

# Understanding European Reference Networks

## Cooperation on rare diseases across Europe

### SUMMARY

European Reference Networks (ERNs) are newly established virtual platforms for voluntary cross-border collaboration between specialists in rare and complex diseases. ERNs were set up under Directive 2011/24/EU on the application of patients' rights in cross-border healthcare, and go back to a 2009 Council recommendation on an action in the field of rare diseases.

Since specialist knowledge of rare diseases is both scarce and scattered across countries, the EU-level cooperation afforded by ERNs is regarded as bringing added value through maximising synergies. Currently, 24 thematic ERNs involve more than 900 specialised healthcare teams in over 300 hospitals in 25 EU Member States plus Norway.

A public consultation fed into the establishment of the ERNs, and a number of stakeholder views were presented on the occasion of their launch. The ERN initiative has generally been well received. According to stakeholders, its strengths include opportunities for carrying out research and new treatments, breaking the isolation of specialists and patients, reducing inequalities in care, and fostering patient involvement. Among the challenges that need to be addressed, stakeholders mention questions concerning reimbursement, interoperability and data confidentiality, and legal issues.

The ERNs are currently in their deployment phase, and expected to reach full capacity over the next five years.



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## Launch of the European Reference Networks

The first European Reference Networks (ERNs) became operational on 1 March 2017. ERNs [are defined as](#) 'virtual cross-border cooperation platforms between specialists for the diagnosis and treatment of rare or low-prevalence<sup>1</sup> complex diseases' (see box). They were launched by the European Commission as a formal structure of voluntary collaboration connecting healthcare providers or centres of expertise across Europe. Currently, [24 thematic ERNs](#) are active, involving more than 900 healthcare teams in over 300 hospitals in 25 EU Member States plus Norway.

## Purpose, structure and functioning

### Legal basis

The need for gathering expertise at the European level to ensure equal access to accurate information, appropriate and timely diagnosis, and high-quality care for rare-disease patients was underlined in the 2009 [Council recommendation](#) on an action in the field of rare diseases.<sup>2</sup> The ERNs were set up under [Directive 2011/24/EU](#) on the application of patients' rights in cross-border healthcare (the 'Cross-border healthcare directive'), which requires the Commission to support the development of ERNs, particularly in the area of rare diseases (Article 12). In line with the directive, the Commission adopted a legal ERN framework in March 2014.<sup>3</sup>

### Rationale

Specialist knowledge of rare diseases is both scarce and scattered across countries. As the Commission explains, the idea behind establishing ERNs is to make medical expertise, rather than patients, travel: the resulting consolidation, coordination and sharing of knowhow will enable healthcare providers to access a larger pool of expertise. This, in turn, will increase the chances of rare-disease patients to receive a fast and accurate diagnosis,<sup>4</sup> and to benefit from the best treatment and advice available for their specific condition. EU-level cooperation is regarded as bringing added value by maximising synergies.

### Scope

[Beyond](#) sharing knowledge about the diagnosis and treatment of patients with rare diseases, ERNs are envisaged to facilitate the development of:

- research cooperation and knowledge generation, for instance, through joint research projects and large clinical trials to improve the understanding of diseases;
- medical guidelines and training activities;
- new medicines and medical devices, by means of gathering large volumes of patient data;
- new care models and [eHealth](#) solutions and tools, including [telemedicine](#)<sup>5</sup> and mobile health ([mHealth](#)) applications.

### What are 'rare' and 'complex' diseases?

For the purpose of ERNs, 'complex' diseases or conditions [are defined as](#) those that combine a number of factors or symptoms requiring a multi-disciplinary approach and a well-planned organisation of services over time.

In Europe, any disease affecting not more than five people in 10 000 is considered rare (in line with [Regulation \(EC\) No 141/2000](#) on orphan medicinal products). An estimated [5 000-8 000](#) rare diseases affect 6-8 % of the population – that is, between 27 and 36 million people.

