

Wednesday 28 March 2018

ERN



GUARD-Heart

Gateway to Uncommon And Rare Diseases of the Heart



ERN GUARD-HEART BIMONTHLY NEWSLETTER

YEAR 2018 NUMBER 2

Assessment of ERN Members (Healthcare Providers) by EU

Brussels, 16 March 2018



DG SANTE and Consumers, Health, Agriculture and Food Executive Agency (CHAFEA) of the European Commission (EC) are about to sign the contract with the Independent Assessment Body (IAB) to carry out the technical assessment of a sample of ERN members' applications received under the framework of the call for interest for European Reference Network in 2016.

In particular, 79 ERN healthcare providers (HCPs) will be selected to undergo the documentation assessment against the specific criteria of the self-assessment checklist for healthcare providers and 23 of them will also receive the IAB on-site visits (audit).

As it has been the case in 2016, the sample is identified respecting objective criteria such as geographical balance and the size of the ERNs.

The exercise is expected to start in the month of April. All ERN HCP members which are part of the sample of HCPs to be assessed will be contacted by the IAB in due course.

The EC has asked the Coordinator of ERN GUARD-Heart you to pass this message to the members of the ERN and to remind the members to have ready the documentation that justify their compliance with the specific criteria and conditions for HCP with regard the area of expertise. ♥

TYPE 5 LONG QT Registry

The Type 5 Long QT Syndrome (LQT5) Registry has been initiated to further characterize the clinical, electrocardiographic, and genetic features of this condition. LQT5 accounts for ~2% of all LQTS cases, corresponding to an overall prevalence of ~0.001% within the general population. Partially stemming from its rarity, dedicated LQT5 reports in the literature have generally been confined to individual families and small case series, limiting insight into its clinical phenotype.

The LQT5 Registry is an international multicenter study that endeavors to enroll a large number of affected patients in order to robustly evaluate its clinical features and natural history and to statistically assess the clinical efficacy of treatment strategies. The anticipated large number of pathogenic *KCNE1* genetic variants that will be collected will serve to help clarify their clinical significance and allow for potential genotype-phenotype correlations to be explored. It is hoped that establishment of the LQT5 registry will lead to further insight into this inherited channelopathy and lead to improved care of affected patients.

The LQT5 Registry is coordinated by Jason Roberts (London Health Sciences Centre, Ontario, Canada). Members of ERN GUARD-Heart will be approached by Dr. Roberts for participation and/or can contact the ERN management office for information on how to participate in this Registry.

(See page 2 of this Newsletter for a full list of all ERN GUARD-Heart patient registries)



ERN GUARD-Heart Patients Registries



Amsterdam, 1 March 2018

ERN GUARD-Heart members have established the following patients registries (ongoing or new):

Registry	Registry leader	Registry coordinator	Link - Host	Minimal no. of patient to include
CALM genes	Peter Schwartz & Lia Crotti <i>Milan, IT</i>	Carla Spazzolini (c.spazzolini@auxologico.it)	https://redcap.heart-institute.nl AMC, Amsterdam, NL	1
CPVT	Arthur Wilde <i>Amsterdam, NL</i>	Krystien Lieve (k.v.lieve@amc.nl)	https://www.openclinica.nl AMC, Amsterdam, NL	10
Short QT syndrome	Silvia Priori & Andrea Mazzanti <i>Pavia, IT</i>	Maira Marino (maira.marino@icsmaugeri.it)	https://redcap.heart-institute.nl AMC, Amsterdam, NL	1
PRKAG2 gene	Philippe Charron <i>Paris, FR</i>	Gabriel Laurent (gabriel.laurent@chu-dijon.fr)	https://redcap.heart-institute.nl AMC, Amsterdam, NL (under development)	1
Type 5 long QT syndrome	Jason Roberts <i>Ontario, CA</i>	Jason Roberts (jason.roberts@lhsc.on.ca)	https://redcap.lawsonresearch.ca Lo London Health Sciences Centre, Ontario, CA	1
Long QT syndrome (GWAS)	Connie Bezzina <i>Amsterdam, NL</i>	Najim Lahrouchi (n.lahrouchi@amc.nl)	https://redcap.heart-institute.nl AMC, Amsterdam, NL	10
ARVC	Peter van Tintelen <i>Amsterdam, NL</i>	Peter van Tintelen (p.vantinetelen@amc.nl) Nynke Hofman (n.hofman@amc.nl)	https://redcap.heart-institute.nl AMC, Amsterdam, NL (under development)	5

How to participate

For including patients in the registries, please check the minimal number of patients that are required for inclusion (see table) and contact the specific study-coordinator by e-mail. He/she will request for a log-in account. Only registry leaders and coordinators have access to the complete data of their registry. As a participant you will receive access to the patients of your own HCP.

