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Call to Action

from the Expert Conference on Rare Diseases

Towards a new European policy framework on rare diseases:

“Building the future together for rare diseases”

On 25 and 26 October 2022, in Prague

The Czech Presidency of the EU Council organised the Expert Conference on Rare Diseases in Prague on 25-26 October 2022 to explore how the European Union can take continued steps towards a coordinated strategy for rare diseases to better addresses current unmet needs by setting meaningful goals for patients, families and for society at large, integrated at the national and regional levels.

Rare diseases, including rare cancers, are a heterogeneous group of largely incurable, complex conditions. There are over 6000 rare diseases, and more than 70% have a genetic origin. Although individually characterised by low prevalence, the sheer number of rare diseases results in a directly affected community of 20 million people across the EU. Rare diseases are chronic, progressive, degenerative, disabling and frequently life threatening. They are typically accompanied by a scarcity of knowledge and expertise.

In 2021, an average of 5 years is still needed to obtain a diagnosis, and only 6% of rare diseases can benefit from a specialized treatment. People living with a rare disease experience a high psychosocial, emotional and financial burden and are often excluded from society. The COVID-19 pandemic has exacerbated their vulnerabilities, with 84% of people living with a rare disease in Europe having experienced disruptions to their care during this period. Scarcity and scattered nature of data and expertise single out rare diseases as an area of very high added community value, demanding interdisciplinary as well as cross-border collaboration in terms of sharing knowledge, data, and research.

Despite tremendous progress demonstrated by the measures already implemented, the ongoing commitments and major investments in addressing the challenges of rare diseases from the side of the European Commission, the need for an updated framework of EU actions and support for national plans and strategies on rare diseases remains. The 2008 Communication on *Rare Diseases: Europe's challenge*, which aimed to “encourage cooperation between the Member States and set out an overall strategy for support to



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Member States”, was a cornerstone policy for today’s progress, but drafted in an era during which scientific breakthroughs, technological potential and crisis and values were not the same as today.

A Conference focused on strengthened European collaboration on rare diseases

Participants, patient advocates, healthcare professionals, researchers, government representatives and industry set out how strengthened cooperation and coordination of Member States could be outlined in a European Action Plan for Rare Diseases. By bringing together current initiatives under one framework that would provide a roadmap leading towards common measurable goals that respond directly to unmet needs and ensure that inequalities are not exacerbated by a person’s country of residence.

The Conference marked another significant milestone in the proposal for a policy framework for rare diseases following the conclusions of the European Court of Auditor’s report n°7/2019, the cross-sector consensus from over 250 stakeholders in the EU spearheaded Rare 2030 Foresight Study, the 43 cosignatory members of the European Parliament in their letter of support for Europe’s Action Plan, the recognition of the “undeniable benefit” of stronger cooperation during the Informal meeting of Ministers of Health in Grenoble earlier this year and the support of patients, key opinion leaders and policy makers presented at the High Level Ministerial Conference: ‘Care and innovation pathways for an EU policy on rare diseases’ (28 February 2022) in support of the proposal for a European Action Plan on Rare Diseases.

In line with the political support and increased momentum for a stronger European approach to rare diseases, the Conference participants explored what meaningful steps could be taken by the European institutions and Member States to improve the lives of people living with a rare disease.



The Expert Conference on Rare Diseases focused on five blocks that make up key pillars of a European strategy on rare diseases and led to five key recommendations:

1) A call for coordinated European Action Plan on Rare Diseases to address the challenges of people living with rare diseases and their families

CZ PRES calls upon the European Commission to adopt a European Action Plan on Rare Diseases to support and complement on-going and future efforts at both the EU and Member State level to reduce unmet needs of the 20 million people living with a rare disease in the EU.

Specifically, a European Action Plan on rare diseases should:

- Bring together existing EU strategies and actions in a comprehensive framework (e.g. cancer, data, research, pharmaceuticals, social rights)¹.
- Integrate and sustain EU and national plans and strategies for rare diseases on a long-term basis.
- Update and reinforce the last rare disease strategy from 2008/2009, to prepare better for the next 10-15 years and the continued challenges in terms of genomics, technology and scientific advances.
- Create an informal multistakeholder, multi-country working group to support the European Commission in establishing a scoreboard of indicators to monitor the implementation of the Action plan at the EU and national level, and to identify good practices across disciplines and countries.
- Introduce measurable goals to ensure that all Member States are working to the same objectives to reduce inequalities across the EU.

¹ This should include: revisions of legislation of Orphan Medicinal Products Regulation, Paediatric Use of Medicines and adoption of the 'general pharmaceutical legislation), Europe's Beating Cancer Plan; non-legislative policy actions; and recent Commission initiatives such as the European Health Data Space, the European Pillar of Social Rights Action Plan and the European Care Strategy



2) Early Diagnosis of Rare Diseases

Early diagnosis (notably via preconception carrier testing and newborn screening) can significantly decrease mortality and morbidity caused by selected rare diseases and improve quality of life by expediting access to the most effective care and treatments. Yet the quest for diagnosis often remains an odyssey. Better use and accessibility of current effective and available diagnostic tools and technologies, best practices and programmes should be considered as part of a continuum of health strategies along the life course of any person living with a rare disease in Europe.

