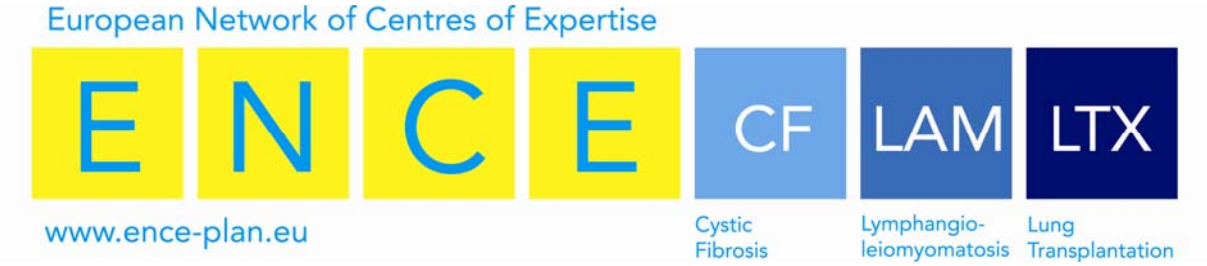

ENCE-CF-LAM-LTX

European Networks of Centres of Expertise for CF (Cystic Fibrosis), LAM (Lymphangioleiomyomatosis), and LTX (Lung Transplantation)

Grant Agreement No. 223355

Final Report

Submitted by the Project Coordinator
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European Network of Centres of Expertise

ENCE CF LAM LTX

www.ence-plan.eu

Cystic Fibrosis | Lymphangio-leiomyomatosis | Lung Transplantation

Final Report
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4.1 Final Publishable Summary Report

Executive Summary

Based on DG Research's "HEALTH-2007-3.4-1: Disease networks of centres of reference" call, the main goal of ENCE-CF-LAM-LTX has been to further the optimisation of the delivery of health care to European citizens by developing a general blueprint of how to implement quality management and guidelines for Rare Diseases and how to develop and build European Networks of Centres of Expertise for Rare Diseases. This was done by looking at three exemplary rare entities: cystic fibrosis (CF), pulmonary lymphangioleiomyomatosis (LAM), and lung transplantation (LTX).

An extensive mapping and analysis of available resources and structures, a thorough scoping exercise to design a framework of what such networks should look like, and a consensus process are crucial for developing the generally applicable requirements for building these networks. This was done separately for each of the project's three model entities. Out of these efforts, which were marked by the integration of the needs and expectations of all stakeholders on national and European levels (patients, doctors and other care team members, clinical researchers, health administration, health insurers), a set of elements for the formation of such European Networks of Centres of Expertise was determined for each entity. Among these elements are patient registries, clinical trials networks, the involvement of patient organizations, basic research, biobanking, etc. In a next step, these criteria were recorded in separate consensus statements for CF, LAM, and LTX, outlining the specific requirements for the formation of such networks for the respective entities.

While some of theses requirements differ or are more or less prominent in CF, LAM, and LTX (and, by extension, other Rare Diseases), there are also a few overarching elements that have to be considered regardless of the disorder one is dealing with. Correspondingly, the final step in the process consisted of filtering common denominators out of the three entity-specific blueprints and of subsequently developing from these a more general blueprint that is usable for the construction of networks of centres of expertise not only, for instance, for other rare lung disorders (e.g. Alveolar Proteinosis – an extremely rare disease with good treatment options only in the hands of those with some experience), but to many other Rare Diseases as well. Entitled "How to Build European Reference Networks (ERNs) for Rare Diseases – Elements, Considerations, and Materials" ("ENCE Elements" for short), this general blueprint is meant to be a guiding document for the design of networks of Centres of Expertise in Rare Diseases. It marks ENCE's major achievement and constitutes a significant contribution to Rare Disease care. The "ENCE Elements" are attached to this report.

