Euro-Histio-Net 2008
Meeting March 20th, Vienna

Held on March 20th, 2009 1.00 p.m. – 5.30 p.m.

at Children's Cancer Research Institute, St Anna Kinderspital, Kinderspitalgasse 6, Vienna, Austria.

Present:
- M. Aricò, Azienda Ospedaliero-Universitaria Meyer, Firenze, Italy
- I. Astigarraga, Hospital de Cruces, Barakaldo, Spain (BIOEF)
- J. Donadieu, Hôpital Trousseau, Paris, France (AP HP)
- L. Filipovich, Children's Hospital Medical Centre, Cincinnati, OH, USA; President of the Histiocyte Society, Pitman, NJ, USA
- H. Gadner, St. Anna Children's Cancer Research Institute, Vienna, Austria (CCRI); intermittent
- M. Girschikofsky, Austrian Working Group for Histiocytic Diseases in Adults, Austria
- R. Haupt, Istituto Giannina Gaslini, Genova, Italy (IGG)
- B. A. Miller, Histiocyte Society / Histiocytosis Association of America, Pitman, NJ, USA
- M. Minkov, St. Anna Children's Cancer Research Institute, Vienna, Austria (CCRI)
- V. Nanduri, Watford General Hospital, Watford Hertfordshire, UK
- R. Price, The Histiocytosis Research Trust, Sutton Coldfield, UK (HRT)
- C. Rodriguez-Galindo, St Jude Children's Research Hospital, Memphis, TN, USA
- S. Van Gool, University Hospital Gasthuisberg, Leuven, Belgium
- J. Visser, University Hospitals of Leicester, Leicester, UK
- S. Weitzman, Sick Children Hospital, Toronto, Canada
- E. Schäfer, Project Manager

Observers:
- J. Dersch, Histiocytosis Association of America, USA
- M. Nykiel, St. Anna Children's Cancer Research Institute, Vienna, Austria (CCRI)
- A. Safer, Histiocytosis Association of America, USA
- E. Thiem, St. Anna Children's Cancer Research Institute, Vienna, Austria (CCRI)

1. Opening of the meeting and welcome (Jean Donadieu)

Jean Donadieu, Chair, opened the meeting at 1 pm., welcomed all attendees and distributed a folder containing the meeting agenda, the minutes of the Euro-Histio-Net meeting in Paris 2008 December 18-20, the current version of the consortium agreement, the catalogue of mandatory data as agreed in the Paris meeting, a catalogue of data which will be common for Euro-Histio-Net and the Histiocyte Society data base, and a catalogue containing all data which is currently collected in Europe from different groups dealing with LCH.

He recalled the five **major objectives** of the Euro-Histio-Net project:
1. To facilitate the access to information in LCH and associated syndromes
   - For the patients and the families
   - For the doctors
2. To increase the knowledge about epidemiology, risk factors, and sequelae by setting up an international database in order to determine better therapeutic measures.
3. To share expertise in difficult cases and to create an online tool to meet experts.
4. To disseminate guidelines for the diagnosis work up, the therapy, and tissue banking.
5. To stimulate the links between patient associations.

Jean Donadieu shortly outlined the three mandatory work packages (coordination, dissemination and evaluation) and the five technical work packages (web portal, data base, meet the expert, and patients as the four IT related work packages plus guidelines in LCH).

He continued with a short description of the situation of the project: After the application in May 2007 and the answer of DG sanco/EAHC in October 2007, the contract was finally signed in July 2008. The official start of the project was in September 2008, in October a project manager was selected and by November the budget was distributed. From November 2008 to March 2009, the project team handled contractual and organisational issues.
In December 2008 the project partners met to conclude on a consortium agreement, the frame of the data base and the external audit committee.

Aims of the today's meeting are:

- Final validation of the consortium agreement
- Final validation of the mandatory data for the data base
- To define an agenda to validate the complete catalogue of data, i. e. the core of the technical specifications for the data base
- To examine the other work packages

2. Adoption of the Agenda

On request of Eva Schäfer the attendees unanimously decided to exchange agenda item no. 6 (Consortium agreement) with agenda item no 5. (Reports on the Status quo of the Work Packages).

3. Procedural Matters (Eva Schäfer)

a. Required Improvements concerning Project Organisation.

On the occasion of the "collaborating questionnaire" which was sent to all project partners in February, it was also queried if the work on the project should be improved in any way. No suggestions were made. Nevertheless, some collaborating partners sent statements showing some confusion about their role and involvement in the project. Therefore a clear definition of involved partners and their role is needed. The list of results of the collaborating questionnaire (attachment 1) shows all partners that want to contribute and the tasks they want to fulfil.

b. Communication Network.

As the table of attachment 1 lists all interested partners, it will be the basis for any communication concerning the different work packages. Each work package leader has to discuss the role of her/his collaborating partners with the latter to define exactly their contribution. The project manager will ensure information and work-flow between the partners and support the realisation of the objectives.

c. Project Review and Evaluation.

A first **Project Review** is planned for the end of the first year (i.e. by September 2009). The aim will be to assess the work carried out over the first period. Independent experts shall be involved. The review shall consider an overall assessment of the project, the extent of achievement of objectives, the use of resources due to defined conditions, the implementation of the project and dissemination, and other issues like ethical or safety questions.

Questions and remarks:

- The review shall also consider legal questions.

For the **Project Evaluation** some indicators for the different work packages (WP) are already defined:

- For the WP Coordination, the Steering Committee shall meet twice a year and the Advisory Board once a year.
- For the WP Dissemination, a yearly participation at the Histiocyte Society Meeting as well as the participation in national meetings of patient associations is planned, and two publications about the Euro-Histio-Net web portal in professional journals with peer review shall be realised by the end of the project in 2011.
- For the WP Web portal, 100 contacts per day in 2011 and the availability in at least five European languages are defined as indicators to evaluate the success.
- For the WP Web data base, data of 3.000 patients shall be entered in 2011.
- For the WP Guidelines it is planned to provide them in seven European languages.

Further indicators are needed to evaluate the success of the project. They have to be quantitative (measurable), easily to present and ranked concerning their importance. The WP leaders are invited to suggest indicators; otherwise Eva Schäfer will send her suggestions. Most important aspects to evaluate are the migration of historic data to the web data base, the quality of the Frequently Asked Questions and the Web sessions for the WP Meet-the-expert, the quality of the Guidelines and the realisation of the WP patient/parent web site.

4. Project Budget (Eva Schäfer)

a. Total Budget 2008-2011.

The comparison of the initially planned project budget and the finally realised amount shows that the project team has to develop some good ideas to realise all contents that are necessary to make the project successful. Especially for the work package data base, the reduction to less than 50 % of the initially planned budget requires to take adequate measures.

All project partners (associated partners as well as collaborating ones) have a high own contribution to realise the Euro-Histio-Net project.

Questions and remarks:

- In order to apply the budget most useful and to minimise maintenance costs as well as data entry effort, it would make sense to have one database, commonly used by Histiocyte Society and Euro Histio Net.
- Some participants stated clearly that from their point of view it does not make sense to have two different data bases as the persons dealing with both of them to a great extent are the same.

b. Budget for the Period September 1st, 2008 to August 31st, 2009.

A general overview of the budget for the first year was given by means of diagrams. Eva Schäfer will send a detailed compilation to the associated partners.

c. Requirements for the Intermediate Financial Report.

- For the Financial Reports, the partners must prove 100 % of the project budget to receive the complete European funding which averages ca. 40 % of the project budget.
- To prove staff costs, salary slips and time sheets are required. The declaration should conform to the detailed budget of annex II of the grant agreement (i. e. do not prove working hours if annex II declares working days).
- Travel costs must be proved by means of the tickets or the passenger receipts.
- Subsistence allowances must be calculated following Council Regulation (EC, Euratom) No 1066/2006.

5. Consortium Agreement – Approval of the Final Version (Eva Schäfer)

In addition to the modifications decided in the Euro-Histio-Net meeting, December 18 to 20 in Paris, the associated partners have agreed on some further changes. The modifications concern the guidance of the Euro-Histio-Net web data base in order to reduce the responsibility of the steering committee and to increase the influence of project groups and study committees respectively. The steering committee (composed of the associated partners) shall govern changes concerning the Catalogue of variables and their definitions as well as changes to legal regulations and general terms of use. The project groups / study committees shall be responsible for regulating access and user rights within the general rules defined by the steering committee. The final version of the consortium agreement had been sent to the project partners prior to this meeting. It was not finally approved due to the following considerations.

Questions and remarks:

- The sentence "The *associated partners* will jointly assume ownership of the web portal and of the data base software and the table structure" might raise problems if the Histiocyte Society (HS) data base shall be used commonly by HS and Euro-Histio-Net. The influence of both, the HS and the partners of Euro-Histio-Net on the governance of the data base must be assured.
- The Euro-Histio-Net partners are obliged to fulfil their contract. Therefore if a common data base shall be realised, the project partners must be able to decide on data which is needed additionally to what the HS data base already collects. Data concerning adult patients and those who are suffering from associated syndromes have to be considered as well as data regarding therapy and sequelae.

6. Reports of the Status quo of the Work Packages (Eva Schäfer)

Work package Meet the Expert

Itziar Astigarraga is reviewing examples for web solutions as regards the Frequently Asked Questions (FAQ) and the Web Sessions. After the review is done she will compile a collection of ideas. Any partner that is interested in contributing ideas or web addresses is invited to contact her (itziar.astigarraga@osakidetza.net). On March 26, Itziar Astigarraga will meet Raul Suarez, President of the Spanish Patient Association, who will contribute ideas to the work package.

Questions and remarks:

- Itziar explained that Raul Suarez has set up the web site of the Spanish association which contains a web forum for asking questions. This forum has a good functionality and is contacted very often.
- She also mentioned that she is in contact with Carlos Rodriguez-Galindo. His hospital (St Jude Children's Research Hospital, Memphis, TN, USA) provides a web solution that allows for contacting experts to get some advices. Itziar intends to create a function for expert sessions that permits to ask questions in real time in the Euro-Histio-Net web portal.
- A tool for exchanging diagnostic details and imagery is planned to enable experts to discuss complicated histiocytosis cases.
- The meet the expert web site shall enable patients and non-specialised doctors to find contact information of histiocytosis experts.
- All partners of Euro-Histio-Net that have stated to be interested in contributing to this work package will receive information how to get involved.

Work package Guidelines

For the guidelines in diagnosis and therapy of LCH, Riccardo Haupt has started to collect all material which has already been produced and could be useful. Any contribution of material is welcome (riccardohaupt@ospedale-gaslini.ge.it). The demand was sent out via email and should be circulated to other colleagues who might be interested to contribute. Riccardo will write a first preliminary draft based on the collected material.

For the guidelines in tissue banking, Riccardo has distributed a draft of a questionnaire which aims at getting answers to questions like where exist tissue banks, when started the collection, which cases of LCH are stored, from what time of the disease course, and what type of tissue is stored? Comments and suggestions to improve the questionnaire are welcome. Afterwards, Riccardo will send it to all national coordinators (to circulate it among the participating centres) as well as to all European scientists interested in LCH. With all answers to the questionnaire, an inventory of LCH tissue banks will be produced.

Questions and remarks:

- At least three different groups have already produced some guidelines in LCH.
- It would make sense that Riccardo contacts the responsible persons to collect the produced documents and to coordinate an exchange to reach a collective consensus.

Work package Patients/Parents Web site

The work package of Richard Price will be the last one that has to be accomplished. Richard has already created a multilingual web forum on the web site of the H R Trust which constitutes some basic work for the patients/parents web site. A letter of invitation will be sent to all European patient associations to ask for their contribution to the work package.

Work package Web portal

Two web domains are already booked for the web portal: www.eurohistio.net and www.histio.net. Today Jean Donadieu will present a proposal for the technical specifications.

Work package Web data base

The basic regulations and the mandatory data for the database were concluded during the Paris meeting in December 2008. They are defined in the consortium agreement which still has to be finalised. A proposal for the technical specifications as well as for the complete catalogue of data will be presented today.

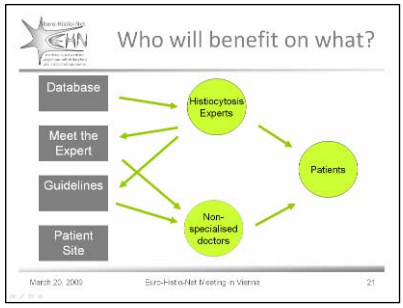
Questions and remarks:

- Using the Histiocyte Society data base would have different advantages: It is already developed even though not yet available online. The IT Company which has realised the data base has high expertise in the high Austrian and German requirements for storing patient data. Any data input of patients enrolled in clinical studies can be governed in a way that automatically fulfils the required conditions for these studies.
- The use of a common data base has the following disadvantages: an enlargement of the Histiocyte Society data base is required and has to follow the conditions defined by the Euro-Histio-Net project. The regulations of property and administration of the data base must consider all conditions defined by the International Histiocyte Society, based in the USA, as well as all requirements of the Euro-Histio-Net project.

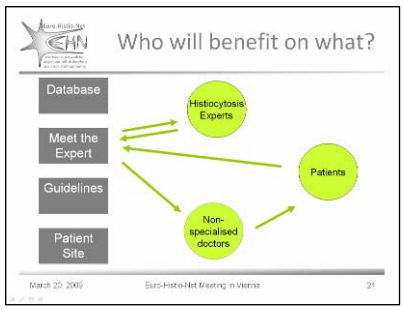
- Due to the special characteristics of histiocytic diseases, for all patients who are enrolled in clinical studies, many aspects of the natural history of the disease are already queried by the clinical study case report forms. It should be avoided to have two different data bases with some overlapping.
- The content of the technical specifications of the web data base depends on whether there will be a common data base or two data bases will exist in parallel. Therefore they cannot be specified unless a decision is taken. This might result in a delay of delivery no 3.
- From a technical point of view it is not a problem to have two different data bases which are able to exchange data.

Who will benefit on what?

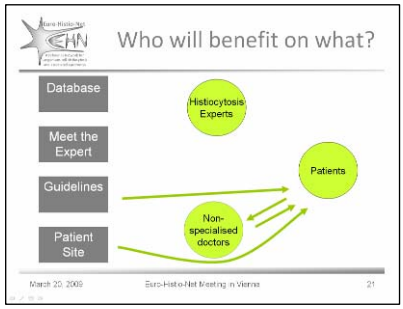
A comprehensive collection of patient data and disease courses will help histiocytosis experts to increase the knowledge about the disease to determine better diagnostic and therapeutic measures and therefore improve the patients' treatment. It will also enable them to constantly improve the contents of the Euro-Histio-Net web sites Meet the Expert and Guidelines. Non-specialised doctors will benefit on access to better information and therefore also be able to improve the patients' treatment.



European patient associations will be asked about all questions that were frequently asked but could not be answered by their treating doctors. So histiocytosis experts will be able to answer these questions and to add them to the FAQ on the Euro-Histio-Net web site Meet the Expert.
Non-specialised doctors will benefit on these answers as well as histiocytosis patients.



Patients can consult the Euro-Histio-Net web sites Patients and Guidelines to get a better understanding of their disease. This will allow for better communication between them and their treating doctors.



7. Web Portal and Web Data Base (Jean Donadieu)

a. Approval of the Definitions of the Mandatory Data for the Data Base.

The list of mandatory data was approved in the meeting in Paris, December 18 to 20. The definitions of the mandatory data will be approved by means of email.

b. Technical Specifications of the Web Portal.

Basic requirements:
Parts of the web portal will address general public and must be comprehensible for laypersons; other parts will address medical professionals.

The web portal has to provide its information in different European languages and shall be a gate to several other links (web data base, web site Guidelines, web site Patients Forum and web site Meet the Expert).

Contents:

- Short introduction (flags by countries)
    - EU and rare diseases
    - Euro-Histio-Net (EHN) organisation
        - EHN aims
        - EHN partners
        - EHN documents
        - EHN minutes of meetings and presentations
- Presentation of the disease
- Guidelines for diagnosis and work up, and general recommendations for patient care
- FAQ for public
- FAQ for professionals
- Contact to all referent centers in all European countries
- Access to the web data base
- Access to other web sites

Further specifications:

- The site should meet W3C compliance standards wherever possible.
- All pages (except video or multimedia) must download in less than 10 seconds over a 56k modem connection.
- All pages must display correctly within a web browser displayed on a computer set to a minimum of 800 x 600 pixels.
- The site must be cross browser compatible with numerous platforms, in particular, Internet Explorer 6 and above, Firefox 2 and above, and Netscape 6 and above.
- The site should not use frames.
- All site pages, excluding the secure administration section, should be available for search engine indexing.
- Ease of use, with structured navigational methods.

Agenda:

- Technical specifications written in detail by May 1st
- Call for tender May-June 2009
- Opening September 2009

c. Technical Specifications of the Web Data Base.

The draft of the document was not presented by reason of the consideration to have a common Euro-Histio-Net and Histiocyte Society data base.

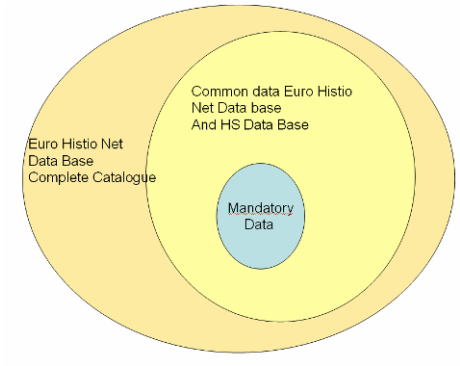
d. Requirements for the Subcontractor Appointment.

The requirements for the subcontractor appointment depend on the decisions as regards to the web data base. Therefore this issue was postponed.

e. Catalogue of Data/Variables for the Web Data Base.

- Presentation.
    - The complete Catalogue was sent to all project partners prior to the meeting and distributed on paper to all meeting attendees.

- The aim of the Euro-Histio-Net data base will be to provide a technical tool in order to collect a comprehensive catalogue of patient data. Questions of data management and monitoring, and how to generate studies with the collected data, have to be addressed by defined project groups or study committees. Each user of the data base (data controller) has to respect his national regulations concerning patient consent for the storage and use of patient data. Each data controller will keep a veto right concerning access to and use of the patient data he has delivered to the data base.
- The question which data will be hosted in the Euro-Histio-Net data base can be answered in two different ways: Either, a 100% agreement of all users on the complete catalogue of data is required, or the Euro-Histio-Net data base will be able to support different national and/or institutional users.
- In Paris it was decided to have a list of mandatory data which has been defined in the meeting (see EHN_minutes_2008_12_18-20) and which will be obligatory for all users. In addition, all data which at present are collected in Europe shall compose the complete catalogue of variables for the data base (which will not be obligatory for all users) in order to enable all partners of Euro-Histio-Net to use a common data base for their work. The Histiocyte Society data base already collects a big part of the complete catalogue for all patients who are enrolled in the LCH IV study. Several teams collect additional data, e. g. for adult patients, for patients not enrolled in the LCH IV study by reason of specific diagnostic or therapeutic characteristics, and for the follow-up of sequelae.



- Discussion, Suggestions for Improvement, and Further Proceeding.
  - An official consultation of all project partners regarding the complete catalogue shall take place until April 15.
  - The document shall be validated and finalised by May 1st.
  - In parallel, the technical specifications for the web data base will be finalised.

8. Discussion of Open Questions and Remarks.

It must be clarified quickest possible, if a common data base for the Histiocyte Society and the Euro-Histio-Net project can be realised and what legal issues have to be considered.

9. Final Conclusions – Allocation of Tasks.

“Euro-Histio-Net work package no. 5 shall be realised as follows:

The budget shall be used to extend the LCH IV database which already exists.
Basis for the extension shall be the “Catalogue of data for data monitoring in Langerhans cell histiocytosis – Euro Histio net data base – Complete set of data” as distributed in the meeting, which has to be approved for this purpose by the project partners by the end of May.
The EAHC shall be asked to approve in advance that this process is possible.”

[Unanimously decided by all participants.]

Eva Schäfer will write the minutes and prepare a request to the EAHC which shall first be discussed with the associated partners and the representatives of the Histiocyte Society.

10. Arrangements for the Next Meeting.
The next meeting will take place mid-September on the occasion of the Histiocyte Society Meeting 2009 in Bilbao, Spain.

11. Any other Business.
No other matters were discussed.

Jean Donadieu closed the meeting at 5.30 p.m.

These minutes arise from the project *Euro-Histio-Net 2008 - A reference network for Langerhans cell histiocytosis and associated syndromes in EU* which has received funding from the European Union, in the framework of the Public Health Programme. Sole responsibility for the content of this document lies with the authors. The Executive Agency is not responsible for any use that may be made of the information contained therein.

	Knowledge to WP					IT knowledge to WP					Dissemination act. for WP					Translations of contents									Fin. Sup.	Fundraising						Inf	Min	Not int.
Representative of Partner	4	5	6	7	8	4	5	6	7	8	4	5	6	7	8	D	F	G	Gr	It	P	Sp	Sw	Other		Pr	4	5	6	7	8			
Astigarraga, I.	X		X		X	X		X		X	X	X	X	X	X							X							X	X		X		
Donadieu, J	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X									X						X		
Fichter, J			X	X	X			X	X	X			X		X			X				X									X		
Girschikofsky, M		X	X	X	X						X	X	X	X	X			X													X		
Haupt, R		X			X							X			X					X											X		
Kaltsas, G		X	X		X						X	X	X	X	X				X												X		
Makras, P		X	X		X						X	X	X	X	X				X												X		
Minkov, M	X	X			X		X								X									Russian Bulgarian							X		
Nanduri, V		X	X		X																										X		
Rodriguez-Galindo, C	X	X	X		X						X	X	X		X							X				X					X		
Stefaniak, M																					X										X		
Van Gool, S		X			X							X		X	X										X					X	X		
Visser, J			X		X																										X		
Weitzman, S			X	X	X																										X		
Beinö, U																							X								X		
Debar, L																															X		
Delestinne, H				X								X		X	X										X					X	X		
Endress, K				X		X		X	X		X	X	X	X	X										X	X					X		
Kauschka, D																													X		X		
Price, R	X			X		X	X	X	X		X	X	X	X	X									see mail	see mail						X		

All columns correspond to the questions in the collaborating questionnaire, sent by mail on 24 February 2009.