Programme of community action in the field of health (2008-2013)

European registry and network for Intoxication type Metabolic Diseases (E-IMD) Contract no: 2010 12 01

Deliverable 07: Annual meetings

June 2014

Description of the deliverable

E-IMD meetings will be held as satellite meetings at the annual SSIEM meetings (M9:Geneva, M21:Birmingham, M33:Barcelona) to allow for maximal dissemination. The advisory board meetings which are closed meetings will be held during the same period.

EXECUTIVE SUMMARY

All associate and most collaborating partners have systematically participated to the Advisory board meetings. Numbers increased every year.
In the evaluation report E-IMD partners stated that the meetings were one of the most important activities of the network: the platform to meet, team work, exchange of knowledge and being able to compare practice and ultimately improve patient care. Nearly 80% or members agreed that annual meetings are sufficient, preferably before or after the annual metabolic meeting (SSIEM)

Partners of E-IMD have enthusiastically embraced the principles of sharing knowledge and improving access to information. Many have said that this is an extraordinarily valuable project that must continue. The project was praised in its initiative to extend to other rare intoxication type metabolic diseases: homocystinurias, methylation and folate defects (E-HOD) and sharing meetings.

1. KICK OFF MEETING

E-IMD kick-off meeting, 1-2 February 2011, Luxembourg
Summary of proceedings

E-IMD: history, overall objective, strategy, deliverables and project management

Stefan Kölker summarized the objectives of E-IMD (see presentation in annex) as well as the management of the network:

1. E-IMD is one of the European Reference Networks (ERN) financed by the DG Sanco. An ERN helps professionals and centres of expertise in different countries to share knowledge. E-IMD has two specific objectives: 1/ to set up a European patient reference on OA's and UCD's and 2/to develop European evidence-based consensus care protocols

2. We have 13 associate partners and 21 collaborating partners (academics, non-profit and private). Associate partners participate in the project, for which their costs are borne and to which they contribute financially. Collaborating partners have no contractual relationship with the EAHC, nor do they receive any EC funding.

3. Heidelberg will circulate an agreement between all associate and collaborating partners concerning access to knowledge and data, governance, publication rules and so on. This agreement should be signed by all partners.

Financial overview and reporting

4. The total E-IMD cost is 1.3 m€ of which the European Commission DG Sanco will co-fund 58%. The 58% will cover staff specifically hired for the project, travel, subsistence and subcontracting i.e. translations and development of a website. No partner will receive money for his/her time, this time contributes to the 42% co-funding.

5. The project started on 1st Jan 2011; partners must keep all invoices for travel, hotel etc. Partners will be asked every 12 months to state exactly how much money they have used and how much time they have spent on the project. Heidelberg has distributed a timesheet.

6. Associate partners were invited, during the meeting, to individually discuss pre-financing with SP. Based on these discussions each partner will be receiving a percentage of the money to start work.

7. We discussed financing travel and subsistence for the collaborating partners. The patient groups and Marshall Summar are members of the evaluation committee and will have their costs borne in WP3 (evaluation). Birmingham

has received funds for meetings to develop consensus protocols and can, from this budget, cover the costs for Matthias and Johannes to the steering group meetings.

The role of Eurordis and patient associations: the patients' perspective

8. Lut de Baere presented the patient perspective and their expectations from RD registries and networks. This was summarized in one of the slides:
    a. Improved quality of information, care and services
    b. Earlier diagnosis and recognition of the importance
    c. Creation of multi-disciplinary teams
    d. Harmonisation and standardisation of best practices / guidelines
    e. Access to the best European resources for rare diseases
    f. Better incentives for research by pooling patients / registries
    g. Increased recognition of rare diseases and thus of their specific features in regards to care through communication and trainings
    h. Less travelling for patients
    i. Better coordination between medical and social care professionals and the PO's expect to be consulted on how this could best be done

Applications for research projects within the E-IMD network: the scientific perspective

9. Matthias Baumgartner gave an overview of the different mechanisms for EU funding for rare disease research and networks. Matthias has led two COST applications which failed. The group felt that this was likely to do with the priorities of the COST rather than the quality of the application.