Overall, then, ENCE-CF-LAM-LTX has translated the concept of clinical networks of expertise for Rare Diseases into an operational stepwise approach of analysing and then designing several distinct networks of expertise, only to arrive at general principles of construction of such networks that can be used as a blueprint for setting up European Centres of Expertise Networks for many Rare Diseases. The added value of such an endeavour is manifold. On the

one hand, the implementation of networks of expertise across Europe will allow for the integration of knowledge and experience beyond national borders and thus further the accumulation of knowledge among care team members by learning from the best. On the other hand, it will allow for a bundling and hence a much more efficient use of resources for patient care and clinical research. All of this will, of course, translate to the greatest benefit – a much improved level of care for the patient by raising the standards of care to the highest levels available throughout Europe.

Summary Description of Project Context and Objectives

Motivation

Rare Diseases (RD) have been one of the priorities in the EU Public Health Programmes since 2003. Among the main lines of action in this area have been:

- the exchange of information via European information networks on RD
- the development of strategies and mechanisms for information exchange and c-o-ordination between people affected by a rare disease, volunteers, and professionals at EU level to encourage continuity of work and trans-national co-operation
- the support of the exchange of best practice and developing measures for patient groups with special support to Eurordis
- the definition of relevant health indicators to develop comparable epidemiological data at the EU level
- the development of the concept of European Reference Networks of expert centres for RD

European Centres of Expertise Networks for Rare Diseases have been identified by the European Commission as one important area of future activity in the attempt to achieve one of the main objectives across the EC endeavour of optimising health care for European Citizens. It is obvious that especially in Rare Diseases the joined forces of the experts networking throughout Europe are more likely to meet the needs and expectations of patients than national services.

Approach

The construction and implementation of European Networks of Centres of Expertise (ENCE) calls for input from many different stakeholders: patients, doctors and other care team members, clinical researchers, health administration, and health insurers have to be heard to come to a model of such networks that can easily be used as a blueprint for most rare disorders. Networking in this European sense will make the best possible use of resources already existing and remaining in the responsibility of the individual member states by interfacing and complementing these present and future elements. This will help the health care system partners to learn from the best and improve the quality of care to the highest European level of expertise.

To achieve this goal, first a scoping exercise was performed to set the framework of how such European Networks of Centres of Expertise should be built, which structural requirements must be fulfilled, which procedures will be necessary to ensure and assess professional quality should be implemented, and how it will be possible to establish quality control and benchmarks for outcome across Europe. Parallel to this, a mapping exercise of existing networks and elements needed for such networking was carried out. This was done for three quite different rare entities – cystic fibrosis (CF), pulmonary lymphangioleiomyomatosis (LAM), and lung transplantation (LTX), all of which comply with the European Commission's definition of a rare disease.

Why CF?
Cystic fibrosis (CF) is the most common fatal autosomal recessive disease among Caucasian populations, with a frequency of 1 in 2000 to 3000 live births. There is a wide variety of national and European activities of the well-structured patient organisations and scientific societies concerning the development of European added value by means of patient advice and quality control, clinical trials networks, and patient registries. As such, while there is, of course, still room for development, CF serves as a good example of how networking can be used to further the standard of care for patients with Rare Diseases.

Why LAM?
Lymphangioleiomyomatosis (LAM) is an extremely rare disease, with a prevalence of sporadic LAM (S-LAM) roughly estimated to be approximately 3-5 per one million people. This will result in very small patient populations of less than 100 patients in most and less than 10 in the smaller member states – a circumstance that makes networking an absolute necessity, as clinical trials, for instance, are almost impossible to carry out without a European multi-centre design. So far, national attempts have been made to launch patient registries and work on international guidelines as well as coordination of national initiatives. It is very important to integrate these existing approaches, since a combined effort across member states is more suitable to satisfy the patients' needs than isolated national endeavours.

Why LTX?
Lung transplantation (LTX) is a well-established though very expensive and very demanding therapeutic option for end-stage lung disease patients, including CF and LAM patients. It is not available in all member states, and expertise is not on the highest level everywhere because the number of procedures per year ranges from one or less than ten to more than 50 and more. The procedure itself is not the only deliverable, but the continued and complicated postoperative immunosuppression and care is comparable to the care of chronic illnesses as far as efforts and cost are concerned. With 338 lung transplantations performed in 2006 according to Eurotransplant, this condition can be considered a very rare entity even though it is not a disease. It has been chosen to be included in this project as one model rare disorder because of the extensive need for cross-border referral and patient care.

