



European
Reference
Network

for rare or low prevalence
complex diseases

⚙ Network
Neurological Diseases
(ERN-RND)

ERN-RND BOARD MEETING

Minutes

Location: Zoom meeting

Date: 02 July 2021, 9:00 - 10:30 (Berlin time)

Attendees:

Alicia Brunelle

Holm Graessner

Bart van de Warrenburg

Alexander Münchau

Alexandra Durr

Alfons Macaya

Antonio Federico

Bernhard Landwehrmeyer

Caterina Mariotti

Dario Ortigoza

Algirdas Utkus

Fran Borovecki

Ivana Babic Bozovic

Jean-Marc Burgunder

Joanna Pera

Johannes Levin

K. Majamaa

Ludger Schöls



Martin Vynalek

Matthias Gerberding

Juidt Molnar

Nicole Wolf

Tamara Martin

Tom de Koning

Wassilios Meissner

Wolfgang Nachbauer

Enrico Bertini

Fina

Pille Taba

Thomas Klockgether

Dario Ortigoza

Jirka Klempir

Odile Boespflug

Victoria Gonzalez

Caroline Sevin

Alberto Albanese

Mary Kearney

Carola Reinhard

1. AGENDA ITEMS

Comments

- Comments by members of Advisory Committee
- Comments by ePAG representatives

Information and reports

- Summary report of management team meetings
- Results of monitoring exercise
- Letter to hospital managers
- Update of disease coverage of existing ERN members
- Status of expansion of ERN-RND
- Results of onboarding meetings
- Results of cooperation meeting with Euro-NMD and EpiCare
- Cooperation with professional organisations
- ECORIS, ERICA and EJP-RD

Decisions

- Participation of new HCPs in ERN-RND activities
- Brexit - approval of permanent guest status for UCL

Planning

- Building blocks and challenges for next five year plan

2. ACTION POINTS

Who?	What?	By when?
Letter to hospital managers		
Coordination office	Collect responses to letter from all HCPs in a structured way	After summer break
Cooperation with professional organisations		
Coordination office	Invite EACD representative to join ERN-RND Advisory Board	After cooperation has been formally established
Orphan drug legislation		
Holm Graessner	Get in touch with RND coordinating panel for RND at EAN and invite them to form a working group.	31 July

3. MINUTES

3.1. COMMENTS

3.1.1 COMMENTS BY MEMBERS OF ADVISORY BOARD

Jean-Marc Burgunder (EAN)

- Collaboration with EAN works well
- Network has been presented in a paper
- Plan for the next 5 years is being established

Alfons Macaya (EPNS)

- Planned joint activities
 - Education and training, webinars
 - Rare disease curriculum
 - Common guidelines, e.g. Flowchart for early onset Ataxias

Holm Graessner

- Collaboration with EAN and EPNS works well
- Start discussion with epiCARE and Euro-NMD regarding future collaboration, including training curriculum

MDS

- Improvement of collaboration has been achieved, but no concrete actions planned yet
- Positive development: Pille Taba and Angelo Antonini now joining ERN-RND
- Pille Taba: Joint activities might include training activities and guideline development

3.1.2 COMMENTS BY ePAG REPRESENTATIVES

Mary Kearney

- Meeting went well, all moderators were well prepared, a lot of future activities have been agreed on
- Presentation by ePAG received a good response
- EURORDIS talk: Concrete examples (e.g. life-threatening events) were missing

3.2. INFORMATION AND REPORTS

3.2.1 LETTER TO HOSPITAL MANAGERS

TO DO:

- **Coordination office to collect responses to letter from all HCPs in a structured way after summer break**

3.2.2 COOPERATION WITH PROFESSIONAL ORGANISATIONS

- New collaboration with European Academy of Childhood Disability (EACD)
- Discussion ongoing with European Federation for Neurorehabilitation (EFNR)

TO DO:

- **Coordination office: Invite EACD representative to join ERN-RND Advisory Board**

3.3. DECISIONS

3.3.1 PARTICIPATION OF NEW HCPs IN ERN-RND ACTIVITIES

- Unanimous decision taken that all new HCPs who have received a positive ERN-RND Board decision can participate in all ERN-RND activities from now on

3.3.2 BREXIT - APPROVAL OF GUEST STATUS FOR UCL

- Decision that a guest status will be given to UCL until the end of the first 5 years period. UCL will not be member of the Board and will thus not be included in formal decisions.
- It should be discussed in the management team which criteria should be applied to grant guest status to European HCPs that are in countries outside the EU

3.4. PLANNING

3.4.1 ORPHAN DRUG LEGISLATION

- ERNs have been informed and will be heard in the process
- Idea to form a working group including the EAN coordinating panel - patients - ERN-RND

TO DO:

- **Get in touch with RND coordinating panel at EAN and invite them to form a working group.**



https://ec.europa.eu/health/ern_en



www.ern-rnd.eu

Co-funded by the European Union





BOARD MEETING

2ND JULY 2021

AGENDA

Comments

- Comments by members of Advisory Committee (annual meeting, cooperation with respective professional society)
- Comments by ePAG representatives (annual meeting)

Information and reports

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- Building blocks and challenges for next five year plan



COMMENTS



SUMMARY OF MANAGEMENT TEAM MEETINGS

MANAGEMENT TEAM MEETINGS

Members:

Judit Molnar, Alexandra Durr, Nicole Wolf, Marina Koning, Thomas Klockgether, Ludger Schols, Antonio Federico, Ludger Schoels, Mary Kearney, Holm Graessner

Office: Carola Reinhard

Exemplary discussion points during monthly meetings

Monitoring

Annual meeting

Report from ERN coordinators meeting

Expansion process

Meeting with EpiCare and EuroNMD

ERN-RND meeting updates



RESULTS OF MONITORING EXERCISE

COLLECTION OF EC DG SANTE INDICATORS FOR THE YEAR 2020

Monitoring, indicators and objectives

The DG Sante of the EC monitors ERNs by **seven indicators**, collected every 6 months. Each indicator measures an objective towards ERN-RND's goal to improve care quality.

