



EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Public Health

RARE DISEASE EUROPEAN REFERENCE NETWORKS:

ADDENDUM TO EUCERD RECOMMENDATIONS OF JANUARY 2013

The decision of the Commission expert group on rare diseases

10th June 2015

Background to the Addendum

Directive 2011/24/EU (Directive on the application of patients' rights in cross-border healthcare) acknowledges the unique potential of European Reference Networks (ERNs) for the rare disease (RD) field: in this Directive, the European Commission (EC) pledges to "support the development of European Reference Networks between healthcare providers and Centres of Expertise in Member States, in particular in the area of rare diseases" (Art.12) and additionally dedicates a separate Article to RD (Art.13).

The EUCERD adopted [Recommendations on Rare Disease European Reference Networks](#) on 31st January 2013. The document was the result of a long process of debate and analysis on the part of several stakeholder groups. In the light of discussion of RD ERNs during the January 2012 EUCERD meeting, followed by a plenary session in June 2012, the EUCERD Joint Action (EJA) organised an expert workshop in September 2012. The outcome of this workshop was a draft set of Recommendations for review and discussion at the November 2012 EUCERD meeting. Following revision, the document was sent to all Members for written review, before a final version was submitted and adopted by EUCERD in January 2013.

The primary purpose of these Recommendations was to "*help focus on the specificities of rare diseases and the criteria for the establishment and evaluation of ERNs in the field of rare diseases*".¹ Once the Recommendations were adopted, the EJA ensured cross-talk, as appropriate, with the Cross Border Healthcare Expert Group in order that the core content of the Recommendations might be considered when elaborating the Delegated and Implementing Acts.

The European Commission published the Delegated Decision (2014/287/EU) and Implementing Decision (2014/286/EU) on 10th March 2014. The Delegated and Implementing Decisions were not intended to define or comprehensively address the specific needs of the RD field, but instead to stipulate transversal criteria for networks to fulfil in order to qualify as ERNs and for healthcare providers wishing to join an ERN. Therefore, further work was conducted in order to explore those areas of the EUCERD Recommendations warranting further attention from the EC Expert Group on Rare Diseases² in the light of the Delegated and Implementing Decisions. An EJA workshop took place in Rome 28-29th October 2014, to affirm and highlight the importance of these RD-specific needs not defined in the legal Acts but nonetheless essential to support applications for ERNs in the field of RD.

At the November 2014 meeting of the EC Expert Group on Rare Diseases, it was agreed that although the Recommendations overall remain highly relevant and comprehensive, two topics should be revisited and elaborated at this stage: the grouping of RD into thematic networks and the necessity of a patient-centred approach to RD ERNs. This Addendum outlines the rationale of these two topics and then makes recommendations accordingly.

¹ Preface to the *EUCERD Recommendations on RD ERNs*

² Established 30 July 2013 via Commission Decision 2013/ C219/04

Rationale for the current Addendum (based on existing policy and legislation)

The Preface to the *EUCERD Recommendations on RD ERNs* acknowledges that “Due to the parallel discussions of the Cross Border Healthcare Expert Group, EUCERD may need to revisit these recommendations at a later date as the conclusions of the Cross Border Healthcare Expert Group become established. In addition, work of other groups (for example conclusions on RD registry platform development) may need to be taken into account as plans for RD ERNs evolve.”

The purpose of this Addendum is to revisit the document, in light of the Delegated and Implementing Acts of 2014, and in view of the first calls for ERNs that will be launched in December 2015. The Delegated and Implementing Acts provide the binding, legal criteria for the establishment of ERNs. They define various stages in the assessment and approval process for a network and its would-be members. In proposing additional RD-related specificities to supplement those highlighted by the original EUCERD Recommendations, it should be noted that although the Delegated Decision provides a list (Annex II) of horizontal criteria for healthcare providers wishing to join a network, this should be viewed as a mandatory minimum and is not intended to be ‘vertically’ restrictive: on the contrary, the Acts expressly call for “a second set of criteria and conditions that may vary depending on the scope of the concrete area of expertise, disease or condition addressed by the Network they wish to join”.³

It is important to emphasise that the EC has commissioned two separate Tenders⁴ to explore and define the process for assessing/approving applications for ERNs and to determine the services and operations of ERNs. This Addendum does not seek to duplicate these tasks.