Consent form

Consent of the patient is required. For new patients and families the new designed ERN-consent form should be used and stored at the local HCPs. This consent form is available on the [IT-platform](#).

Questions

For general questions about existing registries, please contact Nynke Hofman (project/research manager of the ERN GUARD-Heart; e-mail: n.hofman@amc.nl).

Suggestions for new registries can be proposed at the periodic Board Meetings of ERN GUARD-Heart. ♥





Position Statement of the ERN Coordinators Group on UK BREXIT

Brussels, 28 February 2018



The UK National Health Service (NHS) is involved in 23 of the 24 ERNs (approximately 40 NHS hospitals), with NHS Trusts leading a quarter (n=6) of these Networks. It is of the utmost importance to secure the continued and lasting involvement and fruitful collaboration of UK colleagues, especially in the formative years of the ERNs. The Coordinators of the 24 ERNs have issued a statement on the Rare Disease Day (28 February) to call the EU and the UK government to find a solution for UK patients and healthcare providers (HCPs) to continue to benefit from the ERN. The statement is as follows:

“As Coordinators of the 24 European Reference Networks (ERNs), we stand together and united with our 900 strong members (healthcare providers) and the patient community, in the fight against rare diseases. Rare diseases are indiscriminate in nature and do not recognise borders. Individually no one country can successfully address the specific challenges rare diseases presents. Rare diseases clearly evidence the need for continued and enhanced EU-wide collaboration. ERNs bring together the collective knowledge and expertise of clinicians and researchers from across Europe, to take meaningful steps in tackling the impact of these rare diseases, demonstrating EU-added value.

We believe that European Union and its members should remain steadfast in their resolve to tackle rare diseases and complex conditions requiring highly specialised healthcare together, taking steps to safeguard our activity to help the complex needs of this vulnerable patient population. We want to highlight in the strongest possible terms the importance of maintaining our current membership of the ERNs. **We call upon the European Commission and the UK government to ensure that a solution is found so that the UK healthcare providers can continue to participate in the ERNs and all our patients can benefit from our collaboration.**

Rare in presentation, these diseases are devastating for the approximately 30 million EU citizens living with a rare disease. Rare diseases often mean a lifetime pursuit to find an accurate diagnosis, an increasing burden of needs and a significantly reduced quality of life. Patients and experts are few, geographically scattered and often isolated.

Reliable data and information is scarce and research is fragmented, often resulting in limited effective treatments and therapies. This leads to poor outcomes for patients and, in some cases, reduced life expectancy. ERNs represent a paradigm shift in how we work together, breaking the isolation of patients, connecting information and data and fostering collaboration between experts and researchers. ERNs will revolutionise access to care and be the hot-bed for innovation and driving force accelerating the development of research and new therapies. The ERNs have only recently been formally established and are at a crucial stage in their genesis, and we believe that the loss of the active input of the UK groups would be disadvantageous for the UK and the EU for the reasons listed below. The UK National Health Service (NHS) is involved in 23 of the 24 networks (approximately 40 NHS hospitals), with NHS Trusts leading a quarter (6) of these networks and many further lead on delivery of outcomes from within their respective ERNs. It is of the utmost importance to secure the continued and lasting involvement and fruitful collaboration of UK colleagues, especially in the formative years of the ERNs.

1. Pooling of scarce expertise

Rare diseases are rare, experts are rarer. The success of the ERNs will be measured by their ability to draw on and harness the collective (and often limited) expertise and knowledge across Europe. 70% of healthcare provider ERN members come from Western Europe - France, Italy, Germany, the Netherlands and the UK. We, as a community, cannot afford to reduce the pool of scarce experts working together in the ERNs, as this would result in fragmenting the already scarce expertise across the needs of all 28 Member States. This would risk our ability to deliver our mandate and ambition to provide highly specialized advice and recommendations for treatment, drive research and innovation and deliver cross-border training and education.

The legal basis for the ERNs is the EU law on reciprocal healthcare (the EU Directive on Patients' Rights in Cross-Border Healthcare). Ending reciprocal healthcare arrangements with the EU post-Brexit would jeopardise the UK's participation in the ERNs. This would have the effect both of depriving UK patients' access to the best specialised care for their specific condition and of depriving EU patients outside the UK of the benefits of UK specialists' knowledge and expertise.