10. There will also be a call within the FP7 for rare disease with a priority in trans-Atlantic collaboration. The E-IMD and UCDC would be an excellent model for this grant application. (SP to send the draft to MB)

11. The patient groups would like to see improvements in European screening practices and the encouragement of public/private partnerships

Transatlantic collaboration, sustainability and future funding: the US perspective

12. Marshall Summar represented the UCDC and expressed their willingness to collaborate, share data or compare data side by side. Marshall presented learning points from the UCDC registry which included:
    a. It took much longer than expected to start collecting data because of ethical constraints

b. Collecting too much data degrades the quality; it is important to look at what you get compared to the resources used to get the information.

c. The neuropsychological testing was too hard and too long for patients. The UCDC noted that patients would tire in the afternoon and the results would not be representative of their true capacity

d. Data from the IC unit is very hard to understand and enter into the database

e. Defining protein intake varies between centres

f. Some information was not collected at the beginning i.e. immunization; so it was necessary to go to back to the files

g. Surprisingly it was necessary to define criteria of a UCD

h. Units and dosing will need to be defined i.e. citrulline dosing

i. Learnt that patients who were thought to be fine i.e. OTC carrier boys, were not so fine

j. It took longer than expected to publish data (4-5 years)

13. We agreed to make links between the E-IMD and UCDC websites

14. It was suggested that we plan the registry for the long-term and not just for the project duration

15. The US collects quality of life questionnaires completed by parents and older children. The parents complete the forms for children less than 10 years.

16. We can expect in the coming years a whole new series of issues rising from the ageing patients. We could most likely learn from the Down syndrome experience.

EU health programme description of priorities, ERN's, strategic relevance and EU added value of E-IMD

17. The roles of the DG Sanco and Executive agency were described:

18. DG Sanco is the acronym for the Directorate General for Health and Consumer Affairs. It establishes the priorities in areas of high value for EU collaboration. Rare diseases, ERN's and registries are a priority of the DG Sanco 2008-2013 programme

19. The Executive Agency for Health and Consumers implements the EU Health Programme. The Agency provides a professional service in performing the tasks and activities entrusted to it by the European Commission, and it works closely with the Health and Consumers Directorate General.

20. A key message was that the group should dedicate time to thinking about sustainability as the DG Sanco will not be capable of funding all the networks on a long-term basis. Orphanet and Eurordis should be included in this reflection. We were further advised to integrate the networks and registries within each national rare disease plan.

European patient registry (WP4)

21. A list of items to be collected has been circulated to the group

22. Issues of data duplication were discussed – before recruiting new patients, centres should ask patients if they are already registered in the database

23. Concern was raised about the risk of missing data. If incomplete dataset, centres will be contacted by the database manager

24. In principle patients from non associate partners should visit the primary site once and then paper questionnaires will be sent by the non associate to the associate partner. We recognize that this method will not work in all centres. Collaborating centres with large numbers of patients will most likely want to have access to the database with an individual password.

25. All partners will be able to access, extract and analyse their own data

26. *Heidelberg has received ethical approval for the registry. SK has circulated the German application to the group*

27. *Neuro-psychological tests to be used…*

Consensus care protocols (WP5)

28. Anupam Chakrapani is currently making an inventory of all guidelines available in different MS. Once we have an overview, we will evaluate the content and decide whether to endorse and translate. A second step will be to look at significant gaps

29. A separate group for the patient / parent information will be established

30. Three sets of guidelines are already available to be published on the website

31. Marshall agreed that we can use the PA guidelines with the E-IMD stamp

32. Adult guidelines should be developed with the help from an adult metabolic specialist

33. Guidelines have a shelf life and sustainablity should be discussed early

Evaluation of the project (WP3)

34. E-IMD will be evaluated by a multi-stakeholder external group composed of patients, UCDC representative and a EUCERD member (European Expert Group on Rare Diseases)

35. The group will monitor and measure the project to ensure that we achieve the intended impact. We will look at process indicators: how well is the network working? Items to be included in the registry, meetings on schedule, hits and enquiries on the website

36. We will look at outcome indicators and the real benefits of the project: improvement in time to diagnosis, satisfaction of patients, and adherence to guidelines.

37. It is the responsibility of the evaluation group to consider indicators within the larger health system dimension including the availability of diagnostic tests, screening programmes and rare disease plans.

Dissemination of the project (WP2)

38. Dries Dobbelaere is responsible for the dissemination WP

39. We are currently working on the website and a promotional leaflet (available in English)

40. Summary of meetings will be included on the web

41. The website will include information on the collaboration with the UCDC

42. It was suggested that we could have a repository where publications can be downloaded avoiding copyright issues.

43. Funding of the website by private companies would, in principle, not be allowed.

Future meetings

44. We will organize steering group meetings in Paris on M3, M15 and M27

45. Advisory group meetings will be held at the SSIEM in Geneva, Birmingham and Barcelona. We would like to have a formal session in Barcelona

46. Registry group meetings will be held in Heidelberg on M6 and M15

47. Matthias will check for small meeting rooms for the evaluation group and guidelines meetings on Tuesday 30th August in Geneva

List of Participants

- Persephone Augoustides-Savvopoulou,Thessaloniki University A'Pediatric Dept-Metabolic Lab,Greece
- Ivo Baric,Sveuciliste u Zagrebu, Mediciniski fakultet,Croatia
- Matthias Baumgartner ,Kinderspital Zürich, Universitäts-Kinderkliniken, Eleonoren-Stiftung,Switzerland
- Peter Burgard,Universitätsklinikum Heidelberg, Zentrum für Kinder- und Jugendmedizin, Klinik I,Germany
- Alberto Burlina,Azienda Ospedaliera di Padova,Italy
- Anupam Chakrapani,Birmingham Children's Hospital NHS foundation trust,UK
- Ernst Christen,Copenhagen (KGARH),Denmark
- Lut de Baere,BOKS (Belgian patient group),Belgium
- Linda De Meirleir,University Hospital Vrije Universiteit Brussel (AZK-VUB), Department of Pediatric Neurology,Belgium
- Dries Dobbelaere,CHRU LILLE, France
- Angeles Garcia-Cazorla ,CIBERER, Spain
- Wanda Gradowska,Instytut "Pomnik-Centrum Zdrowia Dziecka", Poland
- Stéphanie Grünewald,Great Ormond Street Hospital, UK
- Claudia Kiener ,SHS International, Germany
- Stefan Kölker,Universitätsklinikum Heidelberg, Zentrum für Kinder- und Jugendmedizin, Klinik I, Germany
- Elisa Leao Teles, Hospital de Sao Joao, EPE, Portugal
- Begoña Merinero , CIBERER,Spain
- Hanka Meutgeert, VKS (Dutch patient group), The Netherlands
- Hélène Ogier,Paris, Hôpital Robert Debré, France
- Markus Ott , Milupa Metabolics, Germany
- Samantha Parker, Orphan Europe Sarl (OE), France
- Ute Spiekerkötter, Zentrum für Kinder- und Jugendmedizin, Universitätsklinikum Düsseldorf,Germany
- Nathalie Stroobant, BOKS (Belgian patient group), Belgium
- Marshall Summar, Washington University Children's hospital, USA
- Jolanta Sykut-Cegielska, Instytut "Pomnik-Centrum Zdrowia Dziecka", Poland
- Isabel Tavares de Almeida, Unidade de Doenças Metabólicas, Serviço de Pediatria Hospital Santa Maria Lisboa , Portugal
- Vassili Valayannoupoulos, Hôpital Necker (AP-HP), France
- Laura Vilarinho, Hospital de Sao Joao, EPE, Portugal
- Frits Wijburg, Academisch Medisch Centrum, The Netherlands
- Monique Williams,Erasmus MC-Sophia Kinderziekenhuis, Erasmus Universiteit Rotterdam, The Netherlands
- Jiri Zeman, Charles II University Hospital Prague, Czech Republic

2. 1ST ADVISORY BOARD MEETING

E-IMD Advisory Board Meeting, 29 August 2011, Geneva
Summary of proceedings

Coordinators report (see attached presentation)

48. A welcome note was addressed to new members. E-IMD has evolved from 27 partners in January 2011 to 46 partners in August 2011 from 19 countries.

49. New members "collaborating partners" can join E-IMD by contacting an E-IMD partner or the coordinator directly or current members can encourage centres or individual physicians to join. Partners outside Europe can also apply. Collaborating partners have no contractual relationship with the EAHC, nor do they receive any EC funding.

50. New applications will be put on a waiting list and discussed during the steering group meetings.

51. All partners must sign up to an internal agreement. This agreement is not financially binding but outlines the general networking processes and principles on ownership, publications and so on.

52. An outline of the project was presented including the objectives, management structure and deliverables. It was suggested to include a summary of the number of records in the database public homepage.

53. Guideline development: four groups have been set up:

    a. GA1 group to discuss gaps and improve current guidelines

    b. UCD and MMA combined groups as overlapping interest

    c. IVA is a new group with EU/US collaboration

54. Training: E-IMD has partnered with Orphan Europe Academy. We have specifically developed two programmes including organic acidurias (OA's) and urea cycle disorders (UCD's) www.orphan-europe-academy.com:

    a. E-learning on hyperammonemia available on line from 1st December 2011

    b. 9th European metabolic course, hosted by the Children's Memorial Health Institute in Warsaw,

    MS also suggested the NAMA courses in the US

55. The next E-IMD advisory board meetings will be held in synergy with the SSIEM meetings 2012 (Birmingham) and 2013 (Barcelona)

Finance

56. The total E-IMD cost is 1.3 m€ of which the European Commission DG Sanco will co-fund 58%. The 58% will cover staff specifically hired for the project, travel, subsistence and subcontracting. It was highlighted that partners must hire staff promptly as this is almost 50% of the commission funding. Delays in hiring staff may jeopardize our 2nd pre-financing.

57. SP concluded that:

    a. Essential to promptly respond to requests for financial information

    b. All costs related to the project as agreed in the grant application should be reported

    c. Report costs including tax if your organisation does not claim back the tax

    d. Report costs excluding tax if your organisation claims back tax

    e. if non € costs, please report in local currency or apply EU conversion rules

    f. Please keep a scanned copy of all invoices and send these to SP with financial summary

Orphan Europe Collaboration with the E-imd registry for carbaglu post marketing surveillance

1. Carbaglu is designated as an orphan medicinal product with market authorisation in the treatment of

    a. hyperammonaemia due to N-acetylglutamate synthase (NAGS)primary deficiency;

    b. hyperammonaemia due to isovaleric acidaemia (IVA);

    c. hyperammonaemia due to methymalonic acidaemia (MMA);

    d. hyperammonaemia due to propionic acidaemia (PA)

2. Orphan Europe is required by the European Medicines Agency to design a Risk Management Plan (RMP) which has to characterize the safety profile of the product for all indications. The RMP should follow prospectively all patients using the product.

3. The E-IMD registry data set already encompasses the majority of data required for the Orphan Europe Carbaglu protocol (OE will ask for a few additional questions on drug related adverse events). Therefore, conducting the registry within the E-IMD makes sense thus avoiding the duplication and use of scarce resources.

4. The E-IMD and OE collaboration will be beneficial in:

    a. Improving participant recruitment to the E-IMD registry: The E-IMD use a number of different mechanisms to recruit patients. OE will be able to compliment current mechanisms by identifying physicians prescribing Carbaglu. E-IMD investigators will be able to contact those physicians for potential referral of patients to the Registry.

    b. Expedite activation of Carbaglu registry (CR): The E-IMD registry is already active. Adding the CR to the registry will help avoid lengthy start up times and cost. E-IMD adheres with the standards for data protection, and has full ethical compliance and informed consent in each member state. This collaboration will avoid additional work on consent, methods to preserve anonymised data, ethical committee approval, and issues related to the custodianship of data.

    c. More convenient for Participants: Subjects will be able to enroll in the E-IMD registry and also in the Carbaglu Registry at the same site. Much of the data collection is the same, so they won't need to repeat questionnaires in order to participate in the two registries.

    d. Efforts and costs will be optimized. OE will compensate the E-IMD for extra work involved with recruiting and collecting additional data for the Carbaglu Registry.

5. Additionally, OE and the E-IMD are both partners of the Urea Cycle Disorders Consortium (UCDC) Longitudinal Study in the USA. UCDC is an academically governed Longitudinal Study in UCD. The European and US projects will work together and attempt to secure transatlantic funding through the NIH and EU.

6. This multi-stakeholder approach to a sustainable international registry in UCD's and OA's will be a model for all rare diseases. It addresses issues raised by the European Medicines Agency and the European Committee of Experts on Rare Diseases (EUCERD)

7. After much discussion, including issues around data protection, ethics and patient informed consent, the advisory board agreed that they, in principle, support this project. Steps should now be made to make this feasible.

List of Participants

Last name	First name	Organisation
Baric	Ivo	Sveuciliste u Zagrebu, Mediciniski fakultet
Baumgartner	Matthias	Kinderspital Zürich, Universitäts-Kinderkliniken, Eleonoren-Stiftung
Baumjahre?	Regina	Metabolic Unit University Childrens Hospital Basel
Burgard	Peter	Universitätsklinikum Heidelberg, Zentrum für Kinder- und Jugendmedizin, Klinik I
Burlina	Alberto	Azienda Ospedaliera di Padova
Chakrapani	Anupam	Birmingham Children's Hospital NHS foundation trust
Cleary	Maureen	Great Ormond Street Hospital for Children NHS Trust
De Baere	Lut	Belgische Organisatie voor Kinderen en Volwassenen met een Stofwisselingsziekte VZW (BOKS)
Dobbelaere	Dries	Centre Hospitalier Régional et Universitaire de Lille - CHRU de Lille
Gradowska	Wanda	Instytut "Pomnik-Centrum Zdrowia Dziecka"
Haeberle	Johannes	Kinderspital Zürich, Universitäts-Kinderkliniken, Eleonoren-Stiftung
Haliwglu	Göknir	Hacettepe University
Kölker	Stefan	Universitätsklinikum Heidelberg, Zentrum für Kinder- und Jugendmedizin, Klinik I
Leao Teles	Elisa	Hospital de Sao Joao, EPE
Lund	Alan	Klinisk Genetisk Afdeling Rigshospitalet
Meutgeerg	Hanka	VKS
Otrolenghi	Chris	Biochimie Metabolique, Univ Paris Descartes, Necker Paris
Ott	Markus	Milupa Metabolics
Parker	Samantha	Orphan Europe Sarl
Ribes	Antonia	Centro de Investigacion Biomedica en Red de Enfermedades raras (CIBERER)
Rubio	Vicente	Institute de Biomedicine CIBERER
Sass	Jörn Oliver	Universitätsklinikum Freiburg, Zentrum für Kinder- und Jugendmedizin, Labor für klinische Biochemie und Stoffwechsel
Soares	Susana	Hospital de Sao Joao, EPE
Stroobant	Nathalie	Belgische Organisatie voor Kinderen en Volwassenen met een Stofwisselingsziekte VZW (BOKS)
Summar	Marshall	Urea Cycle Disorders Consortium
Sykut-Cegielska	Jolanta	Instytut "Pomnik-Centrum Zdrowia Dziecka"
Valayannopoulos	Vassili	Assistance Publique Hopitaux de Paris
Williams	Monique	Erasmus MC-Sophia Kinderziekenhuis, Erasmus Universiteit Rotterdam
Simpson	Kara	UCDC Washington
Stäbe	Patricia	Patricia

3. 2ND ADVISORY BOARD MEETING

E-IMD Advisory Board Meeting, 4 September 2012, Birmingham
Summary of proceedings

Coordinators report

1. A welcome note was addressed by Jacques REmacle. new to the agency but previously worked on the IRDIRC project. type of project has a storng inmpact on patients suffering from these diseases. How to work with the agency in the future – EU budget been affected and public health programme will have cuts therefore extremely important to focus on delivery. success of programme will be means of fighting for additional budget in the future. feel that the project is very strong scored highly in the evaluation. two things:

    a. Future new health programme "health for growth": call closes March 22nd 2013. new programme will start in 2014. the new programme is an evolution from the 1st. no major differences in objectives which are: 1/contribute to innovative and sustainable healthcare system; 2/ increase access to medical expertise and expectation to improve healthcare safety 3/ prevent disease and promote good health 4/ cross border healthcare threats. Tasks under these four objectives. Developing cooperation on HTA, promote e-health, support sustainability on workforce, provide expertise to assist MS, support to innovative ?, ehealth and health technology, foster health knowledge system, 6 objectives on safer HC for citizens: **support to reference networks**, blood organ donations, foster health knowledge systems. Support chronic disease prevention like cancer. Overall budget 450 million € over 7 years (likely to be cut by about 10% and about 5% in the health). Timing, new proposals based on cuts about 3 weeks ago, hope that European parliament will agree on new programme in June with a budget. Put everything in place to start 1st Jan 2014. Shift to innovation and sustainability. Will still have project grants, operating grants, conferences, joint actions (but may work by negotiating with MS not calls), operating grants based on partnership agreements

    b. Tips and warnings to keep in mind: recommend to deliver. See problems due to misunderstanding how funding has to be spent – all partners must read the contract and annexes. It is very important to read the eligible and non eligible costs and transfers if over 20% will have to request an amendment. Common mistake is the subcontracting, has to be done with the real procedures (public procurement rules that you have to follow in your institute)if you don't

have any should follow the commission rules. Must publish the bid, show how you evaluate the bids. Major changes must be done at least one month before the end of the project. Engineer your budget in such a way that you will be able to use your money. Must inform the agency of major news so that the information can be disseminated by the commission. Must follow local rules for procurement.

c. Mechanism and discussing with DG Research for the RD management

E-HOD overview (Henk Blom)

1. need to use the new logo (Hristina)
2. add the executive summary here and list of partners in the annex
3. add list of project deliverables

Marike

1. Employed as project officer not as a patient organization but is the mother of 3 children with a mild IMD. As project officer her role will be to chase project progress and maintain the project members enthusiasm .
2. From the patient perspective, the EHOD needs to deliver an easily accessible website and information which is relevant for patients with varying disease and age groups. Patients would like to see tangible outputs from EHOD

registry (stefan kölker)

4. the deliverable of the E-HOD registry is
5. the staff from Heidelberg involved are:
6. technical and security aspects of the registry were presented
7. When applicable, the EHOD will apply for an amendment to the EIMD ethical approval
8. Partners can get started on the registry as soon as they receive ethical approval. they will be sent a personalised access code and user manual.
9. the registry has been developed in a user friendly manner in which only questions appear step by step and relevant to data entered
10. there are automatic quality controls of data items including missing data, outliers, or incorrect punctuation
11. Normally there is only one or two access codes per centre. However centres may have additional people supporting patient information and asking for consent etc.

Newborn screening for homocystinurias and methylation defects

g. the subject is likely to cause a lot of discussion about issues and cut offs etc. go back to the question why we want to screen people and go back to the screening criterea. For CBS deficiency that yes it is important etc but not so easy to answer the question on the effectiveness of treatment and the reliability of test. Currently we do not have control studies to show that early treatment is beneficial. For CBS we have good evidence however for Cobalamin C, MTHFR and other defects the benefits are less clear. the future strategy addressed by EHOD is to suse standardized treatment algorithmys and evaluation of treatment. But what about the tests? methionine can be elevated or low and it has been suggested to measure homocysteine. Some countries have discontinued the nbs programme for CBS as they have not found any cases. Methioninge should be elevated in CBS deficiency. there is a broad varieation in cutoff s ranging from 50 6 240 mcmol/L. there are risk factors for missing cases such as early screening, breast feeding, low protein intakd, pyridoxine responsive forms. in conclusion sensitivity of …..the study from Qatar was presented in a population at high risk for pyridoxine non-responsive CBS deficiency. Qatar have offered a model with a cuto off for Meth at 40 and second tier testing for Hcy. but we don not know if this will be adapted for the European population – this needs to be evaluated. Another model is proposed with tandem mass screening. simple algorithym. A more complicated approach to find CblC type (New York). would like to focus group that it is difficult to compare this data with other algorithms. will be able to answer these questions after the project: establishment of sandardisesd treatment strategies, evaluation of outcome, single analyst approach (meth) not sufficient, cutoffs are variable – population based curoffs mandatory complex algorithms seem promising but need evaluation.

dissemination

12. E-HOD logo:

13. website structure will be similar to the E-IMD registry.

presentation agency

14. the agency was established in December 2004 and is operational since 2006 as public health executive agency name since changed to the executive agency for health and consumers. the EAHC manages the health projects and related events, disseminates know-how and best practices, fosters exchange of information, feed-back project results to DG Sanco to develop other policy.

15. the commission sets priorities in the annual work plan and liases with the MS

16. the project officer for E-HOD is Hristina Mireva who will follow for the projects life-time. She participates in the kick off and other meetings if necessary, follows up on project progress and dealing with any enquiries. Projects must focus on deliverables and their quality as they will be published on the website.

17. role of associate collaborating partners and subcontracting

18. Important that communication must go from the coordinating partner to the agency. if necessary the agency will refer the information to the DG Sanco.

19. financial and technical reports should be sent annually with m12 + 2 months. the agency monitors the project from time-to-time on site visits.

20. do not have an official template for the technical report; should take into account the content of the project. for the financial report there are templates on the website. the final report should contain all information and activities over the 3 year project. this report should be accompanied by all deliverables listed in the grant agreement (paper and electronic copies). the final financial report should also cover the duration of the project. The project must have prior approval for travel outside of Europe. should use financial rules of the commission for subcontracting.

21. Summary of which costs are eligible and which are not. Eligible costs are those detailed in the financial annex. they should incur during the lifetime of the action. costs should be identifiable and verifiable and recorded in the accounts.

22. Documents that should be kept by each beneficiary: time sheets and salary slips, invoices related to travel, subsistence, other. All invoices must include the name of the project and the grant agreement. and must have the institution name not the personal name.

23. payments not in Euro should refer to Article II;16.1 of the grant agreement: should use the first day of the month following the end of the reporting period. For EHOD the first report will use the date of xxxx the second the date xxxx the final financial report should forget the previous exchange rate and use the 1st March 2016

24. Changes requiring an amendment are additiona replacement of the main/associated beneficiairies, change of the name fo a beneificiary or budget transfers. first should request an amendment and when we receive the signed amendment

25. when the budget transfer is up to 20% the project officer informs the project officer. If over 20%

26. few practical suggestions: keep a copy of the grant agreement/contract, keep all project documents, correspondence and invoices together. Provide bank details to the project coordinator; ask the project coordinator is something is not clear

27. useful links on the each website can find guidelines for the request of a payment, fact sheets on project management etc.

28. all publications and dissemination related to the project should have the logo

29. work to identify POs that are specific to homocystinurias and methylation defects.

30.

J-UCD

31. The Japanese network for UCD is lead by Prof Fumio Endo and currently has 600 members. The network has identified a need for training general practitioners and they provide courses for 350-400 participants per year.

32. The network has received a grant of 10 million Yen which has allowed them to organise a patient organisation meeting this year in Tokyo and set up the registry. A second grant of 70 million is for the establishment of guidelines of liver and cell transplantation for IEM. A third grant is on-going for 50 million to establish guidelines for diagnosis and treatment of IEM.

33. A main issue in Japan is that IEM patients are not centralised into centres of expertise, but patients can to go any local hospital for care. This is changing.

UCDC

34. Marshall Summar provided an update on the Urea Cycle Disorders Consortium activities. The UCDC conducts several different study protocols. The longitudinal study contains data on 571 patients, of which 421 are late onset. Details of the neuropsychological and behavioural outcomes were presented.

European Reference network & registry policy

35. Stephan Lynn, Treat NMD project manager, Newcastle University and E-HOD collaborating partner, gave an update on the implementation on the Cross-Border Healthcare Directive 2011/24/EU, in particular the provisions pertaining to the European Reference Networks. The Directive is to be transposed by Member States by October 2013. Discussions of the Committee on Cross Border Healthcare are confidential

36. A parallel group at the EUCERD has looked at the experience of EC-funded pilot ERNs. A number of components of networking have been identified such

as databases, registries, biobanks, tele-expertise tools, guidelines, information packages, and training tools covering the medical and social dimensions of diseases. A meeting in September 2012 is planned to define recommendations from the EUCERD for the criteria of ERNs. This work is challenging due to the parallel work of the Expert Group of the Committee on Cross -Border Healthcare as not all the generic criteria are known.

37. In terms of designation, ERNs for RD should be as inclusive as possible in terms of number of diseases and numbers of centres involved, and access to an ERN should be provided to those patients still seeking a diagnosis: thematic networks may be a solution.

Next meeting

38. Day preceding the 2013 International Congress for Inborn Errors of Metabolism in Barcelona

39. List of Participants

Country	Name	Organisation
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4. 3RD ADVISORY BOARD MEETING

1st Joint Advisory Board meeting of E-IMD and E-HOD

Sunday, 1st September 2013, Barcelona

Summary for public dissemination

The 4th E-IMD advisory board, in association with E-HOD, was held in Barcelona on 1st September 2013. E-IMD now has 80 partners from 24 countries in 4 continents. The European registry currently has over 700 patients from 29 partners in 18 countries. The data analysis and publication strategy were discussed. E-IMD has developed guidelines for the UCD and GA1; guidelines for PA, MMA and IVA are in progress. These guidelines should be endorsed by national socieities and translated into local language. Prof Henk Blom presented the E-HOD network and registry for homocystinurias and methylation disorders which started in February 2013. Exciting presentations were given by Jarosław Waligóra on the implementation on the cross-border healthcare directive in particular the provisions pertaining to the European Reference Networks (ERNs) and by Professor Paul Landais on registries and national common data elements for rare diseases.

E-IMD: overall activity and registry report (Stefan Kölker, Heidelberg)

Slides attached. E-IMD has succeeded beyond expectations. Stefan welcomed new members to the network which has now reached 80 partners (60 clinical partners) in 24 countries and 4 continents. Deliverables are on schedule. On 1st September the registry contained data on over 700 patients which have been recruited from 29 partners in 18 countries. The analysis was on 640 patients (cut off 15th August). E-IMD was not aimed at analyzing incidence and prevalence however in small centralized countries, we may be able to estimate minimum prevalence.

It is clear that associate partners receiving resources for data entry are performing better compared to collaborating partners, participating on a voluntary basis. This is an essential point to consider when thinking about sustainability of the registry.

Data analysis by disease shows a likely underestimation of severe early onset OTC. This is not unexpected since the registry only contains data of patients being born or being following by metabolic centres at or after 1st January 2011. All patients (predominantly with a severe phenotype) who have died before this cut-off date are not included in the registry. It is expected that the number and proportion of patients with an early onset disease will increase with the continuation of E-IMD. The interim analysis also highlights the need to focus on collecting the data on the very rare conditions, such as HHH and NAGS deficiency.

The publication strategy was presented. By the end of 2013, a total of five publications are planned focusing on (1) the establishment of the E-IMD network and registry, (2) comparative phenotyping of patients with UCD and OAD, (3) (4) evaluation of the impact of diagnostic and therapeutic strategies and the neurological outcome of patients with UCDs and OADs, and (5) behavioral problems and quality of life assessment.

E-IMD evaluation and PO group report (Hannigan, Crewe)

Steve Hannigan presented the tools to evaluate the success of E-IMD. The first tool is the website whose primary function is to show what E-IMD is doing and help individuals gain a better understanding of OADs and UCDs. However the number of accesses per day, time spent on website and downloads is low and needs to be improved. Results of the survey to patients were also presented and the plan for an end of project survey.

E-IMD dissemination report (Dobbelaere, Lille)

The website is an important part of the dissemination activities and work is being carried out to improve the number of visits e.g. Facebook page, twitter. YouTubes are also in progress and newsletters need to be sent more often with a wide dissemination.

E-IMD guideline report (Presented by Baumgartner, Zurich)

The UCD and GA1 guidelines have been published. The PA, MMA and IVA guidelines are in progress. Each E-IMD member should push for the guidelines to be endorsed by national socieites. It has been agreed to write a short 2-page summary of the guidelines for public dissemination on the website.

E-HOD activity report (Blom, Amsterdam)

Henk Blom is the coordinator of the European Network and Registry for Homocystinurias and Methylation Disorders (E-HOD). E-HOD uses the platform and resources of E-IMD to add fifteen diseases to the registry and network. The specific objectives are to:

a. set up a European patient registry

b. develop guidelines

c. evaluate the new-born screening programme for the homocystinurias in Europe.

Concept and progress on European Reference Networks (Jarosław Waligóra)

Jarosław Waligóra updated the group on the process of defining European Reference Networks (ERN). ERNs are included in the cross border directive that should be transposed by member states before 23rd October 2013. From this date MS are expected to include ERNs in their national health care systems.
There will be a competitive call for networks, expected in 2014. Designated ERNs will be evaluated every 5 years. There will be one common logo for all ERNs to which specific logos can be associated.
Slides attached

Towards common data elements: strategies to proceed (Landais, Paris)

The French national plan for rare diseases includes the project for a national rare disease databank. The overall objective is to improve the quality of patients care by coordinating the rare disease structures by a shared information system. There are two complementary programmes: Bamara (banque maladies rares) and Radico (Rare disease cohorts). The project has defined a minimum dataset, divided into 13 groups of information, which has been agreed for mandatory collection for all RD and reporting at a national level.
Slides attached