European
Reference
Network
for rare or low prevalence
complex diseases

Network
Hereditary Metabolic
Disorders (MetabERN)

SCIENTIFIC REPORT

MetabERN

Board Annual Meeting

April 9th - 10th, 2018
Lindner Congress Hotel
Frankfurt - GERMANY

AGENDA

MetabERN Annual Board MEETING

9-10 April 2018
Lindner Congress Hotel, Frankfurt
Frankfurt, Germany

9 April 2018 Program			**Parallel Session**
9:00-9:40	**Opening remarks: aim of the meeting and network vision** *Maurizio Scarpa*		
9:40-10:10	**White Paper** *Daniela Negri*		
10:10-10:40	**The patients' role in MetabERN: the first year of work together** *Maurizio Scarpa*		
10:40-10:45	**Discussion**		
10:45-11:00	Coffee Break		
11:00-11:20	**The U-IMD Registry** *Stefan Kölker*		
11.20-11.40	**Cooperation between U-IMD and the ERKNet registry** *Franz Schäfer*		
11.40-12.00	**The EU RD Registration tools** *Holger Storf*		
12.00-13.10	Discussion		
13:10-14:00	Lunch		
14:00-14:30	**The CPMS** *Herman Brand (EC)*		
Follow 30 mins Presentations for each WP: What has been done and what needs to be completed (5 mins) Encountered problems (5 mins) Plans for the Second Year (5) mins) discussion and inputs from the Subnetworks & Patient Organizations (15 mins)			
14:30-15:00	**Work Package 5:** Virtual Counseling Framework *Klaus Mohnike & Terry Derks*		
15:00-15:30	**Work Package 1:** Coordination Presentation of the result of the Satisfaction Survey MetabERN *Maurizio Scarpa* **Discussion on Advisory Board** *Daniela Negri & Karen Schober*		
15:30-16:00	**Work Package 4:** Guidelines and Care Pathways and Standardisation *Athanasia Ziagaki & Carlo Dionisi*		
16:00-16:30	**Work Package 3: Evaluation**		

	Viktor Kozich		
16:30-17:00	Coffee break		
17:00-17.30	**Work Package 8:** Continuity of Care *Maurizio Scarpa & Yngve Thomas Bliksrud*	**16.45-18.30**	**Parallel Session: U-IMD Registry** *Stefan Kölker and the U-IMD Team*
17.30-18:00	**Work Package 2:** Dissemination *Mireia Del Toro*		
18:00-18:30	**Work Package 7:** Capacity Building & Training *Nadia Belmatoug*		
18:30-19:00	**Discussion and Wrap-up** *Maurizio Scarpa*		
	Dinner		

10 April 2018	
8:30-9:30	**Work Package 6:** Research, Translational Activities and Clinical Trials *Maurizio Scarpa & Cinzia Bellettato* Work Package 6: Report on advancements in selected fields of IMD research *Jean Michel Heard*
	Coffee
09:45-12:00	**7 parallel breakout sessions of the disease sub-networks**
12:00-13:00	**Sub-networks reports in plenary** (8-10 minutes per group)
13:00-14:00	Lunch
14:00-14:30	**MetabERN involvement in EU projects** *Maurizio Scarpa*
14:30-15:30	**Sustainability of the Network/Stakeholder Meeting/establishment of *MetabERN grant office*** *Maurizio Scarpa & Ans van der Ploeg*
15:30-15:45	**Results Satisfaction Survey** *Maurizio Scarpa & Corine van Lingen*
15:45-16:00	**Getting ready for the annual IAB Assessment** *Maurizio Scarpa*
16:00-16:30	**Discussion and wrap up**
17:00	End of meeting

MetabERN Kick-off Meeting - Participants

110 participants attended the meeting, mainly clinicians (e.g. paediatricians, neurologists etc.) representing 54 of the 69 Healthcare Providers (HCPs).

Importantly, this year, among the participants there were also 13 Patients Representatives (PRs) that were involved to include inputs on patient needs and expectations and to generate support for the MetabERN activities.

The general atmosphere was friendly, free-thinking and productive: all participants were highly motivated and overall there was a strong sense of collaboration and of excitement. The outcomes of the meeting were very encouraging and positive.