Objectives and *indicators* for the full year of 2020

1 European coverage - <i>HCPs</i> in ERN-RDN (full+affiliated members)	< 31+10>
2 access to HCPs - <i>new patients</i>	< 7082>
3 outcomes - <i>panels in CPMS</i>	< 6>
4 capacity - <i>educational activities</i> incl.webinars	< 67>
5 research - <i>clinical trials /studies + publications</i> acknowledging ERN-RND	< 19+49>
6 access to high-quality care - <i>guidelines</i> (adopted+written)	< 4+2>
7 spread of knowledge - <i>congresses</i> attended + <i>website hits</i>	<42+19k>

[transmitted March 2021]

DEVIATION +/- >20% IN NEW PATIENTS JUL-DEC'19->'20 IN 16 HCPs

- **ERN-RND board decision Nov. 2020:** HCPs with changes in number of new patients >20% are asked for an explanation for the change

	N new patients VII-XII 2019	N new patients VII-XII 2020	increase >20%	decrease >20%	explanation provided
Assistance Publique-Hôpitaux de Paris,Neurogenetics ¹	261	357	+26		y
Assistance Publique-Hôpitaux de Paris, centre for Leukodystrophies	85	58		-31	y
CHU de Bordeaux, France	28	14		-50	y
CHU de Toulouse, France	150	25		-83	y
Foundation IRCCS neurological institute Carlo Besta – Milan, Italy	240	95		-60	y
General University Hospital in Prague, Czech Republic	178	96		-46	y
Hospital de Sant Joan de Déu, Spain	98	43		-56	y
Klinikum der Universität München, Germany	72	50		-30	y
Motol University Hospital, Czech Republic	55	42		-23	y
Pediatric hospital Bambino Gesù, Rome, Italy	173	89		-48	y
Radboud University Medical Center Nijmegen, Netherlands	432	322		-25	y
Universitätsklinikum Bonn, Germany	132	78		-40	y
Universitätsklinikum Ulm, Germany	62	107	+72		y
Université libre de Bruxelles, Belgium	14	5		-64	y
University Hospital in Krakow, Poland	50	37		-26	y
Vilnius University Hospital Santaros Klinikos, Lithuania	12	9		-25	y

INDICATOR “NUMBER OF NEW PATIENTS JULY-DEC 2020” DECREASE >20% FROM 2019

Explanations for decrease

- **Barcelona – Ortigoza:** referrals after worst period of March-April down, unclear how long recovery will take
- **Besta, Milan – Mariotti:** Besta is a national center, and travel of patients from outside the region was down during Covid19
- **Bonn – Klockgether:** it was caused by Covid
- **Krakow – Pera:** hospital transferred to new facility, Covid19 fear of infection, teleconsultations for first appointments not possible
- **München – Klopstock:** willingness to travel by patients down in Covid19

INDICATOR “NUMBER OF NEW PATIENTS JULY-DEC 2020” DECREASE >20% FROM 2019 CONTD.

Explanations for decrease

- **Nijmegen – Warrenburg:** Covid19, across all chronic conditions
- **Prague Charles U – Klempir:** Covid19 impacted visits, old patients have died, stopped seeing GPs, IT-Department compiled numbers for the first time
- **Prague Motol – Vyhnalek:** non-acute care down, scheduled hospitalisations down, return to normal expected after summer 2021. During lowered patient load, methodological improvements and changes were made.
- **Vilnius - Utkus/Morkuniene:** small center, fluctuations over the years, Covid19
- **Rome – Bertini:** Covid19 impact on the recruitment of new patients
- **Bordeaux – Meissner:** number supplied by Bordeaux was wrong and too low, new number equal to 2019
- **Toulouse - Pavy-Le Traon:** number supplied was wrong and too low, new number equal to 2019



