NEW e-HEALTH SERVICES FOR THE EUROPEAN REFERENCE NETWORK ON RARE ANAEMIAS

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Acronym:
e-ENERCA

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FINAL PUBLIC REPORT

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## Specification of eENERCA project grant

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<th><strong>Project title:</strong></th>
<th>NEW e-HEALTH SERVICES FOR THE EUROPEAN REFERENCE NETWORK ON RARE ANAEMIAS</th>
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<td><strong>Acronym:</strong></td>
<td>e-ENERCA</td>
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<td><strong>Date(s) of the Project:</strong></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; September 2013 – 30&lt;sup&gt;th&lt;/sup&gt; September 2016</td>
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<td><strong>Starting date of the grant agreement:</strong></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; September 2013</td>
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<td><strong>Priority area:</strong></td>
<td>3.2. Actions under the second objective 'Promote health'</td>
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<td><strong>Sub-action:</strong></td>
<td>3.2.4.3. Support for European rare diseases information networks - Setting up of new rare disease registers or rare disease information networks</td>
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<td><strong>Action:</strong></td>
<td>3.2.4. Prevention of major and rare diseases (Point 2.2.2. in Annex to the Programme Decision)</td>
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Acknowledgements

We would like to thank all persons and institutions that have contributed to making the e-ENERCA project a useful and realistic tool to improve how rare anaemia is dealt with across Europe:

1. The European Commission, by means of its Executive Agency for Health and Consumers (EAHC);

2. The institutions that support the partners that have actively contributed to this project;

3. All the ENERCA centres and experts who have collaborated in the different activities performed across Europe

4. All the patients who have participated in the e-ENERCA symposiums
Rare Anaemias (RA) are Rare Diseases (RD) with prevalence in Europe less than 5 per 10,000 individuals. Major forms require red blood cell transfusions and iron chelating therapy as main therapeutic options. Most prevalent RA group is the haemoglobin syndromes, including thalassaemia and sickle cell disorders. Beta-thalassaemia major is predominant in Italy and Cyprus, and sickle cell disease (SCD) in African population. During the last 30 years, SCD is increasing in Europe due to African immigration, leading to an important impact on health care burden in several countries: England, France, Belgium, Spain, Italy and The Netherlands. Preventive programs aiming to epidemiological control and a better diagnosis and clinical management of major RA are therefore crucial for decreasing the affected birth rate and achieving an efficient balance between disease morbidity and patient’s life capacity.

Since 2003, ENERCA has taken an active role for improving this situation by:

a) the creation of a European Network of Centres of expertise in RA, on the basis of a legal and ethical analysis, technical consensus criteria, and patients’ expectations

b) the promotion of best clinical and laboratory practices

c) the publication of ENERCA recommendations

d) the improving of continuous medical education by the organization of topic specific training courses

e) the empowerment of patients by cooperation with Patient’s Associations and co-organizing a annual European Symposium on RAs with interactive patients-health professionals sessions and educational material in different languages.

All these ENERCA outcomes have had a wide geographical coverage and an efficient impact as a high number of health professionals and patients were implicated. ENERCA website has definitely contributed to this success. [http://www.enerca.org/](http://www.enerca.org/)

e-ENERCA has been based, in part, on ENERCA 3 achievements, but adapted to the Directive on patients’ rights in cross-border healthcare. Accordingly, it has not been just a continuation of ENERCA 3, but a clear real step forward to the consolidation of the European Reference Network of Centres of Expertise on Rare Anaemias (ERN-Rare Anaemias). For this, e-ENERCA intended to incorporate the innovative e-health information and communication technologies (ICT) to create a pan-European interoperable e-health platform for teleexpertise/telediagnosis, electronic registry/epidemiological electronic health records (EHR) and e-learning.
eENERCA Objective

The general objective of e-ENERCA was to provide professionals and patients with e-Health tools to assure the same level of RA services across Europe, independently from the country of practice and the origin of the patient. e-Health services has been developed through the implementation of three e-platforms endorsed on the ENERCA website with the following goals:

1) To set up a e-registry for gathering patient’s data to achieve the required sample size for epidemiological surveillance and clinical research
2) To set up a e-learning platform for the dissemination of knowledge and best practices
3) To develop a telemedicine platform to provide expertise at distance avoiding the need of physical travelling.

e-ENERCA also aimed to promote the recognition of Centres of expertise by the national health authorities necessary for its promotion and its recognition as a European Reference Network (ERN) on RA. e-ENERCA also assessed the implementation of the new Directive 2011/24/EU.

In order to achieve the general objective, six specific objectives were established:

**Specific objective 1 - To enhance the creation and use of the European inventories to gather updated and reliable data on centres of expertise, epidemiological figures and rare anaemia related data**

Since the frequency of RA in Europe is very low, and the expertise in their diagnosis and clinical care is limited to some specific kind of RA and centres, European inventories for patient’s management are crucial.

**Specific objective 2 - To facilitate the continuing medical education (CME) and best practices sharing on rare and congenital anaemias among European health professionals whatever their country of practice**

e-ENERCA aimed to offer a e-learning platform for open access of European experts and health professionals to up-to-dated knowledge and best practices recommendations on RA, based on the state of the art and on the European training courses content.

**Specific objective 3 - To create a telemedicine platform for the provision of healthcare and medical advice to non-experts dealing with rare anaemia**

e-ENERCA aimed to create an expert collaborative network for sharing expertise without the need of travelling (tele-expertise), and for performing diagnosis in the distance (tele-diagnosis).

**Specific objective 4 - To promote the recognition of centres of expertise at national level and ENERCA as the ERN on RAs.**

e-ENERCA aimed to collaborate in the implementation of the objectives of the new Directive 2011/24/EU that recognizes the importance of networking in RD and the key role of the MS in this context.

**Specific objective 5 - To develop e-Health tools in the field of rare anaemias and promote their use among the scientific community and patients’ associations**

e-ENERCA aimed to develop innovative e-tools endorsed in the existing ENERCA website to facilitate the creation of communication channels and strengthen the links among the main communities with an active role in the management and prevention of rare anaemias.
Specific objective 6 - To assure the project’s sustainability in the future

e-ENERCA aimed to explore the mechanisms for the future sustainability of ENERCA at National and European level.

eENERCA Consortium

e-ENERCA project is led by IDIBAPS / Hospital Clínic of Barcelona and coordinated by Prof Joan LLuis Vives Corrons, head of the project, Dr Maria del Mar Mañú Pereira, Project Scientific Manager, and Victoria Gutierrez Valle, Project web manager.

eENERCA has been carried out by 26 partners distributed in 11 European countries: 12 associated partners and 14 collaborating partners. Contributors are professionals from around Europe who played a relevant role in the evolution of the ENERCA project. Most of the partners have been working together since 2002 and all of them are well known and recognized experts in their respective field.
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<th>COORDINATOR</th>
<th>ACRONYM</th>
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<tr>
<td>Institut D’Investigacions Biomèdiques August Pi i Sunyer-Hospital Clinic de Barcelona / Hospital Clinic of Barcelona</td>
<td>IDIBAPS / HCB</td>
<td>Joan Lluís Vives-Corrons</td>
<td>Spain</td>
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<td>Maria del Mar Mañú Pereira</td>
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<td>Victoria Gutierrez Valle</td>
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<tr>
<td>Centre Hospitalier Universitaire de Montpellier</td>
<td>CHUM</td>
<td>Patricia Aguilar Martinez</td>
<td>France</td>
</tr>
<tr>
<td>Hôpital Erasme - Université Libre de Bruxelles</td>
<td>ERASME</td>
<td>Béatrice Gulbis</td>
<td>Belgium</td>
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<tr>
<td>Cyprus Foundation for Muscular Dystrophy Research</td>
<td>CING</td>
<td>Marina Kleanthous</td>
<td>Cyprus</td>
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<tr>
<td>European School of Haematology</td>
<td>ESH</td>
<td>Didi Jasmin</td>
<td>France</td>
</tr>
<tr>
<td>Foundation IRCCS Cà Granda Ospedale Maggiore Policlinico Milan</td>
<td>IRCCS</td>
<td>Paola Bianchi</td>
<td>Italy</td>
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<tr>
<td>King’s College London School of Medicine</td>
<td>KCL</td>
<td>Swee Lay Thein</td>
<td>United Kingdom</td>
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<tr>
<td>Thalassaemia International Federation</td>
<td>TIF</td>
<td>Androulla Eleftheriou</td>
<td>Cyprus</td>
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<td>Michael Angastiniotis</td>
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<tr>
<td>Universidad del País Vasco / Euskal Herriko Unibertsitatea</td>
<td>UPV/EHU</td>
<td>Carlos Romeo</td>
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<td>Pilar Nicolás</td>
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<tr>
<td>University Medical Center Utrecht</td>
<td>UMCU</td>
<td>Richard van Wijk</td>
<td>Netherlands</td>
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<td>University of Cyprus</td>
<td>UCY</td>
<td>Christos N. Schizas</td>
<td>Cyprus</td>
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<tr>
<td>West Hertfordshire Hospitals NHS Trust</td>
<td>UK NEQAS</td>
<td>Barbara de la Salle</td>
<td>United Kingdom</td>
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<tr>
<td>University of Athens, Biomedical Research Foundation</td>
<td>BFR</td>
<td>Dimitris Loukopoulous</td>
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<tr>
<td>Centro di Ricerca per l’Ingegneria Genetica</td>
<td>CEINGE</td>
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<td>Centro Hospitalar Coimbra</td>
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<tr>
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<tr>
<td>Universitá Vita-Salute San Raffaele</td>
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<td>Italy</td>
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<tr>
<td>Hôpital Robert Debré</td>
<td>HDR</td>
<td>Lydie da Costa</td>
<td>France</td>
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<tr>
<td>Aristotelian University of Thessaloniki</td>
<td>AUTH</td>
<td>Panayiotis D. Bampidis</td>
<td>Greece</td>
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<tr>
<td>Institute of Predictive and Personalized Medicine of Cancer</td>
<td>IMPPC</td>
<td>Mayka Sanchez</td>
<td>Spain</td>
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<td>University of Milan</td>
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<td>Domenica Cappellini</td>
<td>Italy</td>
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<tr>
<td>National Centre of Haematological Transfusiology Sofia</td>
<td>NCHT</td>
<td>Mirela Rangelova</td>
<td>Bulgaria</td>
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<tr>
<td>Centro Nazionale Malattie Rare and Europlan Project</td>
<td>CNMR</td>
<td>Domenica Taruscio</td>
<td>Italy</td>
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Project implementation: Methods and means

e-ENERCA methods have been focused on the fostering of European inventories due to their crucial role in tackle RA and the implementation of the new information and communication technologies (ICT) for health practice (e-health). For this, three different platforms accessible on-line through the ENERCA website have been developed in the running time of e-ENERCA project.