Opening remarks: aim of the meeting and network vision

Maurizio Scarpa

Prof Maurizio Scarpa, the MetabERN Coordinator, opened the meeting and welcomed the participants. He gave an overall presentation of the agenda of the meeting and highlighted the importance of creating a collaborative team both at medical and patients level

Aims of the meeting

- To discuss the achievements of the first year of MetabERN activities and any encountered problem occurred during the project's implementation;
- To give an overview presentation of the planning for the second year of activities,
- To share duties creating a good basis for working together throughout the project, especially involving the PRs.

MetabERN in Brief

Today MetabERN involves 69 certified Health Care Providers endorsed by the Ministries of Health from 18 different EU countries. MetabERN is endorsed by and partners with the Society for the Study of the Inborn Errors of Metabolism (SSIEM). All these members aim to work together with POs in a coordinated way to improve quality of life for people who are affected by certain rare metabolic conditions and their families

MetabERN Mission

To generate a patient centered European Reference Network for hereditary metabolic disorders able to bring the best expertise to patients to facilitate prevention and diagnosis, management and access to therapy to patients affected by rare inherited metabolic diseases (IMDs).

MetabERN Vision

- To meet patients 'need in term of diagnosis, management and access to therapy for IMDs;
- To facilitate the cross border access to therapy for patients with IMDs
- To supply the EU community with a tool able to unify and uniform services to meet patients 'need;
- To interact with stakeholders to facilitate the access to therapy and management in a sustainable system.

Aims of MetabERN

- To pool knowledge and improve information exchange between network partners;
- To improve prevention, diagnosis and care in disease areas where expertise is rare;

- To support Member States with a small number of patients to provide highly specialised care;
- To advance innovation in medical science and health technologies;
- To provide cross-border medical training and research.

The importance of having all the members actively participating to the activities of the network in a responsible way was particularly stressed.

HCPs and PRs will in fact be evaluated throughout the project development and eventually invited to step back if not complying with MetabERN quality standards

The patients' role in MetabERN: the first year of work together

Maurizio Scarpa

Ms. Lut De Baere, President of the Belgian Patient Organization for Rare Metabolic Diseases and responsible for the MetabERN Patients organizations (POs) management could not participate in the meeting so Maurizio Scarpa spoke on her behalf highlighting that the patients and patients´ empowerment are at the center of the interests of the MetabERN

Goal	The main goal of Patients representatives inside MetabERN consists in ensuring the largest possible patient involvement in the network.
Objectives	To identify and enrol Patients Organizations representatives that can act as "communication and information" actors, from professionals to patients, and vice versa.
Strategic Actions	To achieve its goal and to facilitate patients participation a series of action has been undertaken: • The establishment of a proactive collaboration with Eurordis: one of the major sponsor of the concept of ERNs • The Collaboration with the 6 representative of the European Patient Advocacy Groups (ePAGs) elected by Eurordis • The identification and mapping of all the known patient groups active in the area of rare inherited metabolic diseases (we have a database that gives an overview of the existing and known POs: 366 POs have been identified and divided per countries and subnetworks • The production of a list of international, national and regional family associations to engage with us. • The sending of formal invitation letter to join the network. • The sending of a letter to miss Theresa May, the Prime Minister of the United Kingdom, and UK government and to PM inside the EU Parliament regarding Brexit to ensure that a

solution is found so that the UK healthcare providers can continue to participate in the ERNs and all EU patients can benefit from a cross border collaboration.:

MetabERN POs Steering Committee

After the MetabERN meeting with POs in January 2017 some people volunteered to take part in the Steering Committee (SC) in charge of involving the POs, defining the different priorities and understanding the needs of patients.

Brown Collin	LSD/Krabbe -	UK
De Baere Lut	BOKS -	BE
Dekker Hanka	VKS -	NL
Devaux Marie	PKU -	FR
Francisco Rita	CDG – Porphyria	PT (ePAG)
Hugon Anne	GSD –	FR (ePAG)
Sestini Sylvia	AKU -	IT
Cristina Lampe	MetabERN Medical PRs Responsible	DE

MetabERN PRs

All the PRs are going to be involved in the different activities of the MetabERN and in particular they will participate in the governance, ethics, care, research, and evaluation of the MetabERN. The network is trying to enlarge the participation of PRs and facilitate the collaboration with SNW and WP leaders. To this aim MetabERN has started the organization of Disease Specific Units .

Survey on patient needs

A survey aimed to identify patient's needs and expectations is under development and is been translated in several languages.