From the information gathered during the mapping and scoping process outlined above, the areas of activity and a detailed set of construction elements for such European Networks in each of these three rare entities were developed.

Outcome

These construction elements (among them are patient registries, biobanks, and clinical trials networks, to name only a few), which are of varying significance for the different entities, will be brought together in a blueprint to be used for other rare pulmonary disorders. With this method of upscaling the set of criteria from (several) single diseases to groups of diseases and then further to the general situation in most Rare Diseases, basic principles and key features of European Centres of Expertise Networks for Rare Diseases can be arrived at. These criteria can then be used for certification, quality control, and funding of a European system of networks. By making sure that the process of development as outlined above is flanked and supported from the beginning by experts in other (common) pulmonary diseases, it is most likely that these principles can be of such a general nature that they might be applied to common diseases as well.

Networking in this European sense will make the best possible use of resources already existing and remaining in the responsibility of the individual member states by interfacing and complementing these present and future elements. This will help the health care system partners to learn from the best and improve the quality of care to the best European level of expertise.

Description of the Main S&T Foreground Results

Potential Impact (including socio-economic impact and wider societal implications of the project so far), Main Dissemination Activities and Exploitation of Results

Potential Impact

The European member states are in the process of defining the structure of better care for Rare Diseases by means of Centres of expertise and European Reference Networks. The ENCE blueprint has already made its way into this European way by being a constitutive element of the documents that have been used within EUCERD concerning these discussions. The pre-final version of the ENCE blueprint has been used and cited by the scientific secretariat of EUCERD for the semantic definitions and descriptions of different levels of Centres of Expertise and Reference networks. Such significant input into the European definitions of CoE and ERN best characterizes the possible impact of this supporting action.

Main Dissemination Activities

Dissemination activities included:

- A press release about ENCE to German media (as the project coordinator is located in Frankfurt, Germany) at the outset of the project

- The implementation of a project website, which, among other things, contains a newsletter feature informing subscribers about the latest project-related developments and events.
- A presentation on the benefits of ENCE for LAM in the context of the 1st European LAM Conference which took place in Udine, Italy, on October 1-3, 2010
- An abstract about ENCE submitted for inclusion in a booklet published by the European Commission/DG Research and listing FP7 public health research projects
- A project poster submitted to the European Commission/DG Research as per their request, to be used for exhibition at conferences
- An abstract about ENCE included in the EURORDIS Technology Marketplace online platform
- Furthermore, the ENCE blueprint as a pre-final version has been made available to the co-ordinating secretariat of EUCERD and via this route has made a significant contribution to the discussion in the Working group on Centres of Expertise as well as the EUCERD meeting in March 2011.

ENCE's main output, the Blueprint on how to build comprehensive Networks of Centres of Expertise for Rare (lung) Diseases, will be submitted for publication in a international peer review journal.

Exploitation of Results

ENCE's main output, the Blueprint on how to build comprehensive Networks of Centres of Expertise for Rare (lung) Diseases, will be made available to all interested stakeholders via EUCERD and other RD activities in Europe (Joint Action RD 2011-2014) and will be submitted for publication in a international peer review journal.

Address of the Project Public Website and Relevant Contact Information

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4.2 Use and Dissemination of Foreground

SECTION A (Public)

ENCE's main output, the Blueprint on how to build comprehensive Networks of Centres of Expertise for Rare (lung) Diseases, will be made available to all interested stakeholders via EUCERD and other RD activities in Europe (Joint Action RD 2011-2014) and will be submitted for publication in an international peer review journal.