Both aspects have contributed to maximize the benefits in patient care; to broaden the services to all MS, and to decrease the inequalities existing in Europe for RA health care. These new e-Health tools arises some legal and ethical issues, namely the identification of the role of all professionals involved, who do not constitute a working team in terms of legality. A legal study has been carried out involving all these issues through WP7 leader – UPV, as experts in the field of Bio-Law. EU directives on e-Health (interoperability, expandability, security, confidentiality, remote access, and patient-centred) has been ensured by the new e-platforms and communication channels.

e-ENERCA methods and means have been split into 4 Core WPs with specific tasks linked to objectives:

WP 4 – EUROPEAN EPIDEMIOLOGICAL SURVEILLANCE FOR MAJOR RARE ANAEMIAS CREATION OF A PAN-EUROPEAN INTEROPERABLE ELECTRONIC REGISTRY FOR MAJOR RA AND OTHER EPIDEMIOLOGICAL ELECTRONIC HEALTH RECORDS (EHR)

WP LEADER: TIF
Associated partners: UCY, UMCU, UPV/EHU and IDIBAPS, HCPB
Collaborating partners: AUTH, UNISR, CEINGE, CTC, NCHT and CNMR

Link to:

Objective 1- To enhance the creation and use of the European inventories to gather updated and reliable data on centres of expertise, epidemiological figures and rare anaemias related data.

Objective 5- To develop e-Health tools in the field of RA and promote their use among the scientific community and patients’ associations

As a previous task, a study of the requirements and EU standards and directives for EHRs, legislation issues and standards for the maintenance and distribution of medical data, the limitations (political, cultural, and economical) that may exist with respect to local infrastructures and policies, and the identification of possible threats was undertaken.

The ultimate goal of the WP4 is to connect the e-Enerca European registry with already existing databases. Accordingly, a survey was conducted in order to establish local and national practices concerning rare anaemia registries across Europe and to analyse the existing registries at National and International level.

In April 2014 the online questionnaire was sent to health authorities, academic bodies and other organisations. Seventy-eight haematology centres in Europe were contacted via e-mail and given the site to respond. 31 completed questionnaires were returned for their analysis (39 %). 27 centers confirmed the availability of a registry, while only 3 centres stated that they had no registry. The majority of people that answered the questionnaire were Doctors and Nurses from hospitals and clinics around Europe. Taking into account the questions related to the structure of the registries, feedbacks were
useful to have an overall idea of the existing databases formats in Europe and their comparison.

A Proposal of an interoperable, extendible and functional model of a database which will enable entering of certified medical data from the available sources was accordingly made. EU and International standards (such as HL7, CEN/tC 251, 13940 etc) were applied ensuring interoperability and patient-centric philosophy. Accordingly, data in already existing databases can be utilised and collected in a central Pan-European registry, administered by the e-ENERCA.

The core team that has developed the registry includes:

- Dr Michael Angastiniotis - TIF
- Prof Christos Schizas – UCY
- Prof Constantinos Pattichis - UCY
- Zinonas Antoniou – programmer (TIF) supervised by UCY and Anastasios Sofocleous (Betologic SME)
- Irene Schizas – database designer - UCY

The design of the system and the structure of the Health record registry were based on Human Computer Interaction principles. The Registry’s prototype development follows the iterative design, which is a design methodology based on a cyclic process of prototyping, testing, analyzing, and refining a product or process. This process is intended to ultimately improve the quality and functionality of a design.

The registry is not a comprehensive clinical record, but designed to fulfil the stated purpose as a tool for epidemiological surveillance of rare anaemias. However, in order to fulfil its purpose, clinical data were included in the form of annual summary reports. This was necessary since epidemiology, to be complete, requires information on mortality as well as on complication rates. Such information is a valuable assistance to health planners. It is potential tool for patient classification and recruitment for clinical trials.

A modular system was agreed for the structure of the registry:

- Demographic data, which are based on the EU minimal common data elements and include patient consent. Patient consent is first obtained after full explanation of the registry and its purpose by the doctor in each case. A patient consent form was designed, on a modified template created by the Global Rare Disease Registry Data Repository (GRDR). Once signed, the consent is placed on the electronic registry, before any other data can be added.
- Anonymisation of the data is an essential feature and so personal data can only be accessed by the treating physician and the patient if requested.
- Diagnosis is an obligatory field and both ICD10 and Orphacode are used for coding and final epidemiological analysis.
- Proof of diagnosis in the form of a droplist of performed tests which have led to the diagnosis is provided although this is not obligatory.
- Patient reported outcomes, a short list with an option to add a Quality of life questionnaire, are included, with a view for future expansion especially if a modification for clinical trials is required.
- Annual clinical summaries, including a list of complications, are available for transfusion dependent anaemias and another for sickle cell syndromes, non-obligatory modules, which however are highly recommended feature.
- Aggregated data is a module mainly designed for countries for centres or countries who are reluctant to provide individual data or who already have a register and wish just to contribute to overall European or international epidemiological information.
• A simple statistical analysis module is offered although more complex statistics may be had by transporting data to a recognised package such as SPPS.

The model includes (a) a list of tests required to firmly establish the diagnosis of the type of anaemia, in order to discriminate these rare anaemias from one another. The list includes routine as well as advanced diagnostic tests in a detailed manner and presented in the form of a diagnostic flowchart, and (b) patient clinical data that is listed to form the basis of the database. The database has a modular architecture.

The front-end has been designed using Django, which is an open-source high-level Python Web framework that encourages rapid development and clean, pragmatic design. The core Django MVC framework consists of an object-relational mapper which mediates between data models (defined as Python classes) and a relational database (“Model”); a system for processing requests with a web templating system (“View”) and a regular-expression-based URL dispatcher (“Controller”). Security is a topic of paramount importance in the development of Web applications and Django provides multiple protection tools and mechanisms.

A web portal was created using technical blueprints and taking special consideration into:
- Interoperability, in order to receive data from existing registries and assist networking
- Extendable system so that users may add fields of interest to their own projects
- Facilitation of research, both epidemiological and clinical
- User requirements have been included through consultation with partners and other users
- Building the infrastructure and web portal for the registry with installation, testing and delivery of a complete system has been completed.

Dissemination of the platform was also performed through:
- A patient flyer was prepared to support any information offered by the doctor.
- A user's manual is accessible through the web portal.

A validation phase was conducted in order to evaluate the registry and test it in a pilot study in a real environment. A minimum dataset including only anonymised patient outcomes was used during the validation phase and more likely to be utilised by participating centres.

Currently, the platform has 51 patients from 3 doctors among the 15 which are registered to the system.

According to ENERCA objectives there is a need to promote e-health tools to patient associations. In this respect the patients and their associations must learn their rights concerning patient registries and what it means to have ownership of the data. The patients also must understand the use of the registry and the possibility of their entering their own data. With this aim TIF has developed an educational platform for patients.

A final improvement of the ENERCA eRegistry was the provision of personalized training and guidelines services for its registered patients through a platform that offers a straightforward authoring environment for interactive virtual scenarios. The specific tutorial is a branching topical selection that guides the user in the exploration of useful medical information about thalassemia. For this purpose, an e-learning module was developed regarding haemoglobin disorders by Panayiotis Bamidis team from Medical School of the Aristotle University in Greece.

A small simple interactive scenario was created based on tutorial for demonstration purposes. This tutorial has been developed with minimal effort in the established by OpenLabyrinth platform. This platform offers a straightforward authoring environment for
interactive virtual scenarios. The specific tutorial is a branching topical selection that guides the user in the exploration of useful medical information about thalassemia.

Enzyme Geocode section

Enzyme Geocode, section located under Activities, was developed under the 2nd period of the project and released in the final period. Geocode was created under request of UMCU partners, Prof Richard van Wijk and in collaboration with IDIBAPS, Dr Mañú Pereira and IRCCS, Dr Bianchi.

This activity developed under WP4-eRegistry aimed to achieve the European Enzyme Epidemiological Geocode in order to give insight in the prevalence of this type of rare anaemia, but also in time to diagnosis and life expectancy. It contained a short questionnaire to be fulfilled on-line by the health professionals about individual patients under care who are diagnosed with hereditary haemolytic anaemia.