Next steps

- Create a better defined governance structure
- Improve the collaboration with the specific working groups
- Improve the EU diseases groups
- Start and involve PRs in the monitoring and evaluation of the network
- Understand whether the right of the patients in EU are equal or not
- Understand and address the significant differences in the treatment and care for metabolic patients across Europe

White Paper

Daniela Negri

A White Paper on access to treatment for rare hereditary metabolic diseases in Europe is being developed.

The aim is to identify the challenges and disparities with regard to access to EMA approved Orphan drugs within EU Member States and to derive Recommendations on how to expand the coverage in term of disease for which a drug exist, drugs availability in the national markets and costs sustainability (for patients and Health Authorities)

To develop the baseline mapping a list of currently EMA-approved drugs has been made available by the Benzi Foundation and it has been cross-referenced with the list of all currently known hereditary metabolic disorders. According to the outcomes the drafting of the first outline of the survey that is at the basis of the White Paper was initiated and today surveys for the collection of data on EMA-approved treatments for three of the MetabERN sub-networks have been produced (AOAs, LSDs and NOMS).

The survey for the LSDs has been already uploaded and tested on Survey Monkey and is ready for distribution.

Areas covered by the surveys

- Availability of pharmacological treatment for LSDs with approved OD treatment in country & centre (e.g. Fabry disease)
- Availability of specific OD treatment
- Limitation to prescription of OD treatments
- Delay in access to treatment
- Barriers to access
- Opportunities for improvement

Patients involvement in this task (as part of the WP6 activities)

- Surveys are supposed to be distributed to professionals but we also want to develop one for patients, and as soon as the first is developed we will work with patients in order to understand communalities and difference among HCPs and Patients answers.

The U-IMD Registry

Stefan Kölker

U-IMD is the acronym for the Unified European Registry for Inherited Metabolic Disorders. The overall aim of this project is to promote health for children, adolescents and adults affected by rare Inherited Metabolic Disorders (IMDs).
MetabERN is proud to provide multidisciplinary collaborations that include the leading experts in the field of inherited metabolic diseases. Besides their expertise MetabERN experts bring their already existing contacts to European scientific societies and to relevant stakeholders into the network.

More info at https://u-imd.org/

Cooperation between U-IMD and the ERKNet registry

Franz Schäfer

Patients with IMDs often present with multiple organ manifestations. For this reason, collaboration with other ERNs is indispensable to achieve the goals of MetabERN. Since kidney malformations, acute and chronic renal disease, and tubulopathies are frequently found in IMD patients and since extracorporeal detoxification is used in the acute setting of metabolic decompensation as well as for IMD patients with chronic kidney disease, MetabERN and U-IMD closely and actively collaborate with the ERN for Rare Kidney Diseases (ERKNet). ERKNet is a consortium of 38 expert paediatric and adult nephrology centres in 12 European countries providing healthcare for more than 40,000 patients with rare kidney disorders. The two ERNs have already identified an important common field for interdisciplinary research and collaboration and, in an unprecedented collaborative effort, are joining forces to develop a standard for minimal core data sets to be used by both ERNs alike, thus reaching for a maximum level of interoperability of patient records. The sharing of these goals and objectives between the two networks will positively influence the natural disease course of IMDs and adds value to the networks involved.

The EU RD Registration tools

Holger Storf

The Medical Informatics Group is working with the Joint Research Centre. The presentation focused on the functionalities of the European RD Registry Infrastructure (ERDRI). The latter uses open source software to develop the ERDRI and the focus is on the technical support of data exchange and interoperability. The underlying principles of the ERDRI-infrastructure are that there is no storage of identifiable data (IDAT) and that there are no whole registries hosted. The data-owner will keep data sovereignty with the data owner or custodian. The directory of Registries (DoR) can be seen as the yellow pages in which the other registries can be found. In the MDR (Metadata Repository), the data elements of the registries are defined. One registry knows what the other one knows.

The question from the room was whether there will be connections between the ERDRI registries and for example hospital databases. This could be possible if the interfaces are connected.

The CPMS

Herman Brand (EC)

The Information Systems unit within the Commission developed the Clinical Patient Management System (CPMS) for the ERNs and launched in November 2017.
The CPMS is the first and only IT data sharing platform which can be used in the 28 Member States
It is a secure web-based application that enables health professionals from the ERNs to discuss complex cross-border cases in a multidisciplinary way ensuring that the needed expertise can travel to the patient, instead of the other way around.
CPMS is based on a set of generic common data elements. The Integrating health enterprise (IHE) can be used in combination with CPMS. Very few hospitals have agreed to start the process of IHE. The system gives the option to register time spend on the different steps so after 1 year it will be possible to start talking about reimbursements.