As recognised during the Expert Meeting on rare diseases, as well as at the technical meeting also held under the Czech Presidency of the EU specifically on newborn screening (23 July 2022, Brno), newborn screening (NBS) has the potential to detect several dozens of rare conditions, providing the possibility of early treatment and a significantly improved long-term outcome while minimizing harms of NBS programmes. Despite these clear benefits, the availability and conduct of NBS programmes varies considerably across the EU and, with the increasing potential of the newly developed genomic testing, it is likely that these differences may become even more pronounced.

Therefore, the CZ PRES calls on the European Commission and the EU Member States

- A. to support initiatives that aim at promoting the best NBS practice to ensure availability and equity of access to well-structured NBS programmes for all EU citizens and that may benefit from coordinated EU-wide approach. Activities that will help support this aim include:
 - The need to document and identify good practice in existing national NBS programmes so that these lessons may be promoted and adopted more widely.
 - The need to develop, collect and collate key performance indicators for all stages of the NBS programmes that will help to evaluate, monitor and improve the quality of NBS programmes.
 - The need for outputs from national pilot programmes in NBS to be shared more effectively to shorten the time needed to introduce screening programmes for new candidate conditions or cease their inclusion.
 - The development of agreed case definitions.
 - The development of interoperable outcome studies for conditions included within existing screening programmes so that the impact and effectiveness of the current programmes can be assessed and improved.



- The formation of an EU-level NBS Expert Advisory Committee, free from bias or national interests, to provide trusted, high-quality information to support decision making at a national level.

Special consideration should also be given to evaluate the rapid development of genomics that may improve the efficacy of diagnosis shortly after birth. The novel techniques provide exciting opportunities to bring significant health and economic benefits to society and particularly to EU citizens with rare disorders, but they also raise important technical, logistic, ethical and economic issues that need to be addressed before they can be recommended as a routine part of public health policy offered on a whole population basis to asymptomatic newborns.

As demonstrated by the SOLVE-RD project, a combination of -omics technologies can also contribute to solving the pathogenicity in different patient cohorts and confirming a diagnosis for rare disease patients who did not receive one with other tools (e.g., molecular diagnosis).

The CZ PRES calls on the EU and its Member States

- B. to support such an approach to an expanded number of disease areas and countries across Europe to better diagnose currently “unsolvable” cases.

Accessibility of medical devices necessary for diagnostics of rare diseases is of crucial importance. Regulation (EU) 2017/746 on in vitro diagnostic medical devices sets several ways for derogation from the generally applicable rules for safety and performance requirements when placing the medical devices on the market. Nevertheless, further specification that would ensure that in vitro medical devices necessary for proper diagnostics of rare diseases remain available on the market is needed. The CZ PRES:

- A. Appreciates the ongoing work of the Medical Device Coordination Group MDCG guidance document concerning the art. 54 of the Regulation that will include clear statement when it comes to possible derogation from the Regulation for medical devices necessary for rare diseases diagnostics.
- B. Calls upon the MDCG and the European Commission to prepare without any further delay guidance document on art. 5.5 of the Regulation that would in detail define based on practical experience and including practical ways for their implementation.



3) Revision of the Orphan Drug and Paediatric Drug Regulations

In many ways, the Regulation on Orphan Medicinal Products implemented in 2000 proved to be a great success, leading to progress of care in many overlooked conditions. Despite this progress, concerns about remaining unmet needs, patient access, affordability, and sustainability of pharmaceutical spending have risen in the past few years. In particular, there are concerns related to the appropriateness of the current regulatory framework to attain the societal goal of reducing unmet needs while ensuring value-for-money.

The CZ PRES encourages the European Commission:

- A. to use the opportunity of the upcoming revision of the Orphan Medicinal Products and Paediatric Regulation, together with the planned revision of General Pharmaceutical Legislation, to evolve the incentives framework to maintain predictability for sponsors while enhancing Europe's competitiveness. This needs to be the main focus of the European Action Plan on Rare Diseases.

In particular, the CZ PRES believes there is a unique opportunity to:

- A. Define a model that is centred on the unmet needs of people living with a rare disease, and includes patient participation in its establishment and implementation;
- B. Transform the European Research & Development for the rare disease ecosystem building upon advances of the past 20 years, for the next 20 years. This must reflect and connect developments across science, technology and policy;
- C. Situate Europe as a global leader in research, development and access to diagnostics, treatment and care, through a regulation that is attractive and competitive globally. Reflections should be made in aligning with and maintaining competitiveness with the USA's FDA system;
- D. Establish a European pathway, from development to access, to ensure innovation coupled with affordability and to gain that crucial strategic autonomy in research and development;
- E. Ensure convergence and coherence of relevant existing as well as currently negotiated legislation.



