conducted by EURO NMD published on the Orphanet Journal of Rare Diseases, to understand the state of play of hereditary NMD screening in Europe and the needs of patients, she highlighted the large unmet need for neuromuscular disease screening in the EU, considering the focus on treatment as the most important turning point in the fight against SMA disease. On the role of ERNs, Prof. Evangelista cited the priorities of training doctors on screening, public awareness, quality assurance, and finally international collaboration. She also pointed out the tremendous advancements in the treatment of SMA in recent years and the relevance of this for NBS programs.

The European Commission provided its support to the initiative by making available a video message from Commissioner Stella Kyriakides which underlines the commitment of the EU executive in recognizing the importance of the activity of ERNs and integrated NBS European programs in the current and next EU policy agenda.

Hosting MEP Kympouropoulos, in the mid keynote speech, recognized the difficulty of creating a pan-European network. The current inequalities in European screening programs for different social groups of patients requires a targeted EU approach to avoid too much local bureaucracy, and collaboration between countries and civil society. The common adoption of new criteria, new diseases and a uniform approach is important to improve the lives of children born with a rare disease and

their families. There is currently a low prevalence for each disease, but the overall impact is devastating. the SMA disease currently has 3 life-saving treatments.

The Chairman of ERN MetabERN, Prof. Maurizio Scarpa, mentioned that his ERN activity contributed for its part with the publication of a study on how to support EU Countries that are only recently interfacing with the development of NBS programs. This approach includes the conduction of a mobility program for hosting physicians in NBS centers across EU to clinically train them.

Prof. Jim Bonham, ISNS' President, delivered the closing presentation focusing on the steps necessary to mitigate harm and maximize benefit for all forms of screening. It is also important to recognize the potential of new technologies and genomics – it would indeed be possible to move from screening 50 conditions to 200 or more. To pursue these objectives in a clear and sustainable way, it is essential to reserve a key role for ERNs' doctors currently involved in the identification and treatment of rare diseases in Europe, and for their collaboration with appropriate professional societies, relevant patient groups and support, and health policy decision-makers. The first objective of S4R is the development of appropriate, well-organized, and equitable NBS, offered on a voluntary and informed basis to families to help identify well-defined treatable conditions where it is clear that their early detection and asymptomatic treatment during "childhood results in significantly improved outcome". The second objective is the formation of an independent and advisory group on NBS.

The Head of European and International Advocacy of EURORDIS, Valentina Bottarelli, spoke underlining the need to agree and share a pan-European approach based simultaneously on legislative actions and initiatives in the next future. It is also important to consider patients' expectations in this dialogue, and the need to make screening more available and accessible.

The final discussion saw general agreement after a successful event on continuing the collaboration between ERNs and civil society organizations for a correct and sustainable dialogue with EU policy makers, especially considering the institutional change that will take place in 2024 with the European elections.