The CPMS has been developed and approved by the EU Data Protection Supervisor and it is set up according to the guidelines of the new EU Data Protection and Privacy legislation, which will come into force on 25 May 2018. Despite this, some countries have raised concerns regarding the need of approval of the informed consent from Ethical Committees, the storage of the data and the liability of the outcome reports.

Presentations for each WP

Strategies and plans for the forthcoming months were discussed. WPs leaders had been asked to present and discuss their work and their proposal for the action plan designed to achieve the results foreseen by the end of 2018 (milestones and deliverables), taking into account specific objectives, indicators, and possible interactions with other WPs, SNWs and PRs.

Work Package 1: Coordination

Presentation of the result of the Satisfaction Survey MetabERN

Maurizio Scarpa

This Work Package is developed for the good management of the project, including the submission of interim and final reports, and for administrative and accounting activities, as well as the disbursement of funds for approved activities. The scope of the work includes activities for the day-to-day monitoring of the project progress.

Main activities performed during the first year

The main structure of the network and all the meetings that enable a smooth running of the cooperation, coordination, management and communication have been set up successfully.

Encountered Problems

- Unresponsiveness of several members
- Difficulties in combining participants availabilities when planning TC/WebEx
- Delays in getting feedback
- Use of the ECP/CircaBC and of the CPMS must be implemented inside the network.

Collaboration with other ERNs

The ERN Coordinators Group (ERN-CG) has been established on April 26th, 2017. It brings together the coordinators of the 24 approved European Reference Networks (ERNs) and is chaired by Maurizio Scarpa.

The ERN-CG focuses on strategic issues relevant to the ERNs implementation, functioning and governance and provides advice to the commission and Member States when needed in matters related to the ERNs. It has created WPs that are working on important topics crossing the different ERNs

Results Satisfaction Survey Coordination & Management

The results of the satisfaction survey developed by the Project Management Team were shared and discussed. The results of this can be found following this link: https://drive.google.com/open?id=1xCKPxXbnF3nqPFPBG0JR3DNb7rOIlgSX.

Change of WP leadership

WP	in the beginnng was led	now is led by
WP2	Eva Morava	Mireia del Toro
WP4	Ursula Ploeckinger	Athanasia Ziagaki
WP8	Shamima Ramam	Trine Tangeraas & Yngve Thomas Bliksrud

Main activities to be performed during the second year

In the second year WP1 will focus on the maintenance of efficient and effective project management. This will be achieved through continuous monitoring of the progress of both Work Packages and Subnetworks, including the preparation of bi-monthly reports that will feed into the annual report. The organisation of Board meetings involving all stakeholders will be crucial to ensure regular information exchange. Moreover, the WPs will focus on creating synergies with other ERNs in order to be able to tap into existing expertise for the benefit of patients. Meetings with other ERNs/RD Connect/EC will be crucial for sharing knowledge and best practices and identifying common strategies to avoid duplication of efforts and to harmonise and integrate expertise and impact of EU rare diseases policy. External subcontractors will be identified to support the management of the Advisory Board and the organisation of the Board Meeting.

Use surveys to address major issues: limit of 1 survey per WP per year

Transfer the coordination

Participants had been asked to vote for the continuity and to transfer the coordination in the case Maurizio Scarpa changes hospital inside the MetabERN: The unanimity of the board (109 MetabERN representatives) is in favour for Maurizio Scarpa to maintain the coordination with him and to transfer it to any Health Care Provider inside the MetabERN. This is very rewarding according to the future movements.