LETTER TO HOSPITAL MANAGERS

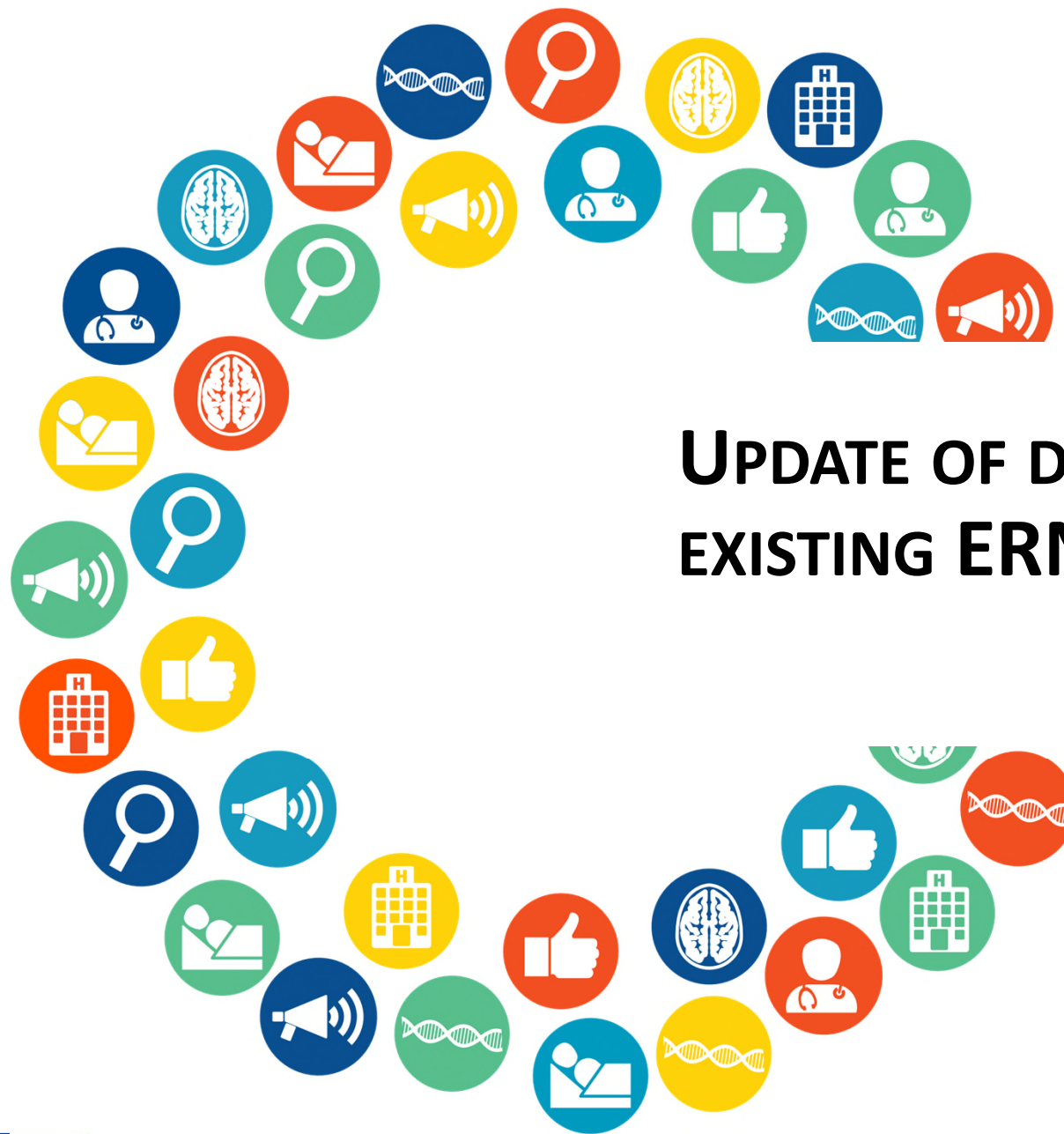
LETTER TO HOSPITAL MANAGERS TO INFORM ABOUT ERN-RND AND TO REQUEST SUPPORT

Status:

- Letter has been sent end of May 2021

Request:

- Please inform us about reaction



UPDATE OF DISEASE COVERAGE OF EXISTING ERN MEMBERS

6 steps to update diseases coverage of existing ERN members

1. Application by
HCP to ERN

2. Endorsement by
national authority

3. Assessment/peer
review by ERN

4. Validation by BoMS

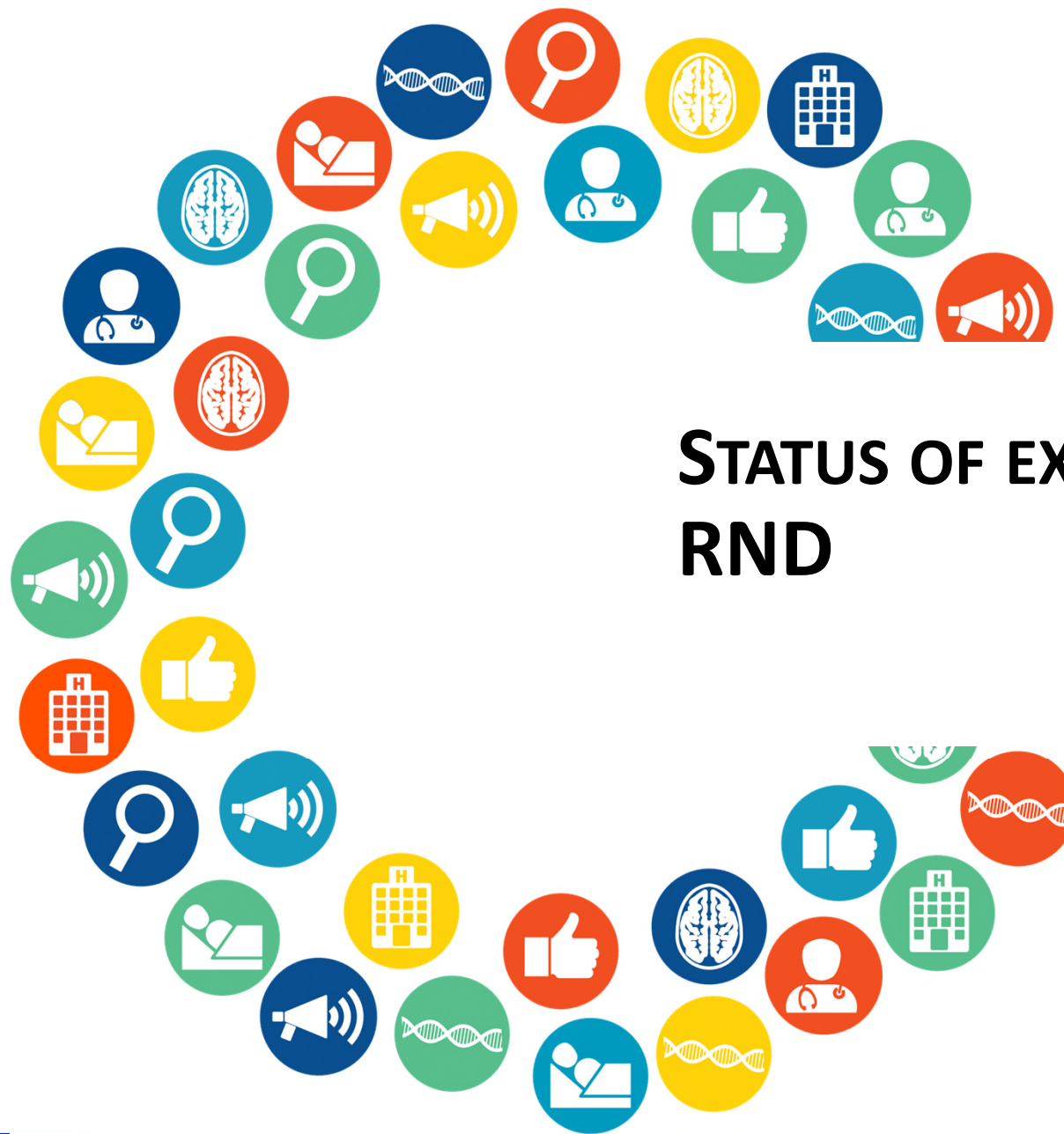
5. HCP and ERN informed,
updated disease coverage
published on website