WP 5 – CONTINUING MEDICAL EDUCATION (CME) ON RARE ANAEMIAS (RAS) AND ENERCA E-LEARNING

WP LEADER: CHUM

Associated partners: ESH, ERASME, KCL, IDIBAPS, HCPB, UMCU, UK-NEQAS and CING

Collaborating partners: UA, CHU, UNIMILANO, HRD, CEINGE, UNISR, IMPPC, CHC, NCHT, UM, AUTH

Link to:

Objective 2- To facilitate the continuing medical education (CME) and best practices sharing on rare and congenital anaemias among European health professionals whatever their country of practice.

Objective 5- To develop e-Health tools in the field of RA and promote their use among the scientific community and patients’ associations

Two training courses were organized by ENERCA, Prof Patricia Aguilar Martínez, and the European School of Hematology, Prof Didi Jasmin. Both courses were accredited from the EHA-ECA

In both courses, the program included clinical and biological small group discussions on specific themes. These sessions were designed to promote informal discussion and interaction. Participants were invited to opt to attend either the clinical or the biological group discussions, according to their main interest. Before the meeting, participants were invited to submit clinical cases or biological abstracts. The scientific committee of the meeting reviewed cases. Selected cases and abstracts were presented by their authors during the meeting and were the object of general discussion led by an expert. This active learning approach proved appreciated and effective.

In addition, the organizers actively promoted interaction between the participants and between participants and speakers, notably via interactive clinical case presentation sessions and the use of voting boxes.

All the oral presentations were video recorded by a professional team and the approved presentation have been published in the ESH websites, also available through ENERCA website.
The first one “Training course on haemoglobin disorders: laboratory diagnosis and clinical management” was held in Barcelona, Spain, the 23-24 January 2015.

Chairpersons course 1
Béatrice Gulbis.......... WP6
Swee Lay Thein......... WP5
Maria Domenica Capellini...... WP5
Patricia Aguilar Martinez.... WP5

The course was developed to provide state of the art knowledge on haemoglobin diseases including practical data for clinicians or biologists who diagnose and/or care for patients with these disorders. Scientific sessions alternated with the presentation of clinical cases by experts. Main topics included epidemiology and screening of haemoglobin disorders, clinical and biological aspects of thalassaemia on day 1. Day 2 was devoted to abnormal haemoglobins especially sickle cell disease and to the complications and treatments.

The second one “Training course on diagnosis and management of very rare red cell and iron disorders” was held in Lisbon, Portugal, the 29-30 January 2016.

Chairpersons course 1
Paola Bianchi (IRCCS) ...... WP4
Achille Iolascon (CEINGE) ...... WP5
Richard Van Wijk (UMCU)…… WP4
Alberto Zanella (IRCCS)…… WP4

The course was developed to provide state of the art knowledge on very rare anaemias, including practical data for clinicians or biologists who diagnose and/or care for patients with these disorders. Main topics included epidemiology, clinical and biological aspects of Disorders of Red Cell Production, Red Cell Survival (haemolytic anaemias) and Very Rare Disorders of Heme Synthesis on day 1. Day 2 was devoted to Disorders of Red Cell Metabolism, Acquired Haemolytic Anaemias and Diagnosis and Treatment of Very Rares Anaemias.
In the field of medical education in haematology, there is a lack of courses or professional training activities targeting rare anaemias. This contributes to the slow implementation of harmonized clinical practices, leading to an unequal awareness of the best practices for the management of the patients among countries.

The aim of the e-ENERCA e-learning platform is to offer an open access distance learning prepared by experts, available to any European health professionals who wanted to update his/her knowledge and skills on RAs. The training is based on the state of the art knowledge provided by ENERCA expert partners, in close connection with the contents of the ENERCA European training courses on RAs.

Accordingly, the e-Learning platform will be a useful tool for initial and continuing medical education in the field of RAs, offering a complete panel of training tools to the registered participants and contributing to reduce inequalities in knowledge accessibility on RAs throughout Europe.

Participants will increase their professional skills in accordance to the requirements established by the “European haematology curriculum/passport”

Accordingly, the specific objectives of the eLearning Platform are:

- To facilitate the harmonization of the haematology and paediatric (haematology) specialities curricula throughout the EU - “European haematology curriculum/passport” [http://www.ehaweb.org/education-science/eha-online-learning/curriculum-cv-passport/]
- To improve continuing medical education on rare and congenital anaemias among European health professionals whatever their country of practice.
- To promote the implementation and dissemination of existing guidelines in the diagnosis and clinical management of rare anaemias, as well as the ENERCA recommendations in the field.
- To create of an on-line training platform on RAs, based on different modules focused on each group of disorders leading to RAs, complementing the ENERCA on-site training courses.

After analysis of several companies, “ENOV formation” [http://www.enov-formation.com/] was chosen for developing the learning platform. This company had developed an original e-learning platform in collaboration with a University professor; the platform was already in use in other domains and could be perfectly adapted to the objectives of eENERCA.

The eENERCA e-learning platform is included in an Academic specialized environment, the University & Hospital of Montpellier, and managed by professionals of education. Contents were built by ENERCA partners involved in WP5, as well as by any partners or contributors of the project with an expertise in RAs.

The structure of the existing platform was adapted as scheduled to fit the requirements of the ENERCA project. The first part was delivered at the end of October 2014. The graphic chart was adapted to the ENERCA project (made similar to the ENERCA website). The EC logo was added to indicate that the platform was developed through an EC grant.

Two “live tests” were performed:

- December 2014: A test was made using a “virtual classroom” composed of CHUM team partners
A second “live test” was done with the students registered to a French University diploma on red cell disorders organized in Montpellier University by CHUM team leader (Patricia Aguilar Martinez).

A “sample e-learning module” (including all the learning process: (pre-test, course, documents, post-test) was prepared by WP5 leader to serve as a model for the preparation of all the different sections of the e-learning courses. A simple general form was prepared indicating the desired learning elements to be produced by the different partners who will produce the contents. The programme of the course (based on the IDC classification) was uploaded by the project assistant on the platform, both in French and English. It was decided that the webcasts of the ENERCA training courses (expected to be held in January 2015 on haemoglobin disorders and in January 2016 on other rarer red cell disorders) would serve as a great basis for the English version of the platform. The courses would be enriched using other learning tools, as the platform allows uploading any kind of teaching material, including videos, PowerPoint presentations, pdf files etc...)

The e-learning platform was made accessible from the ENERCA website by the creation by the coordination team of a specific web page on the ENERCA website linked to the e-platforms, and of a specific page on e-learning.

A “portal page” was also created on the e-learning platform and links between the ENERCA website were prepared. This page contains a description of the tool, the target public, a welcome message by WP5 leader, the programme of e-learning and a few words about the authors.

In January 2015 A “launch event” was organized during training course 2 in order to advertise the opening of module 1. A presentation of the platform was made to the participants in plenary session. Participants were invited to register and to provide their e-mail address in order to be given access to the e-learning platform.

The courses for these new modules 2, 3 and 4 were progressively prepared and arranged.

Accordingly, four modules 1, 2, 3 and 4 were implemented on the platform by September 2016:

- Haemoglobinopathies
- Red Cell membrane diseases
- Red Cell enzymopathies
- Other very rare red cell disorders

Collaboration with the e-HEMATIMAGE project

ENERCA has collaborated with eHEMATIMAGE with the provision of an annual biological case and blood films by ENERCA partners involved in laboratory haematology. ENERCA partners decided to go on with the collaboration with e-HEMATimage paying tribute to Pr Corberand.

On behalf of ENERCA, we would like to express our deep sadness following the death in August 2015 of our eHEMATIMAGE partner Pr Joel Corberand. According to his last message to ENERCA, his collaborator, Dr Rieu will continue the ENERCA-e-HEMATIMAGE collaboration.
**Organization of the ENERCA European Symposium on Rare Anaemias**

In addition to the on-site training courses, eENERCA coordinator organized, as part of WP2 Project dissemination, two European Symposium on Rare Anaemias with the participation of patients

**5th European Symposium on Rare Anaemias**

The 5th European Symposium on Rare Anaemias was held the 15th-16th November 2013 in Ferrara (Italy) with a duration of 1.5 days together with the 1st Italian meeting for patients and health professionals. It was co-organized with the Italian Federation of Associations for Thalassaemia and Sickle Cell Disease (UNITED) and the Thalassaemia International Federation.

The main objectives of the symposium were:

- To provide an overview on prevention, diagnosis and clinical management of thalassaemia and other haemoglobinopathies.
- To provide the current gene therapy approach for thalassaemia treatment.
- To review current situation of other rare anaemias patient’s community.
- Interactive session for patients: For the first time in Italy, patients with rare anaemias will have the opportunity to join, in a common meeting, the most experienced European health professionals in these particular disorders.

A total of 180 participants, 78 patients and 102 professionals from all over Europe participated. There was a total of 22 poster presentation during the session dedicated to posters that was held the 1st day of the symposium.

**6th European Symposium on Rare Anaemias**

The symposium was held the 21st-22nd November 2015 in Amsterdam (The Netherlands) with duration of 2 days. It was coorganized with the Multi-ethnic organisation for patients with Sickle Cell and Thalassemia (OSCAR), Belgic Association of Thalassaemia (ASBL), Aplastic Anaemia and Paroxysmal Nocturnal Hemoglobinuria (PNH) - rare blood disease community (HematosLife), Pyruvate Kinase Deficiency (PKD) Support Group, and Thalassaemia International Federation (TIF).

