Project number: LSSM-CT-2005-516513.

Project acronym: ***ENRAH for SMEs***

Project full title: **EUROPEAN NETWORK FOR RESEARCH ON ALTERNATING HEMIPLEGIA IN CHILDHOOD FOR PROMOTING SMALL AND MEDIUM SIZE ENTERPRISES (SMEs) INTEGRATION**

SPECIFIC SUPPORT ACTION

PRIORITY 1
“Life sciences, genomics and biotechnology for health”

PUBLISHABLE FINAL ACTIVITY REPORT

Period Covered: 01.04. 2005 to 30.06. 2007

Date of preparation: 19.08.2007

Start date of contract: 01.04. 2005

Duration: 27 months

Project coordinator:	Dr. Tsveta Schyns
Project coordinator organisation name:	ENRAH, Vienna, Austria
Revision:	Final Draft / 20.12.2007

Project Objectives

ENRAH for SMEs is a **Support Action** project in the EU Research Program FP6. It is set up to reinforce research and development of new therapies in the area of **rare paediatric neurological** diseases. It focuses on **one single disease**, namely Alternating Hemiplegia in Childhood (AHC), a very rare and poorly defined condition. The project identifies at least three support activities necessary to develop future research on AHC:

- To bring together paediatric neurologists, researchers and patients /patients organizations engaged in AHC into a functional and sustainable **Network of AHC expertise in Europe, ENRAH**
- To identify AHC cases throughout Europe and catalogue scientific and medical information related to AHC into a **European web based Registry of AHC patients**
- To identify additional relevant expertise and potential Network partners, especially among the **SMEs,** and to involve them into the Network and in **projects** under the **European Union Programs.**

Project Partners

ENRAH for SMEs is a **patient- representative coordinated project** in partnership with **AHC patient organizations**, **clinical** and **genetic research centers** with interest in AHC **from Europe**.

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Performed Work, Methodology and Results

Establishing of the European Network of Expertise on AHC

Description: The project gathered many of the Network partners for the first time and gave the opportunity to share their knowledge, experiences, concerns as well as information and tools for support to AHC patients and their families.

Approach: Common Project Goals

Methodology: Project meetings, Working Groups and workshops

Results: International team experienced in working together under common goals and deadlines. Project partners became members of the renewed ENRAH Association at the end of the project time. Currently, ENRAH covers 15 EU countries.

Usage: Future research into AHC; new treatments development; information on AHC and related rare neurological paediatric diseases

Dissemination: www.enrah.net, ENRAH as the Main Partner (coordinator) in the starting project *nEUroped* (2008-2010) under the Public Health Community Program

Comments and conclusions: ENRAH is a patient driven network. The motivation of the project team was the key to the success and in achieving all project goals under the tight deadlines and with insufficient project budget.

Registry of AHC patients in Europe

Description: Within the participating EU countries identifying cases with possible AHC diagnose of all ages, collecting a mandatory set of clinical data for each patient for the purpose of the ENRAH Registry and sharing data into a secured on line format.

Approach: Ensure data collecting costs are covered; involve Patient groups as early as possible; keep time deadlines

Methodology

-- One data providing center per each of the eight participating EU countries
-- Informing and networking patients as early as possible; involve Patient Organisations to support data collection
-- Two project workshops to define the purpose and the content of the Registry
-- A Glossary of terms appended to the Questionnaire for data collection
-- Open for all patients of any age with possible AHC diagnose
-- Patients are known to the data providing center or identified through patient organization/ group or through colleagues
-- Patients are seen and examined by data providers
-- Data collecting costs covered by the project
-- Research Ethics Committees application at each of the eight data providing Centers
-- One site electronic Registry hosting
-- On line data entry, managements and analysis- Internet access via CPS cards

-- Training and on line support for data providers

-- Personal data removed, Unique coding numbers

-- Data validated by expert Committee according to revised AHC diagnostic criteria