Position Statement of the ERN Coordinators Group on UK BREXIT (*continued*)

2. Improving access to high quality healthcare

ERNs are an equalising force for patients to develop and share best practice, offering both the EU and UK patients' quicker access to expert advice, diagnosis and treatment recommendations, drawing on the experiences and knowledge of the ERN members through the new Clinical Patient Management System (CPMS) and to direct care locally.

CPMS is an innovative web-based platform provided by the European Commission that allows healthcare providers in our Networks to provide and receive advice on challenging cases by using an unprecedented Europe-wide consultation technology, responding to the most advanced EU standards in terms of security and data protection. We are now within a critical period as we are all working together to implement the CPMS. Using the CPMS, our ERN healthcare providers are setting up 'virtual' advisory panels of medical specialists across different disciplines and discussing cases in real time.

This is an incredibly exciting time for us as we now have the capability to spread our knowledge and expertise without the need for patients to travel. Our collaborative digital health efforts are also addressing the problem of equity of access of specialist services and overcoming financial obstacles to better care. By safeguarding the continued membership of UK experts in ERNs, this will enable ERNs to harness the rich and diverse experience of rare and complex presentations of patients, to guide prescribing high-cost treatment and optimise patient outcomes and quality of life. Ultimately, this will reduce ineffective tests and treatments.

3. The EU and the UK as a world-leader market for innovation and research

Action which makes it more difficult for the UK and the EU to collaborate will diminish the attractiveness of industry investment in the EU and the UK. Clinical research, including clinical trials, has benefited from UK and EU researchers working together, especially for rarer and paediatric diseases where the UK has the highest number of trials. Because the number of patients with individual rare conditions in each country is low, it is only possible to locate and recruit enough patients for clinical trials by collaborating across countries. A situation whereby UK trials were no longer able to recruit European patients, or UK patients were no longer able to participate in European trials would lessen the benefits for patients in the UK and across the whole of Europe, as well as risking damage to the UK and European scientific reputation.



ERNs are the vehicle to drive forward research and innovation. Bringing together a pan-European population allows the critical mass of expertise, patients and their data in 'ready-made communities'. ERNs are set to revolutionise how research is delivered, with healthcare as research and research as healthcare. We are dedicated to creating an integrated community with our patients that will optimise research and clinical trials, attracting investment in the EU and the UK as a world-leading market for innovation and research.

4. Safe and sustainable supra-specialised workforce

ERNs are ideally placed to collectively develop the safe and sustainable supra-specialised workforce through ERN cross-border training and educational activities. As new technologies, especially in the fields of genomics, imaging and biomarker studies increase diagnosis of rare diseases, the number of patients needing specialised input is expected to increase. We need to build the capacity in the countries currently without expert centres to meet all the needs of their population and train the experts of the future now.

In conclusion, we ask that our patients are put at the heart of the forthcoming EU negotiations with the UK under Article 50. We want to aim for the optimum possible outcomes for our patients. We believe that the ERNs are therefore essential in providing us with the ability to work together, to conduct joint research, to educate our colleagues and in particular to train the next generation. There is no doubt that the ERNs are a landmark opportunity for interdisciplinary collaboration between healthcare professionals working in close collaboration with patient groups."

This position statement of the ERN Coordinators Group was sent on February 28, 2018 to Mr. Michel Barnier, Chief Negotiator of the European Commission in charge of the Preparation and Conduct of the Negotiations with the United Kingdom under Article 50 of the Treaty on European Union. ♥



**European
Reference
Network**

for rare or low prevalence
complex diseases



Network
Heart Diseases
(ERN GUARD-HEART)



Giuseppe Limongelli Director of the Centre for Rare Diseases of the Campania Region

Naples, 27 February 2018

Dr. Giuseppe Limongelli, the representative member of AORN dei Colli, Monaldi Hospital (Naples, IT), has been nominated as the Director of the Centre for Rare Disease of Campania Region, and as the referral person of Campania Region for the Ministry of Health in Italy.



The Centre regulates the health organization for rare diseases in Campania. For more information (in Italian) click [here](#). ♥

Disease-specific patient materials

Amsterdam, 25 March 2018

In the previous Newsletter, the production of six information folders for patients and families with inheritable cardiac diseases was announced.