Rare diseases are serious and often life-threatening. Many of them cause chronic pain and suffering and have no effective cure. About [80 %](#) of rare diseases have genetic origins. Patients affected face common problems. These include lack of access to correct and timely diagnosis, lack of information on and scientific knowledge of the disease, and lack of appropriate quality healthcare.

An existing resource relevant in this context is the [Orphanet](#) portal that 'aims to provide high-quality information on rare diseases, and ensure equal access to knowledge for all stakeholders'.

According to the Commission, ERNs are '[incubators](#) for the development of digital services for the provision of virtual healthcare'. They are conceived as '[part of a broader strategy](#) to make European health systems more efficient, accessible and resilient', which would include the [possibility](#) of scaling up and extending the ERN model to other diseases in the longer term.<sup>6</sup>

### Governance

As the Commission states, the ERN initiative is mainly driven by the **Member States**.<sup>7</sup> An ERN [is composed of](#) at least 10 healthcare providers and/or centres of expertise ('members') from at least eight different Member States. The individual Member States are responsible for the national process of endorsing the applications of their healthcare providers/centres of expertise wishing to become members of an ERN. The final approval of applications is given by the [Board of Member States](#),<sup>8</sup> comprised of representatives of the EU Member States plus Norway.<sup>9</sup> After the Commission's call for proposals in 2016, the board approved the first 23 networks in December 2016 and a 24th one in February 2017.<sup>10</sup> For each ERN, one centre of expertise acts as the coordinating member; this centre in turn appoints one person as coordinator for the given ERN. The framework for the ERNs was created by the **Commission**.<sup>11</sup> Moreover, the Commission has been providing network coordinators with technical networking facilities and support (grants) from different EU funding instruments, including the [EU Health programme](#),<sup>12</sup> the [Connecting Europe facility](#) and the EU research programme [Horizon 2020](#).

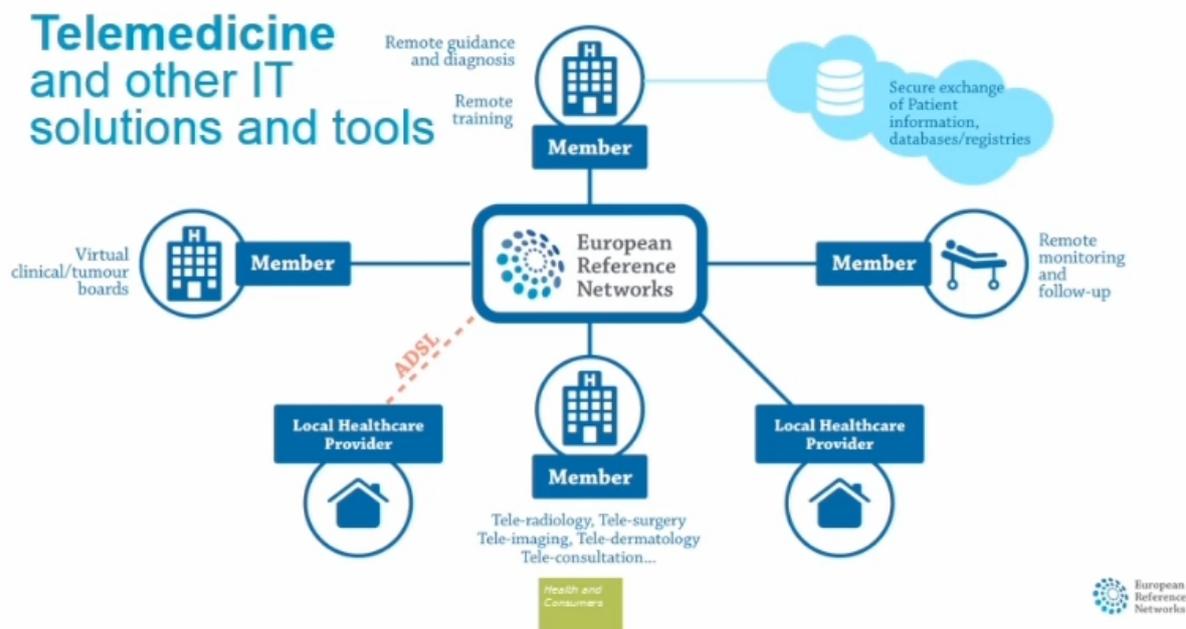
### Organisation

The 24 ERNs are organised as thematic networks around groups of diseases, such as autoimmune diseases, childhood cancers or metabolic disorders, to name but a few. ERNs [vary](#) in size (that is, the number of members) and the range of diseases covered. Resources needed for diagnosis and treatment are likely to differ across ERNs and centres of expertise and to vary depending on the complexity of a specific condition or the requirements of the technological infrastructure (see below). While ERNs are not accessible to individual patients, a patient's case can be referred to the ERN member in their country by their healthcare provider, subject to the patient's consent and in line with the rules of their national health system.

### Infrastructure

Collaboration is facilitated by information technology (IT), using eHealth – and notably telemedicine – tools.<sup>13</sup> Once fully operational, a dedicated IT platform will allow multidisciplinary teams of medical specialists in each ERN to share information and discuss patient cases in virtual clinical meetings ('advisory boards'). The platform is also meant to serve as a repository for the amounts of clinical data processed and collected by ERNs, and thus to contribute to building a bank of cases for further study. The system's main [components](#), which are still [under development](#), include: (i) the ERN collaborative platform for communication and collaboration activities (other than the exchange of patient data), such as document management and event organisation; (ii) the ERN clinical patient management system for the exchange of clinical information and patient data, including such as have been sourced from medical [imaging](#), as well as for web conferencing and virtual clinical meetings; (iii) the ERN public web presence (europa.eu domain and individual ERN websites) to raise awareness of ERNs, to share knowledge with the general public, patients and health professionals, and to issue clinical guidelines, patient guidance, and so forth.

Figure 1 – Telemedicine and other IT solutions and tools used in the ERN infrastructure



Source: European Commission, Commissioner Vytenis Andriukaitis' [presentation](#) at the ERN conference, 9 March 2017.

## Next steps

ERNs are expected to reach full capacity over the next five years. They are now in their [deployment stage](#) (2017-2018). The first version of the ERN clinical patient management system is due to be delivered by mid-2017. Full-service production, continuous monitoring and initial outcome assessment are expected for 2019-2020, with evaluation and update scheduled for 2021. Calls for healthcare providers who would like to join existing ERNs will be launched yearly (the next in November 2017). According to the Commission, there are no calls for new networks planned at this stage.

## Stakeholder views

Prior to launching the ERNs, the Commission carried out a public consultation on the potential scope of the networks and the criteria for healthcare providers wishing to join them. According to the June 2013 [summary report](#), respondents wanted ERNs to 'focus on complex, highly specialised and rare diseases for which expertise is scarce'. A number of stakeholder perspectives were also expressed during the [3rd conference on ERNs](#) and kick-off meetings, held on 9-10 March 2017 in Vilnius ([conference report](#)), and were presented in the Commission's [brochure](#) (see examples below).

## Healthcare providers

Pierre Fenaux, [ERN EuroBloodNet](#) coordinator, [is quoted as saying](#) that the possibility to consult colleagues in other countries will end the professional isolation that experts in rare diseases sometimes face. In his view, the linkages between hospitals around Europe will pave the way for clinical research and may also serve as an advocacy platform by fostering the development of patient associations and offering expert input on innovative treatments. Alberto Pereira, [ENDO-ERN](#) coordinator, [points to](#) the evolving role of patients not only in terms of choosing the best healthcare provider, but also in shared care and decision-making, and thus in management and governance. Maurizio Scarpa, [MetabERN](#) coordinator, [identifies](#) topics that still need further discussion, including the legal entity of ERNs, the reimbursement of ERN activities and the liability of coordinators.

Arimantas Tamašauskas, [ERN EURACAN](#) member and Lithuania's representative on the ERN Board of Member States, [mentions](#) issues such as the different ERN legal bases in different Member States, the relationship with affiliated partners, the costs and responsibility for remote treatment, and intellectual property rights.

In a joint [paper](#), network coordinators Holm Graessner ([ERN-RND](#)), Franz Schäfer ([ERKNet](#)), Maurizio Scarpa (MetabERN) and Thomas O. F. Wagner ([ERN-LUNG](#)) examine the challenges that the integration of ERNs in the German healthcare system will pose. These include the competition between national and European interests in the context of the conflict between national responsibility and intended cross-border availability of healthcare services, the lack of a funding concept and the establishment of ERNs in Member States in which implementation of national action plans on rare diseases is lagging behind.

### Health authorities

Till Voigtländer, chair of the ERN Board of Member States and Austria's representative on it, [points out](#) that ERNs are still in 'progress mode'. The strategic goals to be attained over the next five years include, among other things: approaching the ideal network composition and format, given the broad range in the number of full members per ERN and per Member State; providing evidence for the success of the ERN concept; and solving the reimbursement challenges that virtual cross-border healthcare brings with it. Elisabetta Zanon, director of the UK National Health Service (NHS) European Office, [comments](#) that by pioneering cross-border digital technologies in a real clinical world and at scale, ERNs will also be relevant for the implementation of the Digital agenda.<sup>14</sup> According to Zanon, the infrastructure challenges that will have to be addressed include interoperability<sup>15</sup> of technological solutions, maintenance of patient registries and confidentiality in sharing and re-using patient data.

### Patients

The European Cancer Patient Coalition (ECPC) [has welcomed](#) the activation of the ERNs as a cornerstone in EU cooperation on rare cancers. Eurordis – Rare Diseases Europe [has praised](#) ERNs as a tangible example of the value of EU cooperation in healthcare policy that will directly benefit patients. Eurordis maintains that ERNs will help end the isolation of patients, break the silos in which experts have worked, and reduce the inequality in care both between different rare diseases and between Member States. Moreover, Eurordis thinks that ERNs will provide an opportunity for a new type of public-private partnership, helping to produce the kind of quality data that industry needs to develop new medicines.

### Industry

The Joint Task Force between the European Association for Bioindustries (EuropaBio) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) on Rare Diseases and Orphan Medicinal Products [has expressed support](#) for an increased cooperation between Member States to improve accurate early diagnosis of rare diseases. It supports a joined-up approach that addresses the challenges of patient access to treatments and encourages policy makers to maintain their commitment on what EU health systems can deliver in terms of preventing and treating rare diseases. According to the International Federation of Pharmaceutical Manufacturers (IFPMA), a supportive policy environment for rare diseases is one that helps to increase understanding of rare diseases, stimulate more research, encourage appropriate disease management and empower patients. IFPMA [has stated](#) that political awareness is essential to create

supportive policies for rare-disease patients; furthermore, it calls for multi-stakeholder collaboration and dialogue to ensure patients' access to treatment.

### EU bodies and institutions

#### Members of the European Parliament address March 2017 ERN conference in video messages

[Bryan Hayes](#) (EPP, Ireland), speaking on behalf of the [European Advocates for Epilepsy](#) group in the EP, welcomed the ERN launch as 'the beginning of a new phase of innovation and cross-border cooperation between specialists across Europe'. For [Françoise Grossetête](#) (EPP, France), an 'ambitious dream' was about to become reality: one where clinicians would effectively share their knowledge on rare diseases, patients would have access to the best medical expertise, wherever they come from, and a clear governance structure for knowledge-sharing across countries would make it easier for doctors to adapt the treatments.

On 30 March 2017, the Commission's Directorate-General for Health and Food Safety (DG SANTE) won the European Ombudsman's 2017 [award for good administration](#) for the ERN project. As the [announcement](#) states, the 'strength and weight of the EU is needed to foster cross-border research, alliances and scientific cooperation'.

In his presentation at a roundtable event<sup>16</sup> on 17 May 2017, Guy Dargent, senior scientific project officer with the Commission's Consumers, Health, Agriculture and Food Executive Agency (Chafea), observed that the success of ERNs will depend on how well they integrate with national health systems. Member States have a variety of ways to support ERN members and need to exchange experiences on how this can be achieved.

### Main references

European Commission, [European Reference Networks – Working for patients with rare, low-prevalence and complex diseases](#), 2017.

European Commission, [Share. Care. Cure. European Reference Networks for rare, low-prevalence and complex diseases](#), 2017.

### Endnotes

- <sup>1</sup> 'Prevalence' is the number of people living with a disease at a given moment.
- <sup>2</sup> The 2009 Council recommendation asked Member States to establish and implement, by the end of 2013, plans or strategies to support rare-disease patients. In February 2016, [23 Member States](#) had such plans/strategies in place.
- <sup>3</sup> Including a [Commission delegated decision](#) setting out the criteria and conditions that ERNs and healthcare providers wishing to join them should fulfil, and a [Commission implementing decision](#) with the criteria for establishing and evaluating ERNs.
- <sup>4</sup> According to the patients surveyed in a 2013 [report](#) commissioned by the pharmaceutical company Shire, it takes 5.6 years on average to diagnose a rare disease in the United Kingdom (UK). A 2013 Eurordis [survey](#) found that about 40 % of patients surveyed had first received the wrong diagnosis.
- <sup>5</sup> 'Telemedicine', as per the 2008 Commission [communication](#) on the topic, is 'the provision of healthcare services, through the use of ICT [information and communication technology], in situations where the health professional and the patient (or two health professionals) are not in the same location. It involves secure transmission of medical data and information, through text, sound, images or other forms needed for the prevention, diagnosis, treatment and follow-up of patients.' Telemedicine encompasses a wide range of services, such as teleradiology, teleconsultation, telemonitoring, telesurgery, and videoconferences between health professionals, among others.
- <sup>6</sup> In its May 2017 [mid-term review](#) on the implementation of the Digital Single Market strategy, the Commission refers to ERNs as a 'striking demonstration of what Europe can achieve by pooling medical expertise and data', calling for further EU action in the area of health-data generation and processing to advance research, enable the early detection of infectious outbreaks, accelerate the development of medicines and medical devices, and stimulate innovative healthcare solutions such as telemedicine and mobile health applications.
- <sup>7</sup> Pursuant to Article 168 of the Treaty of the Functioning of the European Union, as EU Member States are responsible for the organisation and delivery of their healthcare, national participation in the ERNs is voluntary.
- <sup>8</sup> See also the [list of members](#) of the Board of Member States (as of September 2016). The board is currently co-chaired by Austria and the Commission's DG SANTE.

- <sup>9</sup> Member States without representation in an ERN can designate healthcare providers as 'associated' and/or 'collaborative' national centres. The first affiliated partners are expected to be nominated by the end of 2017.
- <sup>10</sup> See also the [list of approved ERNs](#). Six of the 24 networks are coordinated by UK centres of expertise.
- <sup>11</sup> Actors involved in ERN implementation include the [Commission expert group on rare diseases](#), the EU joint actions on rare diseases ([RD-action](#)) and on rare cancers ([JARC](#)), as well as patients' and professional and scientific organisations.
- <sup>12</sup> According to the 2017 [action plan](#) for the EU's Health Programme, an approved ERN is eligible for up to €200 000 of funding covering the years 2017-2021. Actions to be funded are coordination, management and non-clinical activities.
- <sup>13</sup> For more information, see a selection of related [EPRS publications](#) on eHealth and digital health.
- <sup>14</sup> The [Digital agenda](#) is one of the pillars of the Europe 2020 strategy. According to the Commission, it is aimed at boosting Europe's economy by delivering sustainable economic and social benefits from a digital single market.
- <sup>15</sup> 'Interoperability' [can be defined as](#) the ability of applications to communicate seamlessly with each other. Levels include cross-border, semantic, technical, legal and organisational interoperability.
- <sup>16</sup> In the Coalition for Health, Ethics and Society (CHES) Policy Dialogue on 'Strengthening the EU added value in health' hosted by the European Policy Centre (EPC) in Brussels.

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