6. New disease coverage
included in the 5-year re-
evaluation

European
Commission

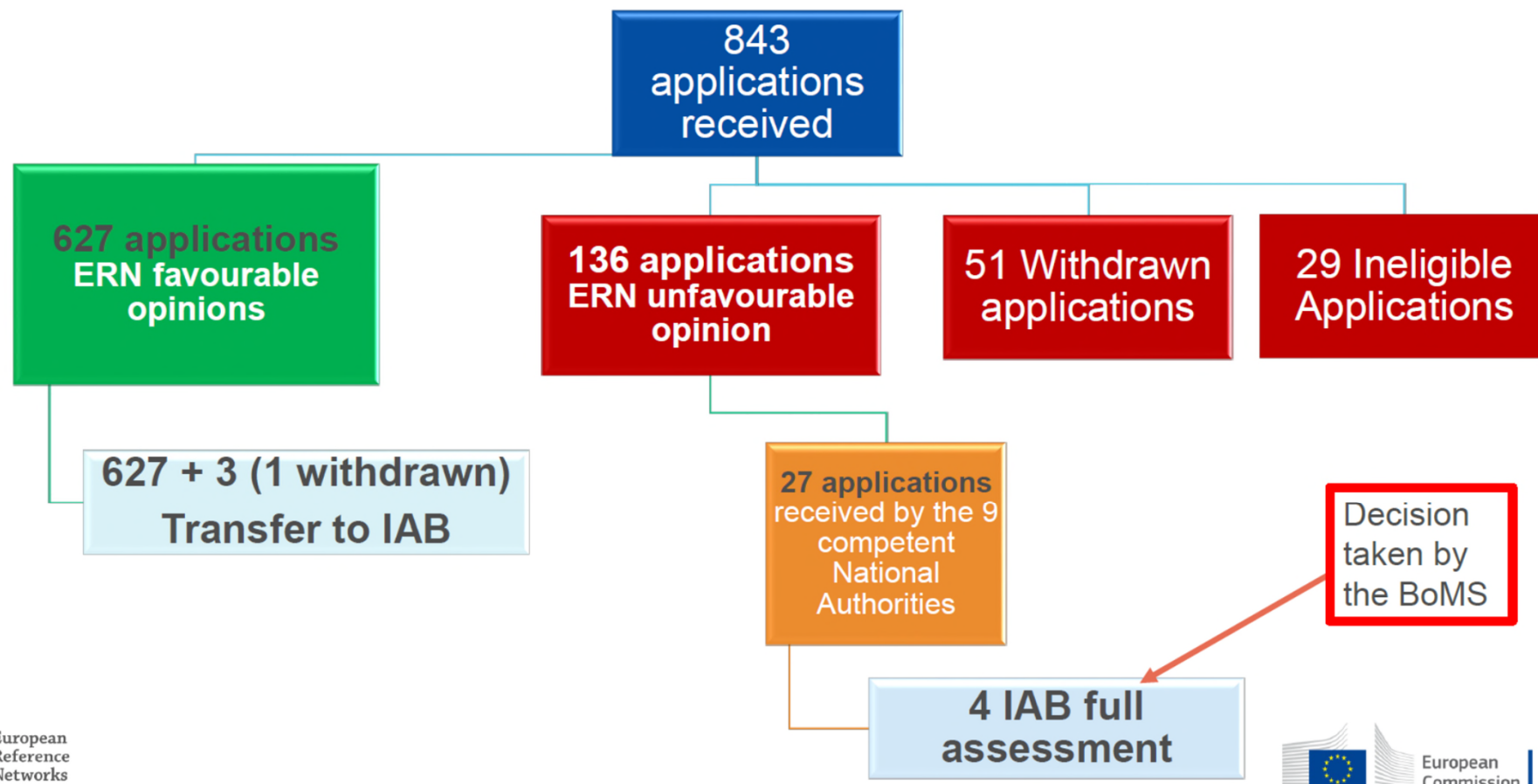
Proposed procedure

- Annual cycle
- No need to assess general criteria, focus on assessment of specific criteria related to the specific disease concerned
- Flexibility for ERNs to arrange the assessment process by, for example:
 - smaller assessment committee of the ERN
 - or evaluation group consults ERN board
 - or the whole ERN board participating in assessment



STATUS OF EXPANSION OF ERN- RND

Current state of play



IAB assessment process



ENLARGEMENT OF ERN-RND

- 33 applicants from 16 countries
 - 20 new ataxia centres
 - 24 new HD/chorea centres
 - 17 new dystonias/paroxysmal disorders/NBIA centres
 - 16 new FTD centres
 - 9 new leukoencephalopathies centres
 - 22 new atypical Parkinsonian syndromes centres