4) Instruments for improving access to rare disease treatments

The revision of the Orphan Medicinal Product and Paediatric Medicines regulations can only address part of the unmet medical needs. Fragmented access to healthcare across the EU precludes many patients from timely access. Desired system should ensure sustainability for healthcare systems and include additional solutions to address a persisting lack of treatments and inequalities across the Member States.

A new approach that balances the incentives needed for innovation, with financial and fiscal sustainability of health care systems, is required. The approach should consider clinical need, proven therapeutic value and cost-effectiveness, volumes of medicines produced and budget impact, while requiring robust evidence generation to reduce uncertainties about benefits. Public and private initiatives developed in response to the ongoing COVID-19 pandemic demonstrate that greater collaboration is possible and reflects shared responsibility between the national health authorities and the pharmaceutical industry, with inherent price transparency².

Further strengthening European cooperation in pricing and negotiations is desirable, while respecting current division of competences.

CZ PRES finds it necessary to:

- A. Explore the feasibility of piloting cross-country mechanisms to improve best practices and information exchanges, value assessments, demand pooling, negotiating and purchasing models, as mentioned by the WHO Europe³ Statement. Such a collaboration, supported by a dedicated platform, should be able to explore new approaches to affordable pricing, reimbursement and funding (for example external reference pricing, price regulation, equity-based tiered pricing, value-informed pricing, and staggered, performance-based or subscription payment models). While joint purchasing has shown to be a rather cumbersome process, joint negotiations have the potential to improve accessibility of complex treatments, since they would significantly increase attractiveness of even smaller EU markets.
- B. Explore opportunities for joint negotiations with producers, and should there be a support of Member States even for opportunities for joint procurement or procurement by the Commission on behalf of the Member States, of complex treatments and treatments for small populations that have the potential to improve accessibility of treatment across the EU providing timely access to patients at an

² Oslo Medicines Initiative - Statement by WHO/Europe (September 2022)

³ Ibid.



affordable manner, in a way that could possibly be incorporated into the revision of Orphan Drug and Paediatric Drug Regulations as regulatory incentive.

As in very small populations and/or complex treatments, such as Advanced Therapeutic Medicinal Products, evidence at time of pricing and reimbursement is often immature⁴, there is a high level of uncertainties at time of Marketing Authorisation which makes clinical value assessment very challenging for all EU Member States. This leads to delays in the HTA processes and results in delayed and incomplete access. CZ PRES believes it is necessary to:

- C. Support the generation of evidence across the whole life cycle of products. The generation of additional real-world evidence data in the years following marketing authorisation for selected, innovative and transformative medicines for complex and low prevalence diseases, with true cross-border value, would ensure attractiveness of the European R&D ecosystem for rare diseases and drive consolidation and structured cooperation. This streamlined approach could be included as a new incentive in the forthcoming revision of the Regulation on Orphan Medicinal Products.

⁴ Rare diseases are not uniformly spread across prevalence: only 4% of diseases sit in the 1-5 in 10,000 prevalence bracket, while 84.5% affect fewer than 1 in 1,000,000 patients. While the more prevalent diseases are less frequent, the size of the populations suffering from each of these diseases is significantly higher, meaning that 80% of all rare disease patients fall in the 150 diseases with the highest prevalence (Nguengang Wakap, S., Lambert, D.M., Olry, A. et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. *Eur J Hum Genet* 28, 165–173 (2020).



5) Holistic healthcare pathways: Integrating European Reference Networks into European health care and social systems

The Expert Conference recognised that European Reference Networks (ERNs) stood out as a success story in how to drive collaboration across the EU. There are now 24 Networks connecting over 1500 clinical centres. Experts at the Conference expressed how crucial the next few years are and the critical importance of European Reference Networks as a pillar within a European Action Plan on Rare Diseases.

CZ PRES would like to emphasise the need for:

- A. Stronger integration of ERNs into national healthcare systems, to enable EU countries to strengthen the resilience of their national health system and improve accessibility of highly specialised expertise.
- B. Sustainable and proportionate investment from national and EU budgets into strengthening the capacities of ERN centres and enhancing their competencies to better serve patients suffering from a rare disease. Sustainable funding mechanisms to accelerate the development and uptake of treatment options for rare diseases within ERNs, as they integrate European-wide clinical research and care settings, supported by registries.
- C. Leveraging network-based health data, experience and knowledge, powered by digital tools, where Centres of Expertise act as a trusted universal source and curators of global knowledge and integrate it to daily clinical practice.
- D. A fully-fledged data strategy for rare diseases, supported by interoperable infrastructures, to collect and exploit the full value and potential of health-related data in alignment with and contributing to the European Health Data Space and the European data strategy.
- E. Implement EU-wide and national policies and programmes to person-centred and integrated care, both in terms of integration across medical disciplines but also bridging the medical and social spheres, with the aim to enable holistic wellbeing of people living with rare diseases and their families.