The main objectives of the symposium were:

- To provide an overview on diagnosis, etiology and clinical management of patients with pyruvate kinase deficiency, paroxysmal nocturnal haemoglobinuria, and haemoglobinopathies (sickle cell anaemia and thalassaemia).
- To provide an overview of general hallmarks of rare anaemias and their clinical management.
- To propose multi-disciplinary comprehensive care for patients with rare anaemias.
To provide a forum for discussion in interactive meetings for patients and health professionals

A total of almost 176 people, 86 patients and 90 health professionals from all over the world participated. There was a total of 6 posters presentation during the poster walk held the 1st day of the symposium.

**WP 6 – ENERCA EXPERT ADVICE: TELE-EXPERTISE AND TELEMEDICINE SERVICES FOR RARE ANAEMIAS**

**WP LEADER: ERASME**

Associated partners: UPV, IDIBAPS, HCPB, CHUM, TIF, UMCU, CING and IRCCS

Collaborating partners: UULM, IMPPC, CEINGE, UM and NCHT

*Link to:*

*Objective 4- To promote the recognition of Centres of expertise at national level and ENERCA as the European Reference Network on rare anaemias*

*Objective 5- To develop e-Health tools in the field of RA and promote their use among the scientific community and patients’ associations*

A previous study of the legal and ethical aspects of the telemedicine and tele-expertise platform was performed by partner UPV/EHU, Prof Carlos Romeo and Prof Pilar Nicolás, with skills in this matter. The study analysed the legal framework of telemedicine services in the European Union (EU) and described the legal requirements for the establishment of a telemedicine platform within e-enerca project in the terms agreed. In July 2014, a legal report was developed as the basis for the establishment of a telemedicine platform within eENERCA project.

The board of the Telemedicine platform is chaired by the leader, Prof Béatrice Gulbis (ERASME) and it is composed by:

- Telemedicine platform coordination team: Prof Béatrice Gulbis and Françoise Neumann from ERASME, and Dr Maria del Mar Mañú Pereira and Prof Joan-Lluis Vives Corrons from IDIBAPS.

- Experts were appointed to specific diseases groups:
  - Aguilar-Martinez, Patricia - Haemoglobinopathies
  - Angastinitis, Michael - Haemoglobinopathies
  - Bianchi, Paola – enzymopathies and membranopathies
  - Cappellini, Maria-Domenica – Haemoglobinopathies
  - Gulbis, Béatrice – Rare anaemias
  - Ignatova, Iglika - Haemoglobinopathies
  - Iolascon, Achille – Bone marrow failures
  - Kaleva, Valeriya - Haemoglobinopathies
  - Kleanthous, Marina – Haemoglobinopathies
  - Mañú Pereira, Maria del Mar - Haemoglobinopathies
Sanchez, Mayka – Iron related disorders
van Wijk, Richard - enzymopathies and membranopathies
Vives Corrons, Joan Lluis – Rare anaemias
Legal team. Experts in biolaw from the UPV/EHU
Romeo Casabona, Carlos
Nicolás, Pilar
Local expert “Moderator” – group of experts from ENERCA members: interface for the 'daily” management of the clinical cases submitted.

The telemedicine platform coordinators prepared a document including the objectives and specifications of the telemedicine platform in order to be presented for the call of tenders for companies. This document also included a table with required specifications to be completed by the companies in order to facilitate the decision process by the platform coordinators.

FARMAVET was selected to develop the Telemedine platform since: they presented a solution based in Python and Django, which was one of the main points to be taken into account for the final decision in order to assure the interoperability of the website. Economical proposal fit the budget, and in addition, Farmavet is not an informatics company but a e-Health, this was valuable for future expansion of the website.

- Final decision: In the light of the presented conclusions Farmavet was selected to develop the telemedicine website in the framework of ENERCA project. Agreement for the final platform was reached with Farmavet in February 2015

The telemedicine platform coordinators worked with Farmavet Company to define in detail the structure of the platform.

Module 1: Telemedicine, use of an interface for remote diagnosis orientation, in view to help at a distance:

1. Non-expert physicians making only on the basis of the information provided by the platform, in a first phase a diagnosis;

2. Although the platform is dedicated to health care professionals, a patient can connect to the platform, introduce his/her data, be offered a diagnosis, and print the report. The patient can then contacts his doctor, submit his report and ask him kindly to log on to the platform and to eventually ask for help to the European experts in rare anaemias.

The telemedicine module is based on decisions trees, generated by the experts involved in the board. Although it is addresses to non-experts health professionals in rare anaemias, it is public and so open to patients who can enter their own data. All data provided is anonym and a code is generated by the platform to be able of tracking the case. A diagnostic orientation is given to the applicant. This is automatically done by the system based on algorithms running in the background of the website according to the decision trees generated by the experts.

For the diagnosis orientation, there are three possibilities:

1. The diagnosis is not related to a rare anaemia:

   - Iron deficiency not excluded
   - Iron deficiency probable
   - Vitamin B12 deficiency probable
• Folate deficiency probable
• Probably no anaemia

The comment given to the applicant is:

"With the given data, the telemedicine website is unable to help you. Your case is probably not related to a disease covered by the ENERCA expertise."

2. Some data is missing, a diagnostic orientation cannot be proposed.

The comment given to the applicant is:

“At this stage, we cannot help you. To be more confident with the diagnostic orientation, results of all or only several tests (i.e. those not given already) are needed: (with the list of data needed). Save your case code and come back with the information requested."

3. The diagnosis might be a rare anaemia i.e. 4 diagnostic groups are offered:

• Thalassaemia and/or haemoglobin variants
• Membrane disorders and enzyme defects and/or haemoglobin variants
• Congenital dyserythropoietic anaemias
• Rare microcytic anaemias

Decision trees are proposed to the applicant (access by clicking on it). The applicant can follow those decisions trees and make a diagnosis by themselves i.e. without the involvement of an expert in the field of rare anaemias.

All decision trees are presented with the same pattern:

1. The clinical signs (in blue)
2. General laboratory tests: “The first level laboratory testing (in green). All the boxes in relation with laboratory testing are in green.
3. A large classification (in black)
4. Screening laboratory data "Laboratory data" (in light green)
5. Possible diagnosis (in red)

All underlined fields indicate a link to relevant literature. There are also general links to the ENERCA website (the same for all the decision trees) and particular links (depending of the decision tree) on the upper right of the screen. The tree is opened in another page and can be printed.

After consulting the decision(s) tree(s), the applicant can report if the diagnosis has been found. There are two possibilities:

The diagnosis has been found which means the end of the process.

The diagnosis hasn’t been found which means that an expert in rare anaemias can be requested: “Ask for an expert”. Link to module 2

A patient cannot ask for an expert, but he can print the structured report with the code number and give it to a healthcare professional who can follow the case and ask for an expert in rare anaemias.

Module 2: Tele-expertise, use of an interface for remotely interactive exchange of information and of anonym data between scientists.
When the applicant asks for an expert, he has to complete new data for the submitted case:

- Family history
- Clinical signs and symptoms
- Treatment given the last 3 months.

A national expert is appointed to the case. The national expert will decide on giving directly an answer to the applicant or share the case with the telemedicine experts’ board depending on the complexity of the case.

**Development of the platform : Testing and improvement**

A parallel work was run since March 2015 with the experts on rare anaemias and Farmavet Company in order to generate the decision trees and the algorithms for decision-making included in Module 1.

In August 2015 internal tests were performed with clinical cases. In September 2015 were updated and re-tested.

From September 2015 to March 2016 both module 1 and module 2 were developed. All the diagnosis proposed and the links to available documents, recommendations and training courses provided by ENERCA and other international societies were implemented. The structured report for the applicant but also for the expert was also implemented. By the end of this period the platform was opened for testing by ENERCA partners.

In addition, the Quarking application was implemented in telemedicine platform for its direct access to the cases through smartphones just by scanning the QR code. This application encrypts your passwords but allows you an easy management of them in a secure way by your mobile phone.

The telemedicine platform was opened to the public since May 2016 for the telemedicine module and since September 2016 for tele-expertise module.

It is accessible through a dedicated section in ENERCA website.
WP 7 – NETWORKING SUSTAINABILITY

WP LEADER: UPV/EHV

Associated partners: IDIBAPS, HCPB, CHUM, ERASME, UMCU, IRCCS and TIF

Link to:

Objective 4- To promote the recognition of centres of expertise at national level and ENERCA as the ERN on RAs.

Objective 6- To assure the project’s sustainability in the future

This WP activities are focussed in a) the promotion of the recognition of the ERN Expert Centres by Member States (MS) and the analysis of the impact of the entry into force of the Directive 2011/24/EU on the application of patient’s rights in cross-border healthcare and b) eENERCA sustainability

eENERCA Legal studies

Legal studies were performed by partner UPV/EHV:

- Prof Carlos Romeo
- Prof Pilar Nicolás
- Dr Emilio Armanza
- Dr Andrea Peris

The first legal study aimed to identify the state of the art of national regulations and policies for identification of centres of expertise in the field of Rare and congenital anaemias. For this, 3 persons in each selected country (Spain, France, The Netherlands, Luxemburg, Italy, Belgium, Cyprus, UK, Poland and Germany) were identified as representative persons.

A survey was conducted by a questionnaire with the key questions to be addressed to the 3 persons selected in each country in order to identify the national regulations and policies for the identification of reference centres.

A report about results and conclusions regarding the state of art of the national regulations and policies with regard to the identification, authorisation or recognition of Reference Centres in the field of Rare and Congenital Anaemias was prepared.

The second legal study was focussed on the analysis of the impact of the entry into force of the Directive 2011/24/EU on the application of patient’s rights in cross-border healthcare.

Legal National experts of ten Member states with experience in medical law were indentified. Experts were contacted and agreed to with the project through the preparation of a report about the impact of the Directive 2011/24/EU in their respective country and legal frameworks.

A questionnaire (list of items for the national legal reports) was prepared in agreement with the Executive Committee members and sent to the national legal experts previously identified. Nine out of ten reports were received for their analysis.
Report on Directive 2011/24/EU application analysis was elaborated for the comparative analysis taking into account the nine national reports received.


The analysis is based on the national reports written by the following legal experts:

- Belgium: Herman Nys, Centre for Biomedical Ethics and Law, Leuven
- Cyprus: Aristoteles Constantinides, University of Cyprus / Savvas Meliniotis, LLB (Cyprus).
- France: Emmanuelle Rial-Sebbag, INSERM Unit 1027, Toulouse
- Germany: Jürgen Simon, Leuphana University, Lüneburg / Jürgen Robienki, Centre for Ethics and Law in the Life Sciences, Hannover
- Italy: Lucia Busatta, University of Trento - University of Padova
- Poland: Miroslaw Nesterowicz / Natalia Karczewska-Kaminska, Uniwersytet Mikołaja Kopernika w Toruniu
- Spain: Fernando Fonseca Ferrandis, Carlos III University, Madrid
- The Netherlands: André de Exter, Erasmus University, Rotterdam
- United Kingdom: Annie Sorbie / Murray Earle, University of Edinburgh.

The questionnaire deals with the following aspects concerning the Directive and its implementation within each legal framework:

1. Description of the National Legal System (centralized or not centralized –Regions, Länders, Autonomous Communities...–; relations between public and private sectors, etc.). Description of the health services system (legal provisions about health services, rights of the citizens, rights of foreigners, etc...). Special reference to Rare Diseases.

2. Description of the legal instrument of transposition. Nature of the legal instrument, structure and general content.

3. Progress in the regulation and implementation in relation with articles 4.2.a, 5.b and 6a of the Directive (National Contact Points. Special reference to Rare Diseases). Progress and implementation in relation with article 4.2.b of the Directive (Information provided by healthcare providers. Special reference to Rare Diseases).

4. Professional liability and complaints procedure (article 4.2.c) Development of specific provisions?

5. Progress in the regulation of the impact in patient’s rights to health data protection (article 4.2.e). Development of specific provisions?

6. Progress in the regulation and implementation of e-health systems. Progress in the regulation and implementation of electronic clinical records. Progress in the regulation and implementation of the electronic pharmaceutical prescription and on the recognition of prescriptions issued in another Member State (articles 11 and 14)

7. Development of provisions regarding the reimbursement of the cost of treatments and the need of prior authorization (articles 7, 8 and 9).

8. Impact in the regulation concerning European reference networks between healthcare providers and centres of expertise (article 12). Related to this issue,
please take also into account the previous conclusions attached about the state of
the art regarding national regulations and policies with regard to the identification,
authorization or recognition of national reference centers in the field of rare and
congenital anaemias.

9. Progress in the instruments for the cooperation in the development of diagnosis
and treatment capacity in relation to rare diseases (article 13)


The structure of this document corresponds to the questionnaire prepared by the WP7.
Each paragraph deals with each specific question, providing the main content of the
national reports and our comparative analysis, as well as general conclusions.

The results of this research, as well as the full text of the national reports and the
comparative analysis, have been published in a eEnerca Special Issue of the Law and the
Human Genome Review, No. 44/2016 (January-June), one of the most important
Academic Journals in the field of Biolaw, was edited and published in Spanish and English
by the Inter-University Chair in Law and the Human Genome (University of Deusto /
University of the Basque Country, Bilbao, Spain)

eENERCA sustainability

eENERCA sustainability is based on the recognition of CoE at the national level as nodes
of the future ERN in Rare Anaemias.

Accordingly, the ENERCA Recommendations on CoE in Rare Anaemias: A whitebook, has
been disseminated among key national authorities representatives.

The on-line version of the WhiteBook was presented through an official letter sent by e-
mail to the Board of MS representatives for the establishment of the ERNs. With this
letter, a face to face meeting with ENERCA national experts representatives was
requested to be considered, in order to present the White Book physically as well as
ENERCA project main outcomes. The official letter and national ENERCA experts were
sent to National authorities representatives of Belgium, Bulgaria, Croatia, Cyprus, France,
Ireland, Italy, Portugal, Spain and United Kingdom.

In addition it was presented at the Meeting with WHO Human genetics programme at
WHO HQ in Geneva (17-18 February 2016)

Patricia Aguilar Martinez (WP5) was invited by the head of the WHO department in
charge of the Human Genetics programme (Dr Edward Kelley) to present the ENERCA
project main outcomes, including the e-ENERCA White Book. In addition, a hard copy
of the White Book was given to the director of the department.

In 2014 the European Commission released two documents regulating the
implementation of the European Reference Networks:

   i. COMMISSION DELEGATED DECISION of 10 March 2014 setting out
criteria and conditions that European Reference Networks and healthcare
providers wishing to join a European Reference.

   ii. COMMISSION IMPLEMENTING DECISION of 10 March 2014 setting
out criteria for establishing and evaluating European Reference Networks and their
Members and for facilitating the exchange of information and expertise on
establishing and evaluating such Networks

At that moment, it is clear for ENERCA Consortium that the best option for ensuring the
long term network sustainability is to prepare a solid application for the recognition of
ENERCA as ERN.
Accordingly, since preparation of the ERN call application was not foreseen by the time of e-ENERCA first application, it was been agreed by the ENERCA Consortium to prioritize the allocation of efforts in tasks aiming to success with the preparation of the proposal for the recognition as ERN. This included:

1. Identification of centers to be included in the ERN
2. Check eligibility criteria established in each MS
3. Study of the main documents published by the EC on the topic
4. Preparation and submission of the proposal

ENERCA aimed to promote geographical expansion in order to cover as many European countries as possible. This is a main consideration in the dynamic and long term evolution of the ERN and this will increase its European added-value. The ENERCA WhiteBook developed in the ENERCA 3 project was designed as a dynamic tool that can be evaluated and adapted according to the new needs and stakeholders’ expectations.

Based on ENERCA Recommendations a discussion was opened within ENERCA members for the establishment of quantitative indicators for evaluating centres fulfilment with criteria to be recognized as Centres of Expertise.

Centres willing to be recognized as European centres of expertise in rare anaemias were evaluated through these indicators.

**WP1- COORDINATION OF THE PROJECT**

**WP LEADER: IDIBAPS, HCPB**

Associated Partners ERASME, UMCU, CHUM, UPV/EHU, UKNEQAS, TIF, UCY, ESH, CING, KCL and IRCCS

The general objective of the Coordination was to establish a management steering programme for the efficient overall coordination of the Project based on a continuous surveillance of all the programmed framework processes necessary for fulfilling Project’s outcomes and specific objectives.

Specific objectives:

- To ensure the effectiveness of Project’s management.
- To facilitate the interaction with EU Commission officers.
- To monitor on-going activities
- To assess that deliverables are submitted on time and under the established standards of quality.
- To ensure the communication flow between partners.
- To promote co-operation between the partners involved in and between WPs
- To complete the project deliverables within the required time
- To solve any problems that may come up during the project’s completion both technical and financial

Project Coordination methodology refers to all aspects concerning the WPs tasks management, quality assurance and assessment of their interactivity, progress and final results. The coordination methodology should assure a full involvement of all participating partners in the programmed tasks, in the collection of data and in the continuous feedback of ideas and needs. This is strictly necessary for guarantee the
compliance with the work plan and the achievement of Project’s objectives and outcomes.

A Consortium Agreement (CA) was prepared at the beginning of the project in collaboration with the European and International Projects Unit of IDIBAPS. The model used for the preparation of this agreement was from DESCA “The simplified FP7 model Consortium Agreement”- March 2011. The purpose of this agreement was to specify with the respect to the Project the relationship among beneficiaries. It was sent to all beneficiaries for agreement and for their signatures. Hard original copies were also sent to all beneficiaries.

**WP2 - DISSEMINATION OF THE PROJECT**

**WP LEADER : IDIBAPS, HCPB**

Associated Partners: CHUM, CING, ERASME, ESH, IRRCS, KCL, TIF, UCY, UKNEQAS, UMCU and UPV

All collaborating partners

*Link to Objective 6 - To assure the project’s sustainability in the future*

Dissemination has been one of the ENERCA key transversal activities, becoming a priority for the whole consortium in order to increase the outreach of the outcomes achieved.

The dissemination of the Project and its sustainability requires permanent contacts between ENERCA Consortium and different stakeholders including National health Providers and authorities, legal and ethical authorities, health professionals and the scientific community, patients with RAs, Patient’s Associations, pharmaceutical industry and public.

The main objective is to create a critical mass of interests necessary for the upgrading of services provided by the experts and expert centres included in the ERN on RAs and assuring Project’s sustainability. Specific objectives:

- To disseminate knowledge and improve the awareness on RAs.
- To facilitate the translation of science from basic and non-clinical research to the clinical practice
- To facilitate the access to the same high quality health care for patients with RAs, independently from the MS where they are from.
- To disseminate ENERCA website and its services.

Project dissemination include all the activities aiming to expand the knowledge of ENERCA project, its website [www.enerca.org](http://www.enerca.org), and its activities and services in order to get the necessary critical mass to make the project fully successful and assure its sustainability.

**Dissemination material**

**ENERCA Leaflet**

The edition of a detailed leaflet about e-ENERCA and the previous editions of the ENERCA project were necessary to contextualize a long term effort that was consolidating an endurable network across Europe. During the first months of the project the ENERCA Leaflet was edited with an appealing design and printed.
Objective: to disseminate the project in a general way and explain the results of over 10 years of work. The leaflet is useful in a first contact but also when a detailed presentation is required. This material offered a professional and attractive look and a glimpse of the project complexity and history.

Contents: 8 pages, edited in English, with general information of the ongoing project and a summary of the achievements of the previous phases of ENERCA. It also included a map with the entire consortium details and explanation about the ENERCA White Book. It also offered a deep explanation about the three pillars of e-ENERCA: Telemedicine, e-Registry and e-Learning. The EC logo (Co funded by the health programme of the European Union) was included in the back cover.

Structure: Project Background; Objectives and outcomes; Network members and distribution; Details about the White Book; WP description with their respective deliverables; Dissemination strategy.

- Publication of the leaflet in the website
  The e-ENERCA Leaflet was uploaded to the website to be used as an element to explain ENERCA to the world. The document was shared online both through a news item (both for the website and the Newsletter) and through the About ENERCA section.

- Distribution of the leaflet among partners and stakeholders
  500 hardcopies of ENERCA Leaflet were printed and distributed among the members of the Executive Committee and the entire consortium and it is also distributed in Congresses and other third parties.

ENERCA website flyer

- Design of the flyer structure and content
  Objectives: The ENERCA flyer was a brief and direct interpellation to readers to visit the ENERCA website. It introduced the e-platforms and services that are endorsed on the ENERCA website. It was edited in English at the beginning and translated into Spanish and Catalan in the second year of the project.

Contents: The messages were especially directed to health professionals and patients, encouraging them to use the ENERCA web services to learn about rare anaemias and receive support in their management. The EC logo (Co funded by the health programme of the European Union) was also included in both front and back cover.

Structure: The format of the flyer was small in order to make it easy to transport it to congresses and meetings involving people related with rare anaemias from different perspectives. It contained short direct messages for different target audiences, both patients and health professionals oriented services. All was combined with an appealing graphic design.

- Publication of the flyer in the website
  The flyer were also available through the ENERCA website, both as a news item and at the About ENERCA section. The translations were available on the intranet.

- Distribution of the leaflet among partners and stakeholders
5000 English website flyers and 1000 translated flyers were printed and distributed with the Executive Committee members and also distributed in Congresses and third parties.

Other dissemination material

- ENERCA poster and power point presentation

A DINA0 Poster and a PPT presentation were created at the beginning of the project in order to explain the objectives and solutions proposed by ENERCA. The new materials were not just an update of previous ones, they were developed from the scratch to present the new challenges faced by ENERCA in e-ENERCA. EC logo was displayed in both materials.

ENERCA Poster: The Poster offered a global view of the project at a glance. After introducing the challenge of rare diseases, it summarizes the objectives of the e-Learning, e-Registry and Telemedicine Platforms. It also underlined the importance of creating Excellence reference networks (ERNs) to facilitate improvements in access to diagnosis and delivery of high-quality, accessible and cost-effective healthcare in rare anaemias. The poster was displayed in a number of events.

ENERCA PPT: Presentation slides were constantly evolving depending on the audience or the subject of the meetings. Having an extensive reference presentation is useful in order to use the most relevant parts for a given audience in every talk where ENERCA is introduced. The e-ENERCA PPT was discussed and designed in collaboration with the ENERCA partners.

- ENERCA Logo

The ENERCA logotype was redesigned in order to express in a graphic way the evolution of the ENERCA project. The new logo illustrated with the first “e” and the new typo the high electronic component in the new phase of the project. There are 3 different versions of the logo with and without the ENERCA title and flag.
A new section dedicated to **Centres of Expertise and European Reference Networks** was drafted in the 2nd year of the project and launched in the 3rd period, including:

**Cross Border Health**

![Image of Centres of expertise and European Reference Networks](image)

- Health services throughout the European Union (EU) have to guarantee quality, security and equality for every EU citizen. Directive 2011/24/EU on patients' rights in cross-border healthcare is an important achievement of the patient empowerment policy of the European Commission (EC). Through this Directive, the EU requires EC and Member states to support the continued development of European reference networks (ERNs) between healthcare providers and the recognition of centres of expertise (CoE) at national level.
- First call for interest to establish a European Reference Network (ERN) has been launched by the European Commission last 16th March and will be opened until 21st June 2016.
- Based on more than 10 years of experience in networking through ENERCA, an application for the upcoming ERN in Rare Hematological diseases (ERN-RHD) is being developed led by its coordinator, Prof Joan Luis Vives Corrons. Network disease coverage will be expanded by including Rare Hematological diseases classified in category 6-8 disease thematic subnetworks coordinated under the umbrella of the ERN-RHD.

- **Recommendations for centers of expertise**
  - A dedicated section for ENERCA White book was created, including:
    - **Why?** a brief explanation of the reasons leading to create this on-line application
    - **Team**: The enerca team involved in this activity
    - **Discover the recommendations**: The PDF on the ENERCA recommendations is linked by sections and also available for downloading
    - **Map of centers**: centres accomplished with ENERCA recommendations will be listed by country in an interactive map of Member states. The on-line application including the set of quantitative indicators will be programmed beyond the final date of the project.
Legal analysis

The documents elaborated by partner UPV on legal analysis of European Directive in cross border health were published here, including:

a) Patients’ rights within the Cross-border healthcare
b) General legislation on patients’ rights
c) Legislation on patients’ rights within the Cross-border healthcare
d) eENERCA reports
e) Links of interest
Disseminate the ENERCA project progress and results

The presence in mass media is important in order to inform patients, experts and the rest of stakeholders related with rare anaemias about the existence of ENERCA and the services it offers. It is also an excellent way to report society about how public funding is being invested.

A press release was sent to international media short after the kick off of the e-ENERCA project, the fourth phase of the ENERCA project. All partners were invited to share the press release with local media. Access the press release:


In order to increase the global audience of the 5th symposium in rare anaemias held in Ferrara (November 2013) a press release was sent to the Italian Mass Media. The Italian TV “RAI TV” was in the event to film and have an interview with the president of UNITED ONLUS. The TV Rai showed it in their night newscast. The press release sent to the Mass Media is included in the Symposium report (See WP2 – Annex 3 – Report on 5th Symposium in Rare anaemias)

In addition, some of the main activities developed by ENERCA in order to disseminate progress and results have been the following:

- ENERCA publishes a report in the new "Journal of Rare Disorders: Diagnosis and Therapy"
- The new ENERCA e-Health Services were presented in the 4th Pan European Conference on Haemoglobinopathies & Rare Anaemias
- Prof. Joan Lluis Vives Corrons approaches Anaemias to population and presents ENERCA features in Catalan TV
ENERCA Newsletter every 4 months

During the last years, ENERCA has disseminated among subscribers up to date information about the main project news and achievements through ENERCA newsletters.

Due to the high density of news publications and in an effort to keep the subscribers informed with the latest progress in the field of rare anaemias, the frequency of sending the newsletter was increased from every 4 months to every 3 three months in the second period of the project.

MailChimp, the tool used for the management of the Newsletter, was incorporated at the end of the first period and has been maintained until the end of the project.

The Activities section of the website offers a list of all the published newsletters and offers visitors the opportunity to subscribe to the ENERCA Newsletter. The Newsletters sent during the project are:

- Number 7 (December 2013)
- Number 8 (April 2014)
- Number 9 (July 2014)
- Number 10 (November 2014)
- Number 11 (January 2015)
- Number 12 (April 2015)
- Number 13 (July 2015)
- Number 14 (November 2015)
- Number 15 (February 2016)
- Number 16 (May 2016)
- Number 17 (August 2016)
eENERCA MAJOR RESULTS AND KEY FINDINGS

The major results of eENERCA project are:

The development of the three platforms accessible through ENERCA website

- The development of the three platforms accessible through ENERCA website

The structure of the platforms section was harmonized, including for each platform the following subsections:

- Why a platform? Where the reasons for its development, the objectives and benefits for the user are fully explained

**eRegistry**

**Why a eRegistry?**

- There is insufficient implementation of comprehensive data collection and analysis systems for rare diseases. Given that more prevalent, as haematological diseases, which are today the most common genetic disorder in Europe, there are poor data on their precise prevalence, overall burden and trends.
- Inventory of expert centres and epidemiological figures will provide eNERCA with comparable data at EU level allowing the promotion of specific actions for primary prevention of rare anomalies in such European countries where its prevalence might be higher than expected from previous estimations.

**Our Objectives**

- Study of the requirements and EU standards and directives for electronic health records.
- Create a pan-European interoperable electronic Registry.
- Raw anomalies and other epidemiological health records ensuring interoperability and patient-centric philosophy.
- Develop an interoperable, extensible and functional model of a database which will enable sharing of certified medical data from the available sources.

**Your benefits**

- Set up your own electronic registry of patients, following the EC requirement for centres of expertise, by downloading the application and adapting it to your needs.
- Share your information in a harmonized way with your colleagues and other experts in Europe.
- Contribute to the European
- Working Team: ENERCA partners involved for their creation, including the links to their personal profiles

### e-Learning

**Working Team e-Learning**

The e-Learning platform, developed in working package 5 of the e-ENERCA project, is led by the Hospital Universitario de Montpellier and coordinated by Patricia Aguilar-Martinez.

### Legal and ethical considerations: legal documents that are related to each platform are available for downloading in this subsection.

### Telemedicine

### Legal and ethical considerations

- Telemedicine is defined as the provision of healthcare services, through the use of information and communications technology (ICT), in situations where the two health professionals or the health professional and the patient are not in the same location.
- The e-ENERCA Telemedicine platform is dedicated to health professionals for sharing complex cases facilitating their diagnosis. Since it is open to public in its first stage, patients can also use it under their own responsibility. This platform has to assure the 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.

### Contact link

- Go to the platform: Direct access for the platform.
A platform for generating electronic health records for patients with RA has been developed - ENERCA eRegistry. The system has been presented in European Forums and a scientific paper has been published on it. It is available through ENERCA website.

It contains six modules:

- Module 1: Patient consent, demographics and diagnosis
- Module 2: Clinical Findings of Thalassaemia and Severe Anemias (not obligatory)
- Module 3: Clinical findings of Sickle Cell Disease (not obligatory)
- Module 4: Patient reported outcomes
- Module 5: Statistical package
- Module 6: Aggregate data

Interoperability has been assured in the software development. In order to be flexible to the different national rules, potential users, have two options in use the software. The first one is to install the system on a private server and use it as in house web accessible software. If this option is selected, the user is kindly asked to provide an annual report regarding the statistical data resulting from the anonymous input data. The second option is to use the platform available on-line. Informed consent form patient is then required. The implementation of EHR at the European level for specific diseases will be done beyond the end of the project.

In the frame of the development of the eRegistry, a tutorial for patients has been developed. Registries benefits are not only directed healthcare providers, but also to patients since they can become an essential tool to provide with valuable sources of information on their disease. A couple of simple interactive scenarios based tutorials for demonstration purposes have been created with the objective of guiding patients users in the exploration of useful medical information about thalassemia alpha and beta. The specific scenarios are adapted for young audiences who are most difficult to inform about the disease. Tutorial for patients is available through ENERCA website – Know Celli!
The e-learning platform was created and made it free available through ENERCA website. All participants to training courses 1 and 2, organized in 2015 and 2016 were invited to log in in the platform to complement their training. In addition, participants to previous ENERCA training courses (Brussels 2011, Paris 2012, Barcelona 2015) from more than 20 different countries, including Southern, Western, Northern and Eastern Europe areas, were also informed of the existence of the eLearning platform through the large ENERCA and ESH e-mailing lists. Currently, 124 students have been registered to the e-Learning platform to the 4th available Modules:

Through the administrator section, tutors can access to some statistics on the courses and participants, eg Progression of learners or the most popular courses within the module.

- Telemedicine platform for remote diagnosis of complex cases - Telemedicine

The Telemedicine platform has been created and made available through ENERCA website. Therefore, objective has been reached. The first step of the platform is publicly open to both patients and health professionals. All data provided is anonym and a code is generated by the platform to be able of tracking the case. A diagnostic orientation is given to the applicant. This is automatically done by the system based on algorithms running in the background of the website according to the decision trees generated by the experts. The second part of the platform is a tele-expertise platform for sharing of data among experts in a secure way. It also allows the sharing of PDFs and images. A report is generated with expert opinion and links to ENERCA documents and website contents.
Two on-site training courses have been organized:

- **ESH-ENERCA Training Course on Haemoglobin Disorders: Laboratory diagnosis and clinical management** - webcasting of the presentations also available
  Barcelona, Spain. 23-24 January 2015
  It was attended by 160 participants from 36 different countries.

- **ESH-ENERCA course on Diagnosis and Management of Very Red Cell and Iron Disorders** - webcasting of the presentations also available
  Lisbon, Portugal. 29-30 January 2016
  It was attended by 150 participants from 29 different countries

Outcome of the courses are assessed by Evaluation sheets distributed to all participants. Most talks were rated +1 (very good) or +2 (outstanding). 90% of participants replied that the course met their learning objectives giving a positive or very positive global evaluation of the course. They particularly appreciated the programme of the course and
scientific level of the presentation, the clinical cases with voting boxes and the clinical discussions.

In addition, webcasting of the presentations are available through ENERCA and ESH website allowing those interested professionals or students not able to attend the courses benefit from them. Regarding course one in haemoglobin disorders, from January 2015 to September 2016, 245 users benefited from the webcasting, 200 visited the website and spent 36 minutes in average, 498 presentations and 13841 slides were viewed. In addition, 45 accessed the contents through smart phones and/or tablets, they spent 24 minutes in average and 105 presentations and 2325 slides were viewed.

Regarding course two in very rare red cell and iron disorders, from January to September 2016, 135 users benefited from the webcasting, 100 visited the website and spent 43 minutes in average, 241 presentations and 7178 slides were viewed. In addition, 35
accessed the contents through smart phones and/or tablets, they spent 31 minutes in average and 85 presentations and 2030 slides were viewed.
Two European Symposia have been organized:

- **5th European Symposium on Rare Anaemias - 1st Italian Thalassaemia Meeting for Patients and Health Professionals** – Slide presentations available
  Ferrara, Italy. 15-16 November 2013
  It was attended by 180 participants, 72 Patients and 102 Health Professionals

- **6th European Symposium on Rare Anaemias - 1st Dutch-Belgian Meeting for Patients and Health Professionals** – Slide presentations available
  Amsterdam, The Netherlands. 21-22 November 2015
  It was attended by 176 participants, 86 Patients and 90 Health Professionals

Slide presentations for both Symposia were made available through ENERCA website to interested professionals and patients not able to attend.

Legal studies regarding national rules for recognition of Centres of Expertise and Impact of the Directive 2011/24/EU in nine MS (Italy, Cyprus, the Netherlands, Spain, Poland, Belgium, France, Germany and United Kingdom).

- **Report on the state of the art of national regulations and policies for Reference Centres in Rare and Congenital Anaemias**


  - The results of this research, as well as the full text of the national reports and the comparative analysis, have been published in a eEnerca Special Issue of the Law and the Human Genome Review, No. 44/2016 (January-June), one of the most important Academic Journals in the field of Biolaw, was edited and published in Spanish and English by the Inter-University Chair in Law and the Human Genome (University of Deusto / University of the Basque Country, Bilbao, Spain). *Hard copy enclosed to this Final Report*

Based on ENERCA recommendations for CoE in RA: A whiteBook, a set of quantitative and qualitative indicators was established. Accordingly, forty-seven centres from 13 MS (Belgium, Cyprus, Czech Republic, Germany, Spain, France, Ireland, Italy, Lithuania, The Netherlands, Portugal, Sweden and United Kingdom) have been recognized by ENERCA as centres of expertise in Rare Anaemias after an assessment process based on the set of indicators.

<table>
<thead>
<tr>
<th>Centre of Expertise in Rare Anaemias recognized by ENERCA (profiles linked)</th>
<th>Country</th>
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</thead>
<tbody>
<tr>
<td>CHU of Liège</td>
<td>BE</td>
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<tr>
<td>Cliniques Universitaires de Bruxelles - Hospital Erasme</td>
<td>BE</td>
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<tr>
<td>Archbishop Makarios III Hospital</td>
<td>CY</td>
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<tr>
<td>Department of Internal Medicine, Hematology and Oncology, University Hospital Brno</td>
<td>CZ</td>
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<tr>
<td>Charité - Universitätsmedizin Berlin</td>
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<tr>
<td>Hospital Universitari Vall d’Hebron</td>
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<td>AP-HP Hôpital Trousseau</td>
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<td>Assistance Publique - Hôpitaux de Marseille</td>
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<tr>
<td>Assistance Publique – Hôpitaux de Paris , HENRI MONDOR Hospital</td>
<td>FR</td>
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<tr>
<td>Hospital Name</td>
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<tr>
<td>Assistance Publique - Hôpitaux de Paris / Hôpital Universitaire Necker Enfants Malades</td>
<td>FR</td>
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<tr>
<td>Assistance publique-Hôpitaux de Paris_Hôpitaux de Saint Louis-Lariboisère-Fernand Widal</td>
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<tr>
<td>Centre Hospitalier Régional et Universitaire de Lille</td>
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<tr>
<td>Montpellier University Hospital (CHU de Montpellier)</td>
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<td>Rennes University Hospital (CHU Rennes)</td>
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<tr>
<td>University Hospital of Pointe-à-Pitre/Abymes (CHU de Pointe-à-Pitre/Abymes or CHUPPA)</td>
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<tr>
<td>Our Lady's Children's Hospital</td>
<td>IE</td>
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<td>ASST Ospedale Papa Giovanni XXIII</td>
<td>IT</td>
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<tr>
<td>Azienda Ospedaliera Ospedali Riuniti Villa Sofia-Cervello Palermo</td>
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<td>Azienda Ospedaliera Università di Padova</td>
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<td>Azienda Ospedaliera Universitaria di Modena</td>
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<td>Azienda Ospedaliera Universitaria Federico II</td>
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<tr>
<td>Azienda Ospedaliera Universitaria/Second University of Naples (AOU/SUN) Pediatria ad indirizzo emato-oncologico</td>
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<tr>
<td>Azienda Ospedaliero Universitaria Careggi (Florence)</td>
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<tr>
<td>Center for Hemoglobinopathies and Iron Disorders - San Luigi Gonzaga University Hospital</td>
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<tr>
<td>Department of Medicine, University of Verona</td>
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<td>E.O. Ospedali Galliera</td>
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<td>Fondazione IRCCS CA’Granda Ospedale Maggiore Policlinico di Milano</td>
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<td>Fondazione Policlinico Universitario A. Gemelli</td>
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<td>Fondazione Toscana Gabriele Monasterio per la ricerca medica e de sanità pubblica</td>
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<td>Istituto Giannina Gaslini</td>
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<td>San Gerardo Hospital - Monza</td>
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<td>University Hospital of Bari - Azienda Ospedaliero-Universitaria Consorziale di Bari &quot;Policlinico-Giovanni XXIII&quot;</td>
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<td>Vilnius University Hospital Santariskiu Klinikos (Lithuania)</td>
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<td>Academic Medical Center -University of Amsterdam</td>
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<td>Erasmus University Medical Center</td>
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<td>Radboud university medical center</td>
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<tr>
<td>University Medical Center Utrecht</td>
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<tr>
<td>Centro Hospitalar do Porto - Hospital de San Antônio</td>
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<td>Centro Hospitalar e Universitário de Coimbra</td>
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<td>Karolinska University Hospital</td>
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<td>UK</td>
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<td>Guy’s and St Thomas’ NHS Foundation Trust</td>
<td>UK</td>
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<tr>
<td>Imperial College Healthcare NHS Trust (ICHNT)</td>
<td>UK</td>
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<tr>
<td>Oxford University Hospitals NHS Foundation Trust</td>
<td>UK</td>
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</tbody>
</table>
Quantitative data on number of patients per year followed-up, number of new patients per year, number of several procedures per year, clinical outcomes indicators and qualitative data on services available have been collected for all these centres in the evaluation process. This gives us the basis for mapping of services and allocation of resources at the European and national level allowing us to establish cross border referral systems for patients and samples. Information is currently being processed in electronic records for its analysis and production of epidemiological figures and publication beyond the end date of the project.

These centres have been included in EuroBloodNet, the proposal submitted to the EC call for ERNs as a result of a joint effort from ENERCA and the European Hematology Association. EuroBloodNet encompasses both malignant and non-malignant rare haematological disorders. Two main hubs of coordination have been established, and network coordinator will rotate in equal periods of time. Prof Béatrice Gulbis, member of the Executive committee of ENERCA since 2002, has been appointed as coordinator for non-malignant hub and EuroBloodNet coordinator for the second period of time. This governance and coordination structure will ensure visibility of non-malignant disorders, distributed in four subnetworks, three of them covered by ENERCA, plus bleeding disorders, covered by EUHANET, the pilot network for Haemophilia and bleeding disorders.

A dedicated section for cross border health was created in ENERCA website, including a section for relevant legal documents for recognition of CoE and establishment of ERNs, as well as legal reports generated through the eENERCA, and a section for disseminating the ENERCA Recommendations for CoE in RA.

ENERCA Website, www.enerca.org, constitutes by itself a major result, since it is the main tool for project and results dissemination. It can be considered by itself an eHealth service for ENERCA, since the disease centered on-line tool for centres and experts nourish a European inventory publicly accessible that allows search by disease and/or country. Currently, 255 health professionals from 179 centres, 150 from European countries and 29 non-European, have created their own profile in ENERCA website.

All these centres have linked their expertise with the RA tackled, age coverage; pediatrics and/or adulthood, diagnostic o clinical services offered and preventive programs.

Activities and results obtained through eENERCA have been disseminated among them by the creation of periodically Newsletter.

For eENERCA project and website dissemination, two leaflets; a brochure and a flyer, were produced and disseminated among educational and scientific events. They are also available at ENERCA website. Hard copies enclosed to this report.
Publications as result of the project:

- **Title:** “Enerca: The European Network for Patients with Rare Anaemias”  
  Authors: Vives Corrons J.L., Mañú Pereira M.M.  
  Journal: J Rare Dis Diagn Ther. 2015; 1:9  

- **Title:** “EuroBloodNet: From Rare Anaemias to Rare Haematological Diseases, a Proposal for European Reference Network (ERN)”. Editorial  
  Authors: “Vives Corrons J.L.”  

- **Title:** “eHealth Services for the European Reference Network on Rare Anaemias (eENERCA)”.  
  Authors: Antoniou Z, Schiza EC, Neokleous K, Angastiniotis M, Pattichis CS, Schizas CN.
Title: Haemoglobinopathies in Europe: health & migration policy perspectives.

“Law and the Human Genome Review No. 44” January-June 2016

Hard copies enclosed in this report
Discussion in relation to project objectives

The general objective of e-ENERCA was to provide professionals and patients with e-Health tools to assure the same level of RA services across Europe, independently from the country of practise and the origin of the patient. e-ENERCA also aimed to promote the recognition of Centres of expertise by the national health authorities necessary for its promotion and its recognition as a European Reference Network (ERN) on RA. e-ENERCA also aimed to assess the implementation of the new Directive 2011/24/EU.

We can say that we have reach the general objective of e-ENERCA project since although it has not been easy the three platforms foreseen for eRegistry, Telemedicine and eLearning have been developed and implemented in ENERCA website. We would have prefer having more time for further exploitation of the platforms however the three of them were delivered later than expected, but in any case the platforms are in place, they have been tested by partners and also opened to the public and they will be further promoted in the coming years. Regarding the promotion of the recognition of centres of expertise and analysis of the legal analysis issues arisen by the platforms implementation and the analysis of the implementation of the Directive 2011/24/EU, ENERCA has play a key role at the European level by establishing objective criteria based on quantitative indicators for the assessment of centres and by the creation of several legal reports, also applicable for other rare diseases, analyzing the impact of the establishment of ERNs and CoE in different MS.

Finally, we consider we have reached the objective of ensuring network sustainability, since a proposal has been submitted to the EC call for ERNs as a result of a joint effort from ENERCA and the European Hematology Association. The proposal is called, EuroBloodNet, and it encompasses both malignant and non-malignant rare haematological disorders. Two main hubs of coordination have been established, and network coordinator will rotate in equal periods of time. Prof Béatrice Gulbis, member of the Executive committee of ENERCA since 2002, has been appointed as coordinator for non-malignant hub and EuroBloodNet coordinator for the second period of time. This governance and coordination structure will ensure visibility of non-malignat disorders, distributed in four subnetworks, three of them covered by ENERCA, plus bleeding disorders, covered by EUHANET, the pilot network for Haemophilia and bleeding disorders.
TARGET GROUPS AND ADDED VALUE

Taking into account the main goals of e-ENERCA, the general target groups to whom these activities were addressed were mainly four:

- **Health professionals, non-experts in RA, and the scientific community:**
  General practitioners (GPs) and specialists in haematology, paediatrics, internal medicine, molecular biologists, genetic counsellors and nurses, Young haematologists or biologists in training. Scientific bodies and EQAS providers.
  - Health professionals non experts in RA can found in ENERCA website reliable and updated information about RA, Centres of expertise and experts, as well as scientific publications linked to the disease. This information can be filtered by disease and/or country in order to look for a centre offering a diagnosis for an specific RA. The last can be of interest also for EQAS providers in order to assess the development of new schemes.
  - Health professionals can be updated regarding news in the field of RA and upcoming educational and training events through ENERCA web News and agenda section and Newsletter
  - Health professionals non-experts in RA can increase their professional skills and promote their professional profile fulfilling the requirements established in the European haematology curriculum/passport by learning the state of the art knowledge on rare anaemias through attending the on-site training courses and/or registering to the eLearning platform.
  - Health professionals non-experts benefit from telemedicine platform by getting diagnosis flowcharts for simple cases and expert advice for the complex. Health professionals are able to share complex cases easily and securely via Internet and increase their knowledge on rare anaemia diagnosis. If needed, they are contacted by a national expert who will present the case in a peer-to-peer expert group through the Telemedicine platform.

- **Health professionals experts in RA:** ENERCA current and former partners
  - Health professionals can be updated regarding news in the field of RA and upcoming educational and training events through ENERCA web News and agenda section and Newsletter
  - Experts in RA can also benefit from training courses on those areas where they do not work in their daily routine.
  - Experts can create their own electronic health records for patients affected by RA by downloading the software developed in the eRegistry platform or registering their patients on-line
  - Experts can share patients’ clinical data through the Telemedicine platform for solve diagnosis of complex cases

- **Patients’ associations:** Patients and their relatives, and patients’ associations
  - Patients can found in ENERCA website reliable and updated information about RA, Centres of expertise, experts and patients’ associations. This information can be filtered by disease and/or country in order to look for a specialist closer to home, or a existing patient association for the disease the patient is suffering from.
Patients can be updated regarding news in the field of RA and upcoming educational and training events through ENERCA web News and agenda section and Newsletter.

Patients benefit from attending the European symposium in RA by learning the state of the art knowledge on rare anaemias and getting in contact with experts in the field and other patients.

Patients can also increase their knowledge through the educational material publicly available in ENERCA website.

Patients benefit from telemedicine platform by getting diagnosis flowcharts and a report that can be given to their physician if expert advice is required.

**Health and Legal authorities:** MS National Ministries of Health and Legal Authorities, European Commission Authorities or related organizations (EUCERD and others).

- Health and Legal authorities benefit from the legal reports produced analysing the national regulations for recognition of centres of expertise and impact of the implementation of Directive 2011/12/EU on cross border health by learning from experiences in other countries and conclusions reported.
- Health and Legal authorities will found in ENERCA website a repository of relevant documents in the field as well as the documents produced by ENERCA and useful links.
- Health Authorities benefit from ENERCA recommendations on CoE and the set of qualitative and quantitative indicators established based on it as a tool for national recognition of CoE in RA and a model for other RD.

**European Networks for Rare Disease (ENRD):** Orphanet, Eurordis and other ERNs.

- ENRD benefit from ENERCA recommendations on CoE and the set of qualitative and quantitative indicators established based on it as a model for other RD.
- ENRD benefit from the legal analysis performed regarding regulations affecting legal and ethical issues raised during the development of eResgistry and Telemedicine platforms.