Status	Country	Applicant	Ataxia/HSP	Choreas/HD	Dystonias/...	FTD	Leukodystrophies	Atypical PD
Applicant	Austria	University Hospital Innsbruck	x	x	x	x		x
Applicant	Belgium	Antwerp University Hospital				x		x
Applicant	Belgium	Ghent University Hospital				x	x	
Applicant	Croatia	Klinički bolnički centar Zagreb	x	x	x	x	x	x
Applicant	Cyprus	Cyprus Foundation for Muscular Dystony Research	x	x	x	x	x	x
Applicant	Czechia	Facultni nemocnice U Sv Anny Brne		x	x	x		x
Applicant	Czechia	Thomayer Hospital Prague					x	
Applicant	Denmark	Aarhus Universitets Hospital	x	x	x	x		x
Applicant	Denmark	Rigshospitalet Copenhagen	x	x	x	x	x	x
Applicant	Finland	Northern Ostrobothnia Hospital District Oulu	x	x		x	x	x
Applicant	Germany	Hannover Medical School	x	x	x		x	x
Applicant	Germany	Katholisches Klinikum Bochum		x				
Applicant	Germany	Universitätsklinikum Aachen	x	x	x	x		x
Applicant	Germany	Universitätsklinikum Würzburg		x	x			x
Applicant	Greece	Eginito Hospital Athens	x	x	x	x		x
Applicant	Hungary	Szent-Györgyi Albert Medical School	x					
Applicant	Ireland	Tallaght University Hospital	x					x
Applicant	Italy	AO di Padova	x	x	x	x	x	x
Applicant	Italy	AOU Pisana Pisa	x					
Applicant	Italy	AOU Policlinico Bari		x				
Applicant	Italy	Azienda Ospedaliera Universitaria Federico II Napoli	x	x				x
Applicant	Italy	UOCD Clinica Neurologica Rete Metropolitana NEUROMET Bologna	x	x	x	x		x
Applicant	Netherlands	Leiden University Medical Center		x				
Applicant	Netherlands	Maastricht University Medical Center		x				
Applicant	Poland	Institute of Psychiatry and Psychology Warsaw	x					
Applicant	Spain	Complejo ospitalario Regional Virgen del Rocío		x	x			x
Applicant	Spain	Hospital Clinic San Carlos Madrid			x			x
Applicant	Spain	Hospital General Universitario Gregorio Marañón		x	x			x
Applicant	Spain	Hospital Universitario Central de Asturias Oviedo	x	x	x	x		x
Applicant	Spain	Hospital Universitario La Paz Madrid	x	x	x	x	x	x
Applicant	Spain	Hospital Universitario Narques de Valdecilla Santander	x			x		
Applicant	Sweden	Centre for Huntington's Disease Sweden		x				
Applicant	Sweden	Karolinska Universitetssjukhuset	x	x				x
Full member	Belgium	Université libre de Bruxelles	x					
Full member	Belgium	University Hospitals Leuven	x	x		x		x
Full member	Bulgaria	University Neurological Hospital "St. Naum" Sofia			x			
Full member	Czechia	Charles University Prague		x	x			x
Full member	Czechia	Charles University in Prague Faculty Hospital Motol	x					
Full member	France	Reference Center (associated center) for Rare Multiple System Atrophy (Bordeaux)						x
Full member	France	Reference Centre for Rare Diseases 'Neurogenetics', Paris	x		x			
Full member	France	Reference centre for rare dementias (Paris)				x		
Full member	France	Reference centre for Huntington's disease (Paris)		x				
Full member	France	Reference Center for Rare Multiple System Atrophy diseases (Toulouse)						x
Full member	France	APHP - Reference Centre for Leukodystrophies					x	
Full member	Germany	Universitätsklinikum Tübingen	x	x	x	x	x	x
Full member	Germany	Universitätsklinikum Bonn	x		x			x
Full member	Germany	University of Lübeck	x	x	x			x
Full member	Germany	Klinikum der Ludwig-Maximilians-Universität München	x	x	x	x	x	x
Full member	Germany	University Hospital Ulm		x	x	x		x
Full member	Hungary	Semmelweis University Budapest	x	x	x	x	x	x
Full member	Hungary	University of Pécs, Medical school	x	x	x	x		x
Full member	Italy	Istituto Neurologico Carlo Besta, Milan	x	x	x	x	x	x
Full member	Italy	Istituto Clinico Humanitas di Rozzano, Milan		x	x	x		x
Full member	Italy	Azienda ospedaliera Universitaria Senese, Siena	x	x	x	x	x	x
Full member	Italy	Bambino Gesù Children's Research, Rome		x	x		x	
Full member	Lithuania	Vilnius University Hospital		x				
Full member	Netherlands	VU University Medical Center, Amsterdam					x	
Full member	Netherlands	University Medical Center Groningen	x	x	x		x	
Full member	Netherlands	Erasmus MC: Universitair Medisch Centrum Rotterdam				x		
Full member	Netherlands	Radboud University, Nijmegen Medical Center	x		x			x
Full member	Poland	University Hospital Krakow	x		x			x
Full member	Slovenia	University Medical Centre Ljubljana	x	x	x	x		x
Full member	Spain	Hospital Sant Joan de Deu, Barcelona	x	x	x			x
Full member	Spain	Val d'Hebron	x					
Guest	UK	University College London Hospitals	x	x	x	x	x	x



RESULTS OF ONBOARDING MEETINGS

ONBOARDING MEETINGS (APRIL/MAY; 11 MEETINGS)

- Per disease group (DG coordinators and ePAGs were also invited)
- Overview presentation
 - Disease knowledge
 - Guidelines
 - Care standards
 - Training and education
 - Research and registry
 - Disease group specific projects
- Discussion
 - How can ERN-RND provide benefit for your centre/hospital?
 - To which ERN-RND activities can/will you contribute? How?
 - Which additional activities would like to see implemented in ERN-RND? How can you contribute?
 - For what kind of cases do you think you will benefit most from using CPMS?

NOVEL ACTIVITIES

Minutes can be found on the collaborative platform

General

- CPMS
 - Disease management
 - Inconclusive genetic results
 - DG overlapping cases
- Guidelines
 - Immune-mediated Ataxias
 - Palliative care – HD/Choreas
 - Video guideline for diagnostic methods – atypical parkinsonian syndromes
- Translation of disease knowledge
- Training activities



EXAMPLE

Outcome onboarding meetings HD and Chorea – 2 meetings with 20 participating new HCPs

(Novel) activities which were emphasised

CPMS

- Bundle cases, have a fixed date for discussion every 1-2 months
- Identified areas

Diagnosis

- Complex cases (both HD and non-HD choreas)
- Diagnosis of non-HD choreas
- Discussion of lab results ("How should clinicians react to a report that NGS does not yield results?")