Folders have been made for the next diseases:

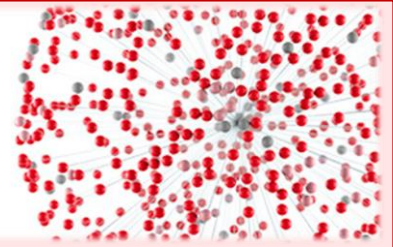
- Brugada syndrome
- Catecholaminergic polymorphic tachycardia
- Long QT syndrome
- Arrhythmogenic right ventricular cardiomyopathy
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy

The folders have been published on the [website](#) of the ERN GUARD-Heart. The patient information folders are only available in English. Unfortunately, the European Commission is (currently) not able to provide expert assistance or financial support to translate the folders in other European languages. If a HCP in ERN GUARD-Heart needs these folders in its own native language, the representative member of the HCP can contact the management office to request a translated version. ♥

ESC Congress Munich 2018

25-29 August

Where the world of cardiology comes together



The fourth meeting of the ERN GUARD-Heart Board will be held in August 2018, in Munich, Germany, during the ESC Congress. Further details on time and location will be announced soon.



In the meanwhile, thematic area leaders can contact the network management office to organize a meeting for their thematic area group (for example at the Heart Rhythm Scientific Sessions in May 2018, in Boston, USA).

Deliverables for 2017-2018 & the Specific Grant Agreement (SGA) for 2018-2019

Amsterdam, 28 February 2018

At the end of February, the Network management office submitted 10 Deliverables to the EU for the Specific Grant Agreement (SGA) for the ERN GUARD-Heart for the years 2017-2018. In the first year, a total of 24 deliverables have been submitted and approved. In addition, the SGA for the second year for the ERN GUARD-Heart has been submitted to the European Commission. The content of the SGA was fully in line with the 5-year-work programme 2017-2021 for the Framework Partnership Agreement (FPA) for ERN. All Deliverables and the SGA's of ERN GUARD-Heart are available at the [IT-platform](#). ♥

**IMPORTANT
NOTICE**

Clinical Patient Management System

The European Commission has released the Clinical Patient Management System (CPMS), a secure online consultation system for second opinion service within the ERNs. CPMS is part of the clinical care and therefore approval of medical ethical committee for research is not required. Using CPMS, ERN experts can discuss their patients within the ERN, and can be invited to provide second opinion advice within the ERN.

Each participating centre within ERN GUARD-Heart will be assessed by the European Commission (EC) with regard to its activities within the CPMS.

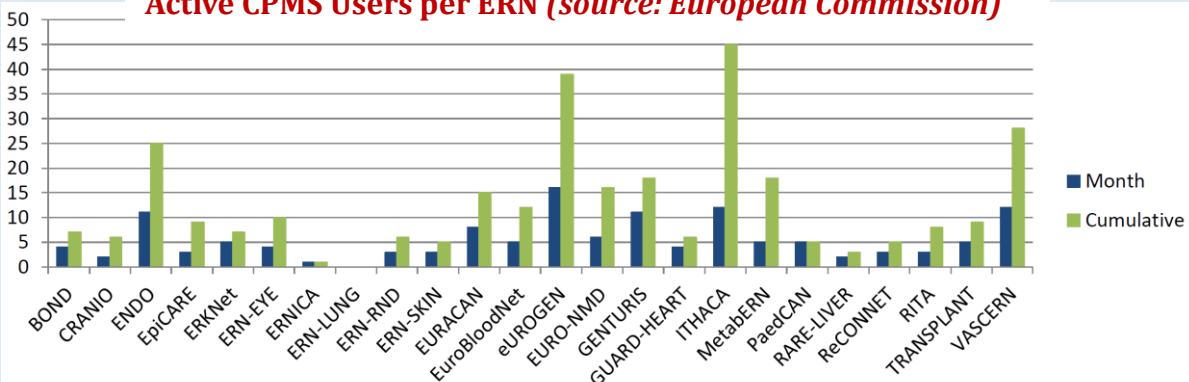
There is a CPMS training area. To use this area visit: <https://cpms-training.ern-net.eu/login/> For logging in to the training environment for CPMS, you need to use one of the following training accounts:

guardheartpuser1
guardheartpuser2
guardheartpuser3
guardheartpuser4
guardheartpuser5
guardheartpuser6
guardheartpuser7
guardheartpuser8