-- Links to existing blood samples collected from the Registry patients

-- Guidelines for the use ENRAH Registry

Results: The electronic on line format (required to facilitate and secure data collection and analysis) of the Registry was subcontracted The vendor -IT provider HC Forum, France - was selected in a competitive call among 5 SMEs candidates. On line secured database with 157 cases/155 coded records (patient are identifiable through the data providing center) which contain: 1) general information (60 parameters) sufficient to categorize the patient; 2) detailed longitudinal clinical information (186 parameters) where available - follow up at 2, 12, 18 and above 18 years; 3) results, if any, of mutation analysis; 4) links to bio-data (blood samples of AHC patients available at five of the data providing centers). The ENRAH Registry organization was set up to target all ages patients with possible AHC diagnose and includes a number of adults up to 51 years. Patent records validated and categorized as typical or atypical. It was not possible to start analysis of the Registry due to the IT product malfunction.

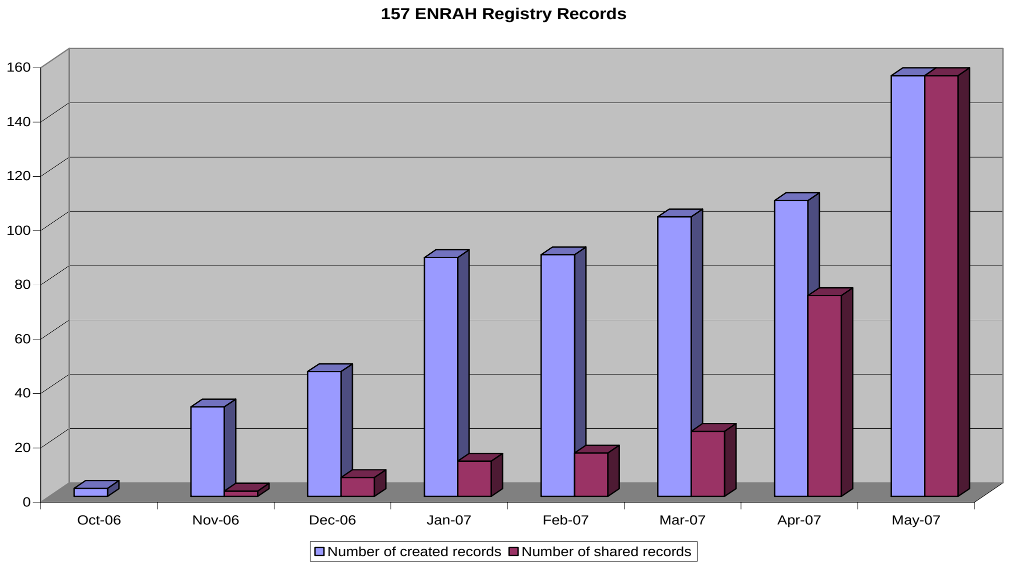

Fig. 1 ENRAH Registry Data collection and sharing

Usage: Longitudinal and natural history studies of AHC, research into AHC, new treatments development and possibly, randomized control trials

Dissemination: Restricted access to the ENRAH for CPS cards users. Access /a CPS card granted to any individual or organization who expresses a legitimate interest in a written application to the ENRAH association Executive Committees (contact through www.enrah.net).

Comments and conclusions:

-- AHC is symptomatically diagnosed and not well recognized by medical professionals. There might be a large number of AHC affected people in all ages which await a proper diagnose. Within two years time we have identified over 200 cases and **catalogued 157 patients from 8 EU countries in the ENRAH registry**. This is an achievement exceeding our best expectations at the start of the project.

-- In France, the Czech Republic and Italy a higher, than the Registry average , number of identified AHC cases as a proportion of the country's inhabitants was identified. We attribute these results to the countries **well established system for AHC diagnosis** but also to the **long history of AHC patient advocacy** and **the involvement of the patient** organizations AFHA and AISEA as project partners.