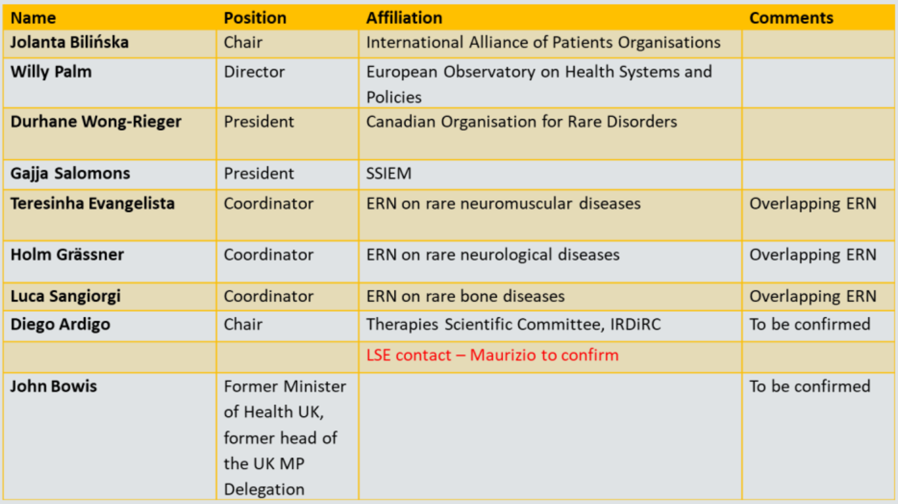
The MetabERN Advisory Board

The MetabERN Advisory Board will bring together representatives of family associations, foundations, policy-makers, representatives from collaborating networks and other relevant stakeholders.

Members serve for a 5-year renewable term.

The purpose of the Advisory Board is to provide input into the planning of activities of the MetabERN, evaluate the implementation of said activities and support their dissemination.

The below proposed composition was unanimously approved



Name	Position	Affiliation	Comments
Jolanta Bilińska	Chair	International Alliance of Patients Organisations	
Willy Palm	Director	European Observatory on Health Systems and Policies	
Durhane Wong-Rieger	President	Canadian Organisation for Rare Disorders	
Gajja Salomons	President	SSIEM	
Teresinha Evangelista	Coordinator	ERN on rare neuromuscular diseases	Overlapping ERN
Holm Grässner	Coordinator	ERN on rare neurological diseases	Overlapping ERN
Luca Sangiorgi	Coordinator	ERN on rare bone diseases	Overlapping ERN
Diego Ardigo	Chair	Therapies Scientific Committee, IRDiRC	To be confirmed
		LSE contact – Maurizio to confirm	
John Bowis	Former Minister of Health UK, former head of the UK MP Delegation		To be confirmed

Patients involvement in WP1

Patient representatives of the steering committee will be the ones mainly involved In the WP1 activities, nevertheless all the patients representatives can contribute to the activities of the WP1 aimed at improve the coordination of the Network and strengthen the collaboration among physicians and Patients representatives (satisfaction surveys and other questionaries' aimed to better identify patients' needs and expectation collecting inputs, comment, ideas).

Work Package 2-Mireia del Toro

Main activities to be performed during the first year

The website (www.metab.ern-net.eu, 4500 visits in the first 3 days), social media channels (Twitter, Facebook, LinkedIn) and the monthly newsletter have all been set up, sent out and kept up to date since January 2018. A press release was issued in March 2017 and the patient brochure has been designed and translated from English into French.

MetabERN members have spread the message of the existence of MetabERN in numerous conferences and meetings where they were invited as speakers. On 13/1/2018 the meeting for Patient Representatives (PRs) took place in Frankfurt. Patients organization per each MS have been identified, contacted and invited to take part ot MetabERN activities as a result 24 PRs from 10 MS (BE, DE, DK, FI, FR, IT, LT, NL, PT, UK) plus Russia and Serbia attended the meeting on January 13, 2018.

One of the questions is whether there should be closed areas on the website.

Encountered problems

The website was online later than expected due to delays at the end of the IT- provider.

Main activities to be performed during the second year

WP2 will implement a series of dissemination activities (presentations at conferences, published papers, patient support group education and conferences, newsletters, videos, educational web presentations, social media channels and website). A dissemination plan defining strategies, processes and tools to promote the projects and its output will be developed. Patient involvement in all dissemination and awareness activities will be ensured. The WP will also ensure continuous liaison with EU policy makers and relevant stakeholders, for example through the organisation of a meeting in the European Parliament that will inform policy makers about the needs of patients with IMDs. To ensure that the materials prepared for the Parliamentary launch of the project are appropriate and suitable for a policy audience, the preparation and organisation of the event will be subcontracted to a third party with proven experience in rare disease policy. A retainer contract will also be granted to a third party for the maintenance of the website and social media channels.

For the patient organisations section in the website we can think about collecting material from/for patients, a make patient oriented newsletter (2/3 months) as well as add links to patient organisations.

With regard to patient involvement: identification of the Patient associations per SNW and country, construction of a list of contact who will be recipients.