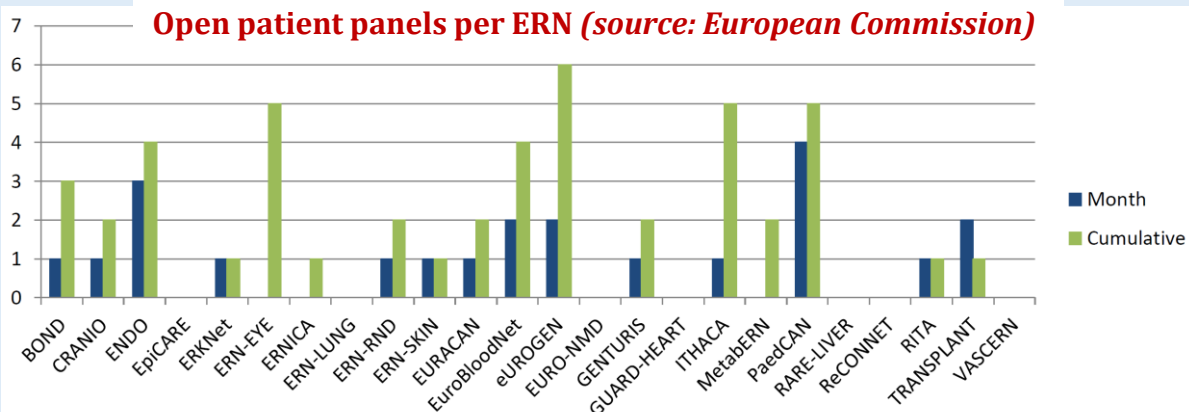
The password for all the accounts is cpmsern. On the login page for the training area you need to select the option: non-eulogin users (test only).

The first patients for online consultation within the ERN GUARD-Heart will be entered in the CPMS before the end of March 2017 by the AMC Amsterdam.

Active CPMS Users per ERN (source: European Commission)



Open patient panels per ERN (source: European Commission)





Collaboration with ERN ITHACA on infantile cardiomyopathy

Amsterdam, 5 March 2018

Dr. Bronwyn Kerr, consultant clinical geneticist at the Manchester University NHS Trust (Manchester, GB), has started a collaboration between ERN ITHACA (the ERN on congenital malformations and rare intellectual disability) and ERN GUARD-Heart. The work will center on new guidelines for infantile cardiomyopathy and the specific questions whether infants with a cardiomyopathy should have a Rasopathy gene panel, and if yes, whether such a panel should include a minimum number of genes? For more information please contact Georgia Sarquella-Brugada (San Juan de Déu - Barcelona Children's Hospital) or Juan P. Kaski (Great Ormond Street Hospital NHS Trust).♥

4th meeting of ERN Coordinators Group

Brussels, 5 March 2018

The 4th meeting of the ERN Coordinators Group was held on 5 March 2018. On behalf of the ERN GUARD-Heart, Ahmad Amin, project manager, participated at the meeting. Important topics that were discussed were the implementation of CPMS (*please see page 6 of this Newsletter*), invitation for HCPs to join ERNs, and monitoring and evaluation of the ERNs.

Before inviting HCPs to join existing ERNs, the EU intends to propose amending the 2014 Commission Implementing Decision criteria for ERNs (Decision 2014/287/EU) to slightly modify the procedure for the application for membership of an existing ERN. The amended procedure will require that each membership application shall be accompanied by a favourable pre-assessment from the Network that the HCP wishes to join. This pre-assessment would reflect the recognition of the high-quality of the application by the other Network members, which is essential for a good cooperation among the members and the effective functioning of the ERN.

The amendment will align the procedure for the application for membership of an existing ERN with the procedure for application for membership in a new Network, which was already implemented in 2016, when the existing 24 ERNs were established.

The amendment of Decision 2014/287/EU is expected to be finalised in autumn 2018 following a vote by the Member States in the Cross-Border Health Care Committee and the adoption of the act by the College. The invitation for HCPs to join existing ERNs will therefore be launched afterwards, most probably in the last trimester of 2018.

With regard to the monitoring and evaluation of the ERNs, the Coordinators Group unanimously selected a set of indicators for monitoring the performance of the ERNs. Definitions of the indicators aim to enable an assessment of any maintenance, improvement or deterioration in relation to the objectives of the ERNs. Furthermore, they aim to permit provision of accurate reporting to healthcare authorities, HCPs, patients, and clinical and research experts.

A total number of 43 indicators have been selected to monitor ERNs, including 5 structure indicators, 25 process indicators and 13 outcome indicators. A number of 8 indicators specifically measure patient involvement. ERNs need to demonstrate that the Networks are functioning and are adding value compared to what exists. Therefore, the indicators have been chosen to capture the added value post the ERN establishment. It is also essential that the selected indicators to monitor ERNs capture successes and failures in trying to fulfil the ERN objectives. The goal has been to define stringent and generic indicators, which are applicable across the heterogeneity of different ERNs, and to collect data pertaining to things which *can* be changed, instead of things over which the ERNs have little or no control. The Coordinators also made suggestions of who will be responsible for collection of the data and how frequently the data is to be collected. The next step is to create protocol/standard operating procedure to comply with this process.

The full list of the common indicators for monitoring the ERNs is available on the [IT-platform](#). ♥



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