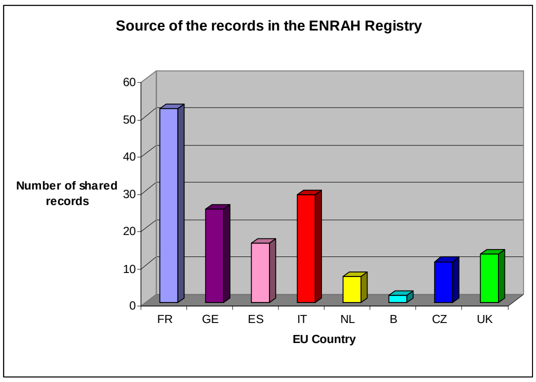

Fig. 2 Number of AHC cases in the ENRAH registry in the participating EU countries

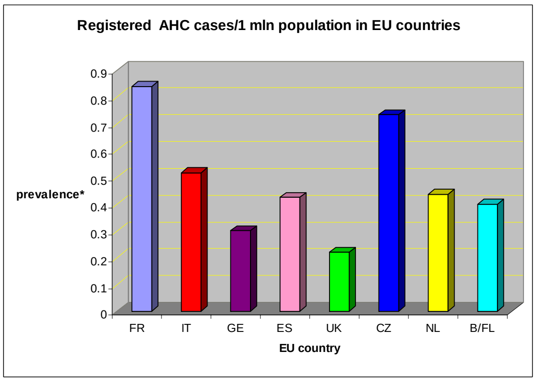

Fig 3. Number of AHC cases per million inhabitants as estimated from the first data collection

-- The ENRAH Registry contains predominantly cases under age of 20 years and that likely reflects the real life situation since:

1) AHC is recently described disease (the name was coined in 1974), thus, most people with AHC currently above the age of 35 may not have been AHC-diagnosed

2) adult neurologist are less aware and familiar with the AHC symptomatic

3) a significant proportion of children affected by AHC die before reaching adulthood.

Further efforts need to be made in order to define **incidence** the disease, to study **disease outcomes** and publish **longitudinal studies**.

-- One line hosting and organization of the ENRAH Registry greatly facilitated data sharing across country borders and across language barriers. On the other hand, unfortunately, our experience with the purchased **IT product** (subcontractor HC Forum, France) which lacked the correct tools for data management and processing shows that, **when not properly designed, it can present a serious threat** to the Registry's data security and patient confidentiality.

Raising Public Awareness

Description: Dissemination of information on AHC, the project, the Network and the Registry for SMEs and for public to extend the Network and integrate SMEs

Methodology: presentations, patient Presentations and summaries on the project for AHC patient organizations at meetings, in newsletters, through emailing

Results: extended Network contacts to include neurologists from Europe and the rest of the world- China, India, New Zeeland, South Africa and Argentina. Also contacts to and between AHC patients groups and the AHC patient organisations have been strengthen and communication has improved through the efforts of the project (partner 6 AFHA and 8AISEA).

A New Research on AHC has been initiated at the Academic Hospital, KULEUVEN thanks to the efforts of partner 4 and the support of partner 10-LUMC. This ongoing project has obtained the **first positive clinical results in five AHC** patients.

Comments and conclusions: Raising awareness and information on the disease is an essential step towards research and new therapies development.

Involving SMEs into the AHC Network and the Community Programs

Description: Identifying, stimulating and supporting SMEs which are relevant to the Network to facilitate the assembling of new Project teams and new project proposals to the European Community Programs.

Methodology: on line experts data base restricted to registered members; literature and databases search; emailing list of SMEs, on line brokerage events; tele-conferences; writing and submitting proposals.

Results: an expert data base with checked research profiles; five on -line brokerage events; three project teams ; two submitted proposals – ISECRARE and *nEUroped* (starting 2008).

Usage: Future research into AHC; new treatments development; information on AHC and related rare neurological paediatric diseases

Comments and conclusions: ENRAH for SMEs involved clinical centers with expertise in rare paediatric neurological diseases – an area little known to the Community programs.

Our experience is that SMEs are very keen in receiving information and in participating in projects in this area and under the community Programs.

Ethical Guidance

Description: Identifying the needs for implementing ethics and GCP related to clinical data registries into the project and developing specific ethics and GCP standards and applications for research involving AHC patients and their families as well as other related rare diseases.

Methodology : working group ethics, working group meetings, survey among project participants.

Results: Report on the needs and challenges in Ethics the ENRAH for SMEs project; Best Practice Guidelines for the Development and Use of the ENRAH Registry

*Usage :*ENRAH and other research Networks utilizing patient registries and sharing research across Europe.

Comments and conclusions:

Ethical Guidance was essential part of the *ENRAH for SMEs* project to provide an ethical and scientific standard for the development and use of the ENRAH Registry.

Dissemination and use

Publication	Type of audience	Type	Partners responsible involved
Examining the Value and Impact of the EU Clinical Trial Directive, 10-11 May 2005, Brussels, Belgium	Industry, EC, clinical	PPT	1. ENRAH
www.enrah.net	General public	Web site	1. ENRAH 2. RTD
Third European Conference on Rare Diseases, 20-22 June 2005, Luxembourg	Patients, EC, Industry, research	PPT	1. ENRAH
9th EFNS Congress(European Federation Neurological Societies)- a stand kindly provided by EFNA, 19-20 September , Athens, Greece	Clinical, Research	Stand, leaflets, poster	1. ENRAH 2. RTD
Spanish Family meeting , Madrid, Spain , 7 May 2005	Patients	PPT	8.AISEA
Sleep Disorders Meeting, Denver, Colorado, US	Clinical, Research	Poster	4.CUP
International Workshop Paroxysmal Disorders in Infancy, 10-13 May 2005, Islay, UK	Clinical, Research	Poster, PPT	4.CUP
US Family meeting, 29 July 2005 Boston , USA	Patients	PPT	1.ENRAH, 6. AFHA
Dutch family Meeting, 11 September 2005, Leiden, The Netherlands	Patients	PPT	1.ENRAH, 11-LUMC
17th Annual EACD Conference Monaco, 21November 2005	Clinical, Research	PPT, session organisers	6. AFHA, 7. APHP, 12.UB ,13.UCL
2nd International Symposium on Paediatric Movement Disorders, 10-12 February 2006, Barcelona , Spain	Clinical, Research, Patients	PPT	all
AHC patient organization meetings Italy, March, 2006	Patients, Clinical	PPT	6.AFHA, 8.AISEA
Eurordis annual meeting Berlin , May 2006	Patients, EC, Industry, research	PPT	1. ENRAH
AHC patient organization UK, July 2006	Patients	PPT	6.AFHA, 13.UCL
International Symposium On Alternating Hemiplegia June 11, 2006 Montreal Neurological Institute Canada	Clinical, Patients	PPTs	4,5,6,7,8,12
Bio-banking Conference, Basel, October 2006	Industry, research, clinical	Chair	1. ENRAH
Rare disease Leadership Summit , December 2006, Arlington, US	Industry, Gov., Research, Patients, clinical	PPT	1. ENRAH
Letter to the identified SMEs	Industry and academic	email	1. ENRAH 2.RTD
Spanish, Danish and Dutch organisations Newsletters	Patients	report	1. ENRAH
AHC patient organization meetings Germany, June 2007	Patients	PPT	1. ENRAH, 14.UKH
Information on the project in the Deutschen Nervenheilkunde , May 2007	Clinical	Report	14.UKH
European Workshop “Gaining Access to Rare Disease Research Resources” Paris, May 2007	Patients, EC, Industry, research	PPT	1. ENRAH, 2. APHP
Participation for a video report on AHC from Picture Art society	General public	interview	1. ENRAH , 6. AFHA

Publication	Type of audience	Type	Partners responsible involved
Presentation at www.efna.net	General public	Web page	1. ENRAH
the International Headache Society Meeting ,Stockholm, June 2007	Clinical, research	PPT	11. LUMC
EPNS meeting, September 2007, Ismir , Turkey	clinical	PPT	7. APHP
Second Rare disease Leadership Summit , December 2007, Washington DC, US	Industry, Gov., Research, Patients, clinical	PPT	8.AISEA
Neuropadiatrie in Klinik und Praxis 6. Jg. (2007) Nr. 2	clinical	Article	14. UKH
Developmental Medicine & Child Neurology 2007, 49: 777–780	clinical	Article	13. UCL

Information, updates, contact information as well as directions for access to all exploitable results can be found on the www.enrah.net .