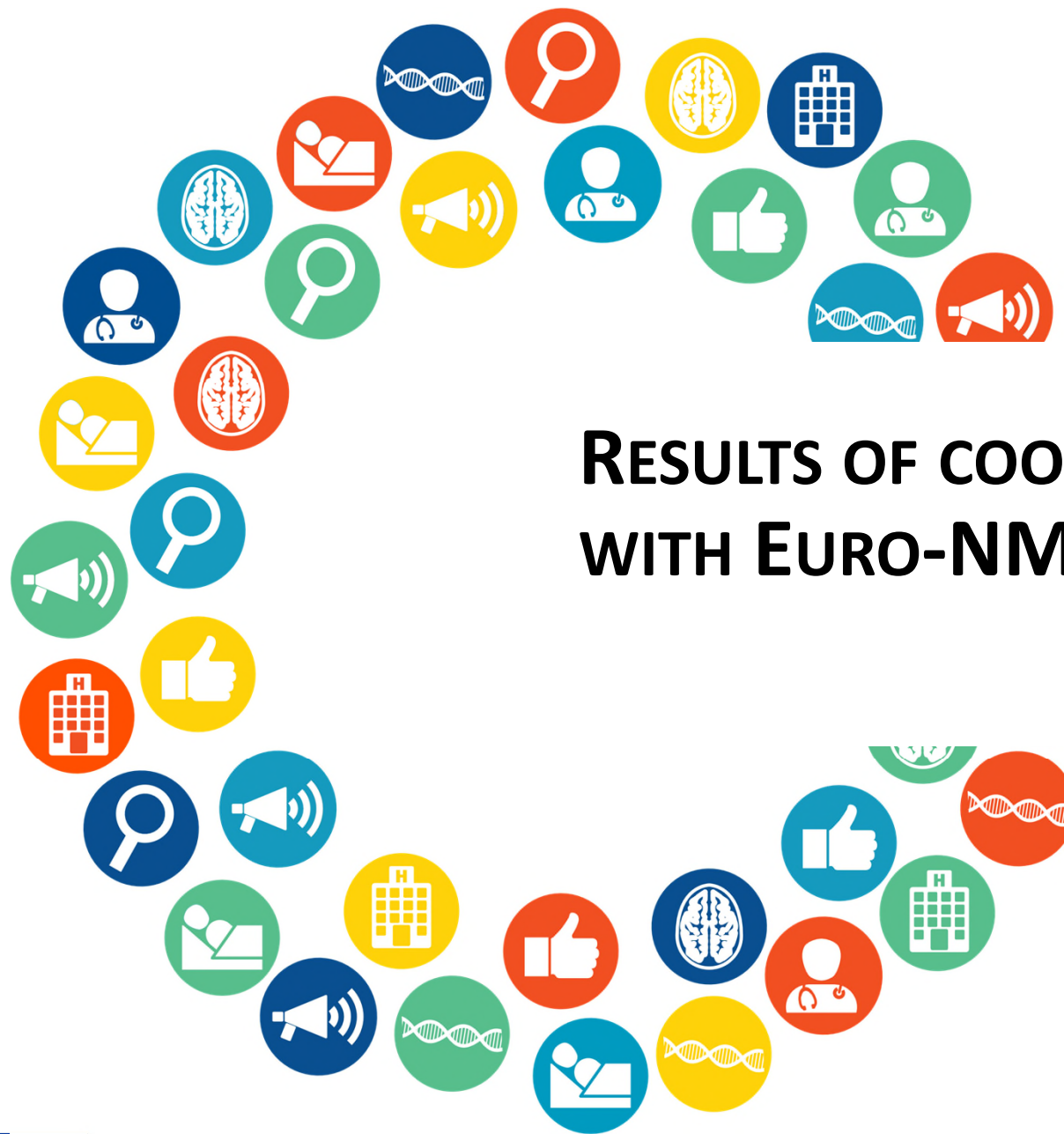
Therapy/management

- Focus can be on "education" (large audience) or a small group can give quick feedback on a specific case (2-3 experts)

Guidelines and clinical practice recommendations

- In most of the countries there are no national guidelines, physicians follow European/international guidelines
- Value in developing European guidelines, but also consensus documents (expert opinion)
- Potential Areas:
 - Palliative care

Translation of disease knowledge



RESULTS OF COOPERATION MEETING WITH EURO-NMD AND EPICARE

Two meetings in June 2021

Identified topics for collaboration:

- Training curriculum
- Next generation sequencing
- Registries and European Health Data Space
- Gene therapy and stem cell transplantation
- Surgical therapies (e.g. epilepsy surgery, DBS)
- Overlapping disease groups: myoclonus, channelopathies, mitochondrial disorders, neurometabolic disorders

Next steps

- Form cross-ERN WG – responsibility: 3 per each ERN

EURO-NMD

Building bridges and breaking barriers
in rare neuromuscular diseases



European
Reference
Network

Neurological Diseases
(ERN-RND)



COOPERATION WITH PROFESSIONAL ORGANISATIONS

COOPERATION WITH PROFESSIONAL ORGANISATIONS

EAN, EPNS, MDS, EFNR:

- Training activities and curriculum
- Guidelines
- Promotion and RD awareness
- Congresses

→ Planning meeting with EAN Board this autumn

EACD:

- Session on rare neurological diseases at next EACD meeting in May 2022
- Joint webinars
- Presentation at young researcher forum
- Developing and implementing standardized/harmonized approaches for the care of pediatric patients.



ECORIS, ERICA AND EJP-RD

EXISTING AND FUTURE* EDUCATIONAL OFFER

1

Fellowships for Mobility Exchanges

Long term exchanges (up to 6 months)

Proposal: research question/project



Training on Research in RD _ 2 calls/ year

Website: <https://www.ejprarediseases.org/our-actions-and-services/training-and-education/ern-workshops/>

Contact:

sanja.hermanns@med.uni-tuebingen.de

Workshops

2-days workshop, 25.000€

Proposal: workshop TOPIC

Shanice Beerepoot, Amsterdam → Tübingen, D; (ERN-RND); “Course of peripheral neuropathy overtime in patients with metachromatic leukodystrophy.”
Carlo Wilke, Tübingen, D → Nijmegen, NL; (ERN-RND); “Beyond family-based exome analysis: advanced cohort-level bioinformatic approaches for assessing genetic burden in rare neurodegenerative diseases”
Alexander Bernhardt, Munich (ERN-RND) → Bologna, IT; (non-ERN); “Advancing RT-QuIC for the diagnosis of rare neurodegenerative diseases”

2

EU Funding for ERN

Short term exchanges (up to 1 month)

Focus: Neurorehabilitation and others

Target group: clinicians, nurses, physiotherapists and other medical personnel

Aim: learn medical processes/techniques, or organizational management



Application monthly

Website: <http://www.ern-rnd.eu/education-training/short-exchange-programme/>

Contact:

Tamara.martin@med.uni-tuebingen.de

ERICA – COORDINATED ACTION

The aim of the ERICA consortium, in which all 24 *European Reference Networks* (ERNs) take part, is to build on the strength of the individual ERNs and create a platform that integrates all ERNs research and innovation capacity.

Through knowledge sharing, engagement with stakeholders in the rare disease domain and assembly of transdisciplinary research groups working across the global health spectrum, ERICA strives to reach the following goals:

- new intra- and inter-ERN rare disease competitive networks;
- effective data collection strategies;
- better patient involvement;
- enhanced quality and impact of clinical trials;
- increased awareness of ERNs innovation potential.



ERICA will strengthen research and innovation capacity by the integration of ERN research activities, outreach to European research infrastructures to synergistically increase impact and innovation. This will result in efficient access and safe therapies for the benefit of patients suffering from rare diseases and complex conditions.