TEMPLATE A2: LIST OF DISSEMINATION ACTIVITIES

No.	Type of activity	Main leader	Title	Date	Place	Type of audience	Size of audience	Countries addressed
1	Press Release	GUF	Frankfurt plant für Europa: Entwicklung von Netzwerken für Seltene Erkrankungen	25 May 2009	Frankfurt	Scientific Community, Civil Society	1 Mill.	Germany
2	Project Website	GUF	ence-plan.eu	22 Sep 2009	Online	All audiences		International
3	Publication	GUF	ENCE abstract in DG Research booklet on FP7 projects	7 Dec 2009	Brussels	Scientific Community, Civil Society, Policy Makers		European countries
4	Conference	UNOTT	1st European LAM Conference	01 Oct 2010	Udine, Italy	Scientific Community, Civil society, Industry, Policy Makers	150	International
5	Poster	GUF	ENCE CF-LAM-LTX	13 Aug 2010	Brussels	Scientific Community, Civil Society, Policy Makers		European countries
6	Publication	GUF	ENCE listing on CORDIS Technology Marketplace	1 Dec 2010	Online	All audiences		International

SECTION B

B1 – List of Applications for Patents, Trademarks, Registered Designs, etc.
Not applicable.

B2 – Exploitable Foreground
The European Member states are in the process of defining the structure of better care for Rare Diseases by means of Centres of expertise and European Reference Networks. The ENCE blueprint has already made its way into this European way by being a constitutive element of the documents that have been used within EUCERD concerning these discussions. The pre-final version of the ENCE blueprint has been used and cited by the scientific secretariat of EUCERD for the semantic definitions and descriptions of different levels of Centres of Expertise and Reference networks. Such significant input into the European definitions of CoE and ERN best characterizes the possible impact of this supporting action.

4.3 Report on Societal Implications

A. Ethics

1. Did your project undergo an Ethics Review (and/or Screening)? No
If Yes: have you described the progress of compliance with the relevant Ethics Review/Screening Requirements in the frame of the periodic/final reports? Not applicable

2. Please indicate whether your project involved any of the following issues :
RESEARCH ON HUMANS
Did the project involve children? No
Did the project involve patients? No
Did the project involve persons not able to consent? No
Did the project involve adult healthy volunteers? No
Did the project involve Human genetic material? No
Did the project involve Human biological samples? No
Did the project involve Human data collection? No

RESEARCH ON HUMAN EMBRYO/FOETUS
Did the project involve Human Embryos? No
Did the project involve Human Foetal Tissue/Cells? No
Did the project involve Human Embryonic Stem Cells (hESCs)? No
Did the project on human Embryonic Stem Cells involve cells in culture? No
Did the project on human Embryonic Stem Cells involve the derivation of cells from Embryos? No

PRIVACY
Did the project involve processing of genetic information or personal data (eg. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)? No
Did the project involve tracking the location or observation of people? No

RESEARCH ON ANIMALS
Did the project involve research on animals? No
Were those animals transgenic small laboratory animals? No
Were those animals transgenic farm animals? No
Were those animals cloned farm animals? No
Were those animals non-human primates? No

RESEARCH INVOLVING DEVELOPING COUNTRIES
Did the project involve the use of local resources (genetic, animal, plant etc)? No
Was the project of benefit to local community (capacity building, access to healthcare, education etc)? Not applicable

DUAL USE
Research having direct military use No
Research having potential for terrorist abuse No

B. Workforce Statistics

3. Workforce statistics for the project: Please indicate in the table below the number of people who worked on the project (on a headcount basis).

Type of Position	Number of Women	Number of Men
Scientific Coordinator	1	1
Work package leaders	1	5
Experienced researchers (i.e. PhD holders)		
PhD student	0	0
Other	5	0

4. How many additional researchers (in companies and universities) were recruited specifically for this project? 0
Of which, indicate the number of men: 0

C. Gender Aspects

5. Did you carry out specific Gender Equality Actions under the project? No
6. Which of the following actions did you carry out and how effective were they?
Design and implement an equal opportunity policy Not applicable
Set targets to achieve a gender balance in the workforce Not applicable
Organise conferences and workshops on gender Not applicable
Actions to improve work-life balance Not applicable
Other: Not applicable
7. Was there a gender dimension associated with the research content - i.e. wherever people were the focus of the research as, for example, consumers, users, patients or in trials, was the issue of gender considered and addressed? No
If yes, please specify. Not applicable

D. Synergies with Science Education

8. Did your project involve working with students and/or school pupils (e.g. open days, participation in science festivals and events, prizes/competitions or joint projects)? No

If yes, please specify: Not applicable
9. Did the project generate any science education material (e.g. kits, websites, explanatory booklets, DVDs)? No

E. Interdisciplinarity

10. Which disciplines are involved in your project?
Main discipline: 3. Medical Sciences
Associated discipline: 3.3 Health sciences (public health services, social medicine, hygiene, nursing, epidemiology)

F. Engaging with Civil Society and Policy Makers

11a. Did your project engage with societal actors beyond the research community? Yes
11b. If yes, did you engage with citizens (citizens' panels/juries) or organised civil society (NGOs, patients' groups etc.)? Yes, in co-operation with patient organizations; communicating/disseminating/using the results of the project
11c. In doing so, did your project involve actors whose role is mainly to organise the dialogue with citizens and organised civil society (e.g. professional mediator, communication company, science museums)? No
12. Did you engage with government/public bodies or policy makers (including international organisations) Yes, in having them take part in the consensus meetings; in communicating/disseminating/using the results of the project
13a. Will the project generate outputs (expertise or scientific advice) which could be used by policy makers? Yes - as a primary objective the consensus statement is a building plan for European Reference Networks which can be adopted by the European Committee of Experts for Rare Diseases (EUCERD)(please indicate areas below - multiple answer possible)
13b. If Yes, in which fields?
Public Health Yes
13c. If Yes, at which level? European level and in addition at local, regional, national, and international levels

G. Use and Dissemination

14. How many Articles were published/accepted for publication in peer-reviewed journals? 0
To how many of these is open access provided? 0
How many of these are published in open access journals? 0
How many of these are published in open repositories? 0
To how many of these is open access not provided? 0
Please check all applicable reasons for not providing open access:
- publisher's licensing agreement would not permit publishing in a repository No
- no suitable repository available No
- no suitable open access journal available No
- no funds available to publish in an open access journal No
- lack of time and resources No
- lack of information on open access No
- other: –
If other - please specify: Not applicable
15. How many new patent applications ('priority filings') have been made? ("Technologically unique": multiple applications for the same invention in different jurisdictions should be counted as just one application of grant). 0

16. Indicate how many of the following Intellectual Property Rights were applied for (give number in each box).
Trademark 0
Registered design 0
Other 0
17. How many spin-off companies were created / are planned as a direct result of the project? 0
Indicate the approximate number of additional jobs in these companies: 0
18. Please indicate whether your project has a potential impact on employment, in comparison with the situation before your project:
None of the above / not relevant to the project
19. For your project partnership please estimate the employment effect resulting directly from your participation in Full Time Equivalent (FTE = one person working fulltime for a year) jobs: 0
None of the above / not relevant to the project

H. Media and Communication to the General Public

20. As part of the project, were any of the beneficiaries professionals in communication or media relations? No
21. As part of the project, have any beneficiaries received professional media/communication training/advice to improve communication with the general public? No
22. Which of the following have been used to communicate information about your project to the general public, or have resulted from your project?
Press Release Yes
Media briefing No
TV coverage/report No
Radio coverage/report No
Brochures/posters / flyers Yes
DVD/Film/Multimedia No
Coverage in specialist press No
Coverage in general (non-specialist) press No
Coverage in national press No
Coverage in international press No
Website for the general public/internet Yes
Event targeting general public (festival, conference, exhibition, science café) Yes
23. In which languages are the information products for the general public produced?
Language of the coordinator Yes
Other language(s) No
English Yes

List of Attachments (uploaded separately)

Project outcome documents:

ENCE Blueprint: "How to Build European Reference Networks (ERNs) for Rare Diseases – Elements, Considerations, and Materials"

ENCE-CF Consensus Report
ENCE-LAM Consensus Report
ENCE-LTX Consensus Report

Project planning and status documents:

ENCE Workflow

Miscellaneous:

ENCE Logo and Website Screenshot
ENCE Poster (scaled down to A4 size)
ENCE Benefits for LAM – Presentation given at the 1st European LAM Conference, Oct. 2010

List of Beneficiaries and Contact Persons