We are also in the process of developing a survey to patients on what they expect etc.

Patients involvement in WP2

- **Organizational level:**
  - Identification of the patient associations per sub network and country
  - Construction of a list of contacts which will be the recipients of the communication
  - Questionnaire:
    - What they expect
    - What they need
    - What they already have
  - **Participation level:**
- Exploiting opportunities to generate exposure of the project and the constant search for appropriate dissemination channels
- Directly participating in dissemination activities
- Giving presentations and publishing papers, with particular attention to acknowledge network affiliation
- Giving talks about the collaboration in the ERN

- Developing or sharing information addressed to a lay audience and for patients and their families as well as for HCP
- Helping the periodically providing contents and news for the website, newsletter
- Sharing MetabERN news on social media
- **Simon James Bond, affected by Mucopolysaccharidosis II B, has been appointed as collaborator to the planning and management of the socials (Twitter, LinkedIn, Facebook etc.) and the management of the MetabERN website.**
-

Work Package 3: Evaluation- Viktor Kožich

Main activities performed during the first year	A policy on continuous monitoring system as well as an approach for periodical self-assessment for all the ERNs have been written by a working group within the ERN-Coordinators Group (ERN-CG), to which MetabERN representatives has actively participated. As soon as this policy is approved by the EC and BoMS, MetabERN will use it as guidance for internal evaluation. The Conflict of Interest policy is being written by the ERN-CG Working Group on Ethics and Legal Issues as well as the form that will be used to disclose conflicts of interest. The survey on patient needs has not been shared yet but is in its final stages of drafting. The delay is mainly due to the fact that MetabERN the network wanted to incorporate more inputs from the patient organisations and representatives. Translation of the survey in several languages are foreseen to enhance the take up and understanding by the respondents. The same is being done for the survey on HCP needs that is also in the drafting phase.
Encountered problems	• originally MetabERN-specific items (COI, evaluation) changed to general ERN policies • Complexity and little minimum of examples • Multiple bodies involved in drafting and revising of documents including Working Groups of Coordinators Group, BoMS and the Commission • Involvement of WP3 members and activity of WP Leader
Main activities to be performed during the second year	WP3 will ensure transparency on possible conflicts of interest and the official adoption of a Conflict of Interest policy. The WP will develop a survey to assess the needs of HCPs and to develop criteria for the evaluation of professional-centered needs for MetabERN services. Surveys will be also used to monitor the satisfaction of HCPs with MetabERN activities in daily clinical practice. Similarly, patient needs and expectations about activities will be identified and specific criteria for the evaluation of the patient-centeredness of services will be developed.
Patients involvement in WP3	• By directly assisting the Coordinator, Management Board and Advisory Board with monitoring progress • By ensuring the interactions between stakeholders involved in the care for patients with IMDs are transparent and credible • By evaluating the impact of MetabERN activities on patient care.

- By actively responding to the surveys and questionaries' that will be shared

Work Package 4: Guidelines & Clinical Pathways – Athanasia Ziagaki

Main activities performed during the first year

- Discussion on Guidelines vs. Clinical Pathway Recommendation (CPR)
- Definition of the Target Groups for CPRs: in this WP there has been progress made on the identification of the primary target group, the setting up of the online platform and the expectations have been drafted.
- Definition of the first 5 Diseases by each Subnetwork group for which CPRs are to be set up
- Building a platform for setting up CPRs; in the Google Drive platform there is an extensive step-by-step approach in order to be able to write CPRs according to the same forms and schedules. The quality assessment uses the AGREE assessment tool or Grade. To pool knowledge and improve information an online accessible information platform on GLs and clinical pathway recommendations (CPR) has been developed and created. It contains all the documentation necessary to produce guidelines and contains guidelines and care pathways recommendations already available for a number of selected IMDs.

WP-4 is proposing to have a 1-day meeting to discuss the setting up of the CPRs with the persons involved in this WP. WP4 Guidelines, Care Pathways and Standardisation for Medical Care and Transition:

Main activities to be performed during the second year

WP 4 will focus on the development of transition guidelines and unmet needs in this area. A consensus statement will contain an overview on transitional requirements in IEM. The WP will also define and prepare a first pilot project for Guidelines/Care Pathways, starting with consensus on the workflow that has been set up for GL/CP documentation. A standardized tool for disease-specific key parameters will be developed in order to be able to evaluate the implementation and impact of GL/CP on disease outcome. Defining measurable disease-parameters will facilitate i) the evaluation of clinical practice, ii) documentation of the natural course of the disease and thus knowledge and treatment options/efficacy. Consultations with all WP and Subnetwork leaders as well as with European and national scientific societies will take place before implementing the final tool.