1 March 2021 – 1 March 2025 → means to achieve things: ERN cross-cutting WG



DECISIONS

- Participation of new HCPs in ERN-RND activities
- Brexit - approval of permanent guest status for UCL



BUILDING BLOCKS FOR NEXT FIVE YEAR PLAN

- Disease Group Activities and Disease Group close WG activities (pediatric issues and neurorehabilitation)
- Cross-cutting structural and supporting activities
 - CPMS (DG, highly specialized services, care/referral pathway)
 - ERN-RND registry
 - Guideline development
 - Training and education
 - Care pathways
- Multi-pillar activities for highly specialized services (for example: DBS, NGS, Stem Cell Transplantation, Genetic Therapies, Neuroimaging, ...)
- Activities in collaboration with EuroNMD and EpiCare
 - Topics of interest that hook up with ERN-RND activities
 - Overlapping disease groups: myoclonus, channelopathies, mitochondrial disorders, neurometabolic disorders
- Collaboration with professional organisations and other networks (EHDN, Ataxia Global Initiative, European Dystonia Network, etc.)

CHALLENGES FOR NEXT FIVE YEAR PLAN

- Size of the network – organization of work and governance
- Resources – spread the work in the entire network even further
- Integration with national networks and healthcare systems / localization of impact
- Coordination with other ongoing activities
- Management of external ambitions



PROTOCOL FOR MANAGING DISEASE AREAS WITHIN CURRENT ERN HEALTHCARE PROVIDERS

EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW PREVALENCE AND COMPLEX DISEASES

Share. Care. Cure.



DOCUMENT INFORMATION

PROTOCOL FOR MANAGING DISEASE AREAS WITHIN CURRENT ERN HCPs

Approved by ERN Board of the Member States in written procedure on 02/07/2021

Short Description

This document describes the procedures for the extension of diseases covered by the existing members of the ERNs (HCPs). The final goal is that this procedure would contribute to reaching as comprehensive coverage of all known rare or low prevalence and complex diseases by the ERN system as possible.

This procedure is inspired by the process carried out in 2019 to extend the coverage of existing ERNs with new diseases in addition to those established in the initial call for ERNs in 2016 (this exercise took place in the context of the call for new members of existing ERNs launched in 2019).

A number of ERNs decided to add new diseases to their coverage in 2019 and the Commission included those new diseases under the eligible areas of expertise for the new applicants who were able to apply for these additional disease areas under the 2019 call.

In this context it is important:

- to set up a mechanism for the validation of the expertise of the already existing ERN members not previously assessed or validated for the new diseases included by their ERNs in 2019.
- to set up a mechanism for existing ERN members to expand into pre-existing disease areas of their ERNs for which they did not initially apply in 2016.



TABLE OF CONTENTS

Background.....	5
1. Proposal.....	7
2. Internal ERN review process.....	8
3. Recommendations for ERN action.....	10

Publication Date

06/07/2021



INTRODUCTION

In 2019, a number of ERNs have updated the disease areas that they cover and added new diseases. It has been possible for applicants to the call opened on 30 September 2019 by the European Commission (EC) for new ERN members to apply for these new disease areas. However there is no mechanism for existing members of ERNs to do so. In addition, existing members of ERNs also need an opportunity to expand into pre-existing disease areas for which they did not apply in 2016.

This document is limited to the extension of expertise of an HCP for new diseases that are already recognised as being within the scope of the ERN by the ERN Board of Member States representatives (ERN BoMS).

This document is addressing the procedure to assess the expertise of an HCP for the extension of its disease-area coverage to those areas:

- already within the scope of the ERN when the HCP joined the network but for which they did not apply.
- that have subsequently been included within the scope of an ERN since the HCP joined the network (in the 2019 call for new members) .

Timing - It is envisaged that ERNs will implement an annual process to expand their disease areas and this is likely to begin once the new members have joined the ERNs.

BACKGROUND

- The disease coverage of the 24 ERNs was analysed and discussed in 2015-2016 following a bottom-up approach in consultation with the broad rare diseases community, including Patient Associations, Scientific Societies, Member States and consultation bodies (Joint Action on Rare Diseases and Commission Expert Group on Rare Diseases).
- 24 ERNs applied to the 2016 call for ERNs, each proposing a defined list of thematic and sub-thematic areas of diseases, alongside the corresponding applicable criteria and thresholds that the individual healthcare providers wishing to join a network would be required to fulfil.
- Although the initial 24 Network proposals were quite exhaustive in terms of the diseases coverage, it has been deemed appropriate to consider in 2019, two years after the launch of the ERNs, whether any major gaps exist in the disease coverage of the Networks that need to be addressed.
- Several Networks have been raising this issue and, in order to better understand the perceived needs and proposals of the 24 ERNs, a survey was conducted in May 2019 on the potential disease expansion of the current 24 ERNs.
- Following the discussion held on this issue in both the ERN CG and the ERN BoMS meetings on the 24-25 June 2019, a comprehensive consultation with the ERNs was carried out with those who wished to extend their disease-area coverage. Based on this consultation, an

update of the disease coverage (including, when needed, new thresholds and criteria) was published on the Commission's website^{1 2}.

- As a result of this, applicants of the 2019 call for new ERN members were able to apply to cover these new disease areas.

¹ In June 2019, 16 ERNs replied to the 'Survey on the expansion of diseases to be covered by the ERNs'. 8 of them proposed the expansion. In September 2019, 8 ERNs included changes in the specific criteria and thresholds to add new diseases and areas of expertise.

² For any future extension of the disease coverage of the existing ERNs, the trigger for expansion should be either a needs analysis regarding new thematic ERNs or an analysis of existing disease covering gaps between ERNs. A procedure should always be in place to cross-check the opinion of other ERNs or their possible own wish to expand thematic coverage in the same direction. Finally, before entering the assessment process, the proposals should be presented to the group of coordinators, patient representatives, the EC ERN Team and the Board of Member States.

1. PROPOSAL

In order to update the disease coverage of the existing members (i.e. a HCP which may include different teams who are experts in different disease groups within the same ERN) and to validate their fulfilment of the new threshold and ERN specific criteria, an application procedure, supported by a peer review by the Board of Network of the ERN in question and further supplemented by the National authorities / ERN BoMS validation, is required.

In order to avoid an overly onerous process for current HCP members (units of expertise) a lighter assessment process can be applied: the HCP have already demonstrated compliance with the General Criteria, under the initial call for application and during the initial assessment of ERNs and their members in 2016. The additional team proposed within this HCP will now have to be evaluated only with regard to the new rare disease(s) for which they are applying. This assessment procedure is proposed to be structured under three steps, as described below.

Following an application submitted by an existing member to be recognised as an expert in a new rare disease area within the scope of its Network, the assessment process will be conducted under the following steps:

- Step 1: The initial step in the process will be for member HCPs to identify any changes to disease areas they wish to cover and provide details of these, along with the appropriate volumes and evidence in an application submitted directly to the Board of the Network of the relevant ERN. A standardised template for the application should be developed for this purpose. HCPs should be advised that they will need a letter of endorsement from the national Ministry of Health or similar certification at national level confirming that the existing member is recognised as an expert centre for this rare disease or complex condition under their respective national legislation.
- Step 2: The member HCP needs to notify a copy of the application to the Member State's competent authority. Upon this notification, the Member State's competent authority may either: (i) endorse the application by issuing a letter of endorsement or similar certification at national level confirming that the existing member is recognised as an expert centre for this rare disease(s) or complex condition(s) in its Member State under their respective national legislation; or (ii) take note of the application without any further action within 30 days after the notification; or (iii) reject the application. This evidence should be submitted by the applicant to the Board of the Network. In cases described under (i) and (ii) the assessment continues as explained under Step 3 below. In case described under (iii) the procedure is terminated at this stage.
- Step 3: The application will be peer reviewed by the Board of the Network of the ERN (see internal ERN review process section below for how this can be managed), and an assessment report issued. Internal review by the Board of the Network (or delegated by the Board of the Network to a dedicated Task Force or Working Group) should include engagement with patient organisations as required by the governance of that network. The Board of the Network will give a favourable or non-favourable opinion. Where this assessment is negative, the member will not be further assessed and therefore not



validated for the coverage of that disease or group of diseases. If the assessment is positive only for some of the diseases that have been assessed, it will be a decision of the Board of the Network whether to ask the ERN BoMS for the validation of only those diseases which have been positively assessed by them or to terminate the process.

- Step 4: Where the assessment by the Board of the Network is positive, the ERN BoMS and the EC will be informed of the changes by a letter from the ERN Coordinator. Applications that secure both an endorsement by the Member State's Ministry of Health and a positive opinion by the Board of the Network will be validated by the ERN BoMS. All the applications with positive assessment from the same network should be sent to ERN BoMS (for decision) and to the EC (for information) jointly on an annual basis (once a year). The ERN BoMS should consider jointly all applications received within the same period of time (annually) and validate all of them at the same (annual) meeting.
- Step 5: After the decision of BoMS the EC will inform the applicants and the ERNs concerned about the decision. The EC and the ERNs will ensure that any changes to the coverage of disease areas are reflected in appropriate information systems and website material.
- Step 6: Follow-up of the extension of the disease coverage should be made a mandatory and integral part of the annual monitoring and 5-year re-evaluation by the IAB.

2. INTERNAL ERN REVIEW PROCESS

Each ERN will need to decide how to organize the internal review process of the applicant healthcare providers (HCPs) within the necessary timeframes, according to the governance rules of each ERN.

The internal review process should reflect, as far as is possible, other internal assessments undertaken by ERNs. The internal ERN review process, for example, will not involve the overall checking of all aspects included in application forms for the calls for new members to join existing ERNs. But the two processes can reflect the same methodology for how the assessments are undertaken across the members of the ERN. The internal ERN review process would need to focus on the specific criteria and check there is evidence that the existing members meet the Network's specific criteria with regard to the specific disease applied for. In the case of a consortium proposal (for e.g. a new partner will join the original application), a specific endorsement shall be issued by the Member State's competent authority.

The ERN Board of the Network is required by the legislation to ensure that every HCP in the network has its representative on the Board of the Network. In addition, all of the ERNs have patient representatives on the Board of the Networks, many of whom have voting rights, depending on the governance rules of the individual ERN. Therefore, the role of the patient representatives in the assessment of the applicant HCP expertise teams will be determined by the Board of the Networks according to any applicable governance procedures of the network in question, including ensuring that any appropriate conflict of interest rules are followed.



The members of the Board of the Network or any member of the ERN involved in the peer review process must ensure that they maintain the highest professional standards of integrity, transparency and independence. All the participants of the Board of the Network shall communicate and notify immediately if they have any conflict of interest. Peer review of existing members should not be undertaken by other members from the same country. Additionally, the members of the ERN Board of the Network have the obligation to respect European laws on the protection of personal data and confidential data and the applications cannot be shared with the third parties. In addition, they shall respect in particular:

- the rules on the protection of personal privacy and personal data,
- the rules and obligations of professional secrecy laid down by the treaties and their implementing rules.

To that end, it is suggested that each ERN will need to decide how to organise the internal review process of the healthcare provider full members wishing to extend their disease areas within the necessary timeframes, according to the governance rules of each ERN.

The following are all possible options that could be implemented:

A. The ERN Board of the Network could delegate the decision making responsibility to a smaller decision making group in the ERN (an evaluation team, for example) and they will take the decision on behalf of the ERN. If the decision making is delegated to a smaller group, it is recommended that the evaluation team members are not from the same country as the applicant being assessed, in order to prevent any conflict of interest.

B. The Coordinator or the evaluation team could disseminate a list of the results of their evaluation (favourable or non-favourable) for all applications for extension of disease coverage with a request for comments within two weeks to the Board of the Network. If no comments are received the list will be accepted as agreed with no changes

C. All ERN Board of the Network members could vote on every application,

In any case, the ERNs should keep a record of their delegated decision process according to their internal governance rules. ERN experts working in the same field as the applicants are not considered as having a conflict of interest.

3. RECOMMENDATIONS FOR ERN ACTION

It is recommended that the ERNs begin immediate preparations internally for their role in assessing their current full member healthcare providers who wish to expand the coverage of their disease areas, specifically by organising any voting that might be needed if delegated decision making is needed which should follow the ERN's governance rules.



European Reference Networks

https://ec.europa.eu/health/ern_en

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