Grouping Rare Diseases in Thematic Networks

Based on the content of the EUCERD Recommendations and the content of the Acts, one purpose of this Addendum to the Recommendations is to suggest an illustrative grouping of RD as a feasible approach to RD ERN planning and to ensure coverage of all RD eventually.

Although in most areas the EUCERD Recommendations are adequate to support the interpretation of the Acts for RD-specific applications, a particular issue is raised for RD in the numbers of healthcare providers who should participate in a network: Networks must include at least 10 healthcare providers in at least 8 MS. It is acknowledged in the Acts that:

*“It might be difficult to reach the minimum number of healthcare providers or Member States for some rare diseases or conditions due to a lack of expertise. It would therefore be a good idea to group healthcare providers that focus on related rare diseases or conditions in a thematic Network”.*⁵

The addendum therefore aims to guide the field towards network proposals able to satisfy this essential criterion. This resonates with the content of the EUCERD Recommendations specifically relating to the grouping of RD:

³ Preface to the Delegated Decision (6)

⁴ N° Chafea/2014/Health/25 and N° Chafea/2014/Health/05

⁵ Preface to the Commission Implementing Decision (6)

- *“Based around the concept of medical specialties and body systems, diagnostic and therapeutic areas can be identified each covering a wide range of rare diseases. Comparison of the systems in place in MS with well developed services for rare diseases shows that the number of diagnostic and systemic areas which might cover the majority of diagnoses could be approximately 20-30.” (Recommendation 19)*

The fact that there are 6,000 - 8,000 separate RD necessitates a comprehensive, overarching framework to avoid establishing potentially hundreds or even thousands of individual networks and ensure that a reasonable number of well-integrated RD ERNs have adequate capacity to address all of these conditions. A sound and sustainable framework will ensure that ultimately all RD patients will find a ‘home’ within an ERN – this is a fundamental concept conveyed by the EUCERD Recommendations:

- *“The overall vision of RD ERNs is that they will provide the framework for healthcare pathways for RD patients through a high level of integrated expertise... This will cover in a stepwise approach all RD patients” (Recommendation 1)*
- *“A step-wise strategy for RD ERN designation should be delineated so that all patients with a rare disease will have access to an appropriate RD ERN in a defined period of time.” (Recommendation 17)*

The table of Thematic Networks proposed below is based on analysis of existing national networks and other groupings of RD and is the result of discussion and consensus during the EJA workshop of October 2014 and subsequent meetings of the EC Expert Group on RD, and of written Expert Group feedback.⁶ ERNs in the field of RD should follow as much as possible the traditional organisation of healthcare services by medical specialty, particularly as this is the way in which Centres of Expertise (CEs) emerged in the MS according to a survey carried out by the EUCERD Scientific Secretariat.⁷

The primary goal of the proposed scheme is inclusivity at the European level – it is important to emphasise that member healthcare providers/CEs will *not* need to be designated (or re-designated) to align precisely with one of the 21 Themes. In all likelihood, the members of any given ERN will not possess the same level of expertise for all the RDs within that ERN; however, organising ERNs at the level hereby proposed will help to close the gaps. Although RD are often multisystemic disorders, they can readily be classified under these headings; the medical expertise necessary for multi-system care will largely be provided -as at present- by CEs involving experts from various disciplines. The success of this framework will be ensured by effective cross-links between the different RD ERNs. This overarching approach to grouping RD will also facilitate the referral of undiagnosed patients, who will always be ‘assigned’ to a broader group of specialists whilst a specific diagnosis is pursued.

Such inclusivity should also relate to the ages of patients. The *EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States* stipulate, as a criterion for CEs,

⁶ To compile the table, the following existing models were compared and amalgamated: ontology in Harrison’s Principles of Internal Medicine; the Orphanet classification (<http://www.orphadata.org/cgi-bin/inc/product3.inc.php>); a preliminary EURORDIS proposal of disease groupings; the French ‘filieres de santé maladies rares’; and the UK NIHR translational research grouping

⁷ <http://www.ojrd.com/content/pdf/1750-1172-7-S2-A5.pdf>

the “Organisation of collaborations to assure the continuity of care between childhood, adolescence and adulthood, if relevant”. By extension, RD ERNs linking CEs in related thematic domains should ensure continuity of care for paediatric, adolescent and adult patients within each overarching Thematic network. It would therefore be anticipated that these networks should not be specific to the paediatric or adult age ranges.

Necessity of patient involvement in RD ERNs

The *EUCERD Recommendations on RD ERNs* stress the critical role of patient representatives and organisations- as experts by experience and co-producers of knowledge- in the functioning of RD ERNs, specifically:

- *“Patient organisations should play an integral role, especially in the evaluation of RD ERNs, where patient organisations exist”.* (Recommendation 8)
- *“The groups providing evaluation of RD ERNs should be multi-stakeholder and include patient organization”.* (Recommendation 4.v.: Mechanisms for evaluation and clear indicators of performance)

The *EUCERD Recommendations on Quality criteria for Centres of Expertise for Rare Diseases in Member States* also promote the role of RD patients and their representatives in the functioning of CEs, recommending:

- *“CEs collaborate with patient organisations to bring in the patient perspective”* (Recommendation 7)
- *“Link and collaboration with patient organisations where they exist”* (Recommendation 29)

The Delegated Decision builds on these EUCERD Recommendations and translates the principles of empowerment, participation and patient-centric care into the horizontal criteria and conditions that all ERN applicants have to fulfill. ERNs must:

‘have knowledge and expertise to diagnose, follow up and manage patients with evidence of good outcomes’, specifically to:

- a. *promote good quality and safe care to patients suffering from certain diseases and conditions by fostering proper diagnosis, treatment, follow-up and management of patients across the Network;*
- b. *empower and involve patients in order to improve the safety and good quality of the care they receive.*

All healthcare providers joining an ERN must comply with the following criteria and conditions for patient empowerment and patient-centred care:

- i. *have put strategies in place to ensure that care is patient-centred, that patients' rights are respected;*
- ii. *provide clear and transparent information about complaint procedures and the remedies and forms of redress available to both domestic and foreign patients;*
- iii. *ensure feedback on patient experience and the active evaluation of patient experience;*
- iv. *apply personal data protection rules and ensure access to medical records and clinical information in compliance with EU data protection;*

- v. *ensure that the informed consent of the data subject complies with the requirements set out in Article 2(e) of this Delegated Decision;*
- vi. *ensure transparency, including providing information about clinical outcomes, treatment options and the quality and safety standards put in place;*

Although these key principles are thus embedded into the legal framework for all Network applicants to fulfil, due to the specificity of RD the role performed by RD patients is actually more fundamental and involved due to the limited body of knowledge, experience and expertise in the field of RD; therefore, a higher level of involvement of patients in decision and opinion-making processes is essential to ensure the successful development of RD ERNs.

The capacity of patients and patient representatives, as experts and co-producers of knowledge in the field of RD, is already well established at a European level, including participation in Scientific Committees, European Medicine Agency, Committee Orphan Medicine Products, and European Commission Expert Groups.

RD ERNs should recognise the critical roles patient and patient representations play, as experts by experience and co-producers of knowledge in all ERN activities, besides demonstrating meaningful involvement, patient-centricity and empowerment in care.

Addendum

Addendum Introduction

This Addendum accompanies the *EUCERD Recommendations on Rare Disease European Reference Networks*, adopted on 31 January 2013, and -in light of the Commission Delegated and Implementing Acts⁸, pursuant Directive 2011/24/EU and adopted in 2014- complements the content of the Recommendations in the following areas:

- The grouping of rare diseases in Thematic Networks;
- The necessity of Patient Involvement in RD ERNs.

The disease-grouping framework and the recommendations to ensure patient-centeredness and patient involvement should be used wherever possible:

- To increase awareness of the specificities of rare diseases amongst Member States' Competent National Authorities (tasked with endorsing healthcare providers as members of a network)
- To support those healthcare professionals preparing Network proposals by promoting key messages related to the specificities of rare diseases
- To inspire the development of the Assessment Manual and Technical Toolbox for network applications and assessment bodies for ERNs, to ensure a clear strategic framework is provided for network applications to be assessed as formal RD ERNs.

Addendum Recommendations

Grouping Rare Diseases in Thematic Networks

It is recommended that broad, Thematic ERNs for rare diseases are established, as this is the only way to ensure all rare diseases have a 'home' within an ERN. This scheme is recommended as **a model** for the purposes of grouping rare diseases thematically and is the result of extensive expert stakeholder collaboration, including the following: the EUCERD Scientific Secretariat Scoping study; the process of elaborating and adopting the EUCERD Recommendations on RD ERNs; presentations and discussions at the 2nd, 3rd and 4th meetings of the European Commission (EC) Expert Group on Rare Diseases; a dedicated workshop in October 2014; and a period of written Expert Group review and revision.

Rare immunological and auto-inflammatory diseases
Rare bone diseases
Rare cancers* and tumours
Rare cardiac diseases
Rare connective tissue and musculoskeletal diseases
Rare malformations and developmental anomalies and rare intellectual disabilities
Rare endocrine diseases

⁸ Delegated Decision Preface (6) and Implementing Decision Preface (6)

Rare eye diseases
Rare gastrointestinal diseases
Rare gynaecological and obstetric diseases
Rare haematological diseases
Rare craniofacial anomalies and ENT (ear, nose and throat) disorders
Rare hepatic diseases
Rare hereditary metabolic disorders
Rare multi-systemic vascular diseases
Rare neurological diseases
Rare neuromuscular diseases
Rare pulmonary diseases
Rare renal diseases
Rare skin disorders
Rare urogenital diseases

*Note: The networking of rare cancers is currently under discussion in EC Expert Group on Cancer Control

Each Thematic RD ERN should ensure continuity of care for patients by bridging the transition from paediatric through to adult care; therefore, it is highly recommended that a single ERN is established in each domain to meet the needs of both paediatric and adult patients, wherever possible.

Necessity of Patient Involvement in RD ERNs

Patients and patient representatives should play an integral role in the decision and opinion making process in RD ERNs and be involved in structural and clinical network activities.

It is recommended that RD ERNs demonstrate meaningful patient involvement, patient-centeredness and empowerment through recognition of the role of patients, as experts by experience and co-producers of knowledge, in RD ERN structural and clinical activities and therefore demonstrate meeting the legal requirements in the Delegated Acts. Patients' involvement depends on the scope of RD ERNs in the following dimensions:

- To advise on planning, assessment and evaluation of Centres of Expertise and European Reference Networks based on their experience, with a consistent approach
- To ensure transparency to quality of care, safety standards, clinical outcomes and treatment options
- To promote and encourage a patient-centric approach in both delivery of clinical care, service improvement and strategic development and decision-making
- To ensure all ethical issues and concerns for patients are addressed, balancing patients' and clinical needs appropriately
- To ensure care is patient-centred and respects patients' rights and choice
- To ensure the application of personal data protection rules, compliance of informed consent and management of complaints

- To ensure feedback on patient experience and the active evaluation of patient experience