TIMELINE

CPRs

- All CPRs should be delivered until November 2018
- All CPRS will be evaluated by the WP4 group for adherance to the quality assessment and form of presentation
- January 2019 all corrections completed and material delivered for MetabERN website

- January 2019 all subnetworks named the next 5 diseases for which CPRs are to be developed

- To be discussed for priorities
- CPRs done

Open Questions

- Should we add to those CPRs emergency recommendations?
- Should we add to those CPRs fertility and pregnancy recommendations?
- Should we add to those CPRs neonatal and pediatric care recommendations?
- Are CPRs translated for patients more important?
- Any ideas on how to proceed with transition?

Guidelines

Develop GP especially for Rare Diseases where no GD exist

Patients involvement in WP4

- By playing an active role in the process of standardization of recommendations, guidelines and care, assuring a patient friendly language.

Work Package 5: Klaus Mohnike, Terry Derks

Main activities performed during the first year

The EC has provided all the ERNs with the Clinical Patient Management System (CPMS) that has been launched in November 2017. This WP has worked on facilitating and promoting the use of the CPMS inside the MetabERN, getting as many patient consultations in the pilot phase done as possible as well as to get all our members registered to the system. We have performed 7 consultations with various results due to technical and performance problems of the system.

Guidelines for intellectual property have not been written since, before setting up a complete intellectual policy including guidelines, the Code of Conduct and the Conflict of Interest policy need to be finalised.

As said in the context of the WP3 this document is being developed within the Ethics working group under the ERN Coordinators Group and will be followed by an internal discussion, which will be done together with the HCPs representatives participating in this WP. For this reason it has not been possible to proceed with the drafting of the IP document.

Encountered Problems

- Technical (Logistics, speed, support, Interconnectivity with existent software) and legal problems limited the use of the CPMS
- Also the fact that hospitals are not paid for second opinion is a limiting factor: CEO are not incentivizing the use of the CPMS
- Expert for 2° opinion should be named by subnetwork coordinators
- EU-Consent form has been questioned at some HCPs
- Active roles for end users (HCPs and patients?) So far the CPMS is not intended for the direct use of patients. A video could be shared with patients in order to let them know how the system works and its potentialities.

- It should be open for collaborations with non-EU colleagues

Main activities to be performed during the second year

WP5 will focus on promoting, implementing and developing the use of the CPMS within the network. Guidelines for the use of the system need to be developed and the system needs to be used on a regular basis by all HCPs in order to improve its use. Continued input and support from the IT Helpdesk is expected. Furthermore, this WP will focus on using the CPMS to develop guidelines for data and DNA sampling collection

Patients involvement in WP5

- By playing an active role: data transfer using existing apps (GSD, Groningen)
- By taking part to group discussions with varying partners: Interaction with the Subnetwork-Patient Representatives (PRs)
- Supporting the structure and the development of the CPMS: (GSD, Groningen)
- Facilitating the creation of cross-border multidisciplinary teams: PRs should inform on CPMS for 2nd opinion

Question

- **What happens if the advisor provide indication that are not valid in the country of the patients?:** The doctor initiating the panel is responsible for the patients, it is up to the physician to decide what really do with the recommendation: the only contact is from the doctor to the patients, not from the counselling team**.**
- If one country is not paying for a drug it will not be reimbursed, but then the patients/medical community could go to the reimbursement system asking for implementation in the reimbursement service

Warning

- **CPMS is a monitoring system on the validity of the established network; we should all start working with it!!!**

Work Package 6-Maurizio Scarpa & Jean Michel Heard

Maurizio announced that Jean Michel Heard (previously director of research for the French Ministry of Research, Paris France) is now collaborating with MetabERN and in particular with the WP6 activities as part of the research working group that is addressed to all the different aspect of research. MetabERN is requested to participate to EU grants so we have formed a sort of unit that will screen the projects and will decide to participate to those projects that will bring effective benefits to the network.

Main activities performed during the first year

WP6 Research, transitional activities and clinical trials: Research is a key component of MetabERN since several issues currently obstruct patient diagnosis and treatment including delayed diagnosis, limited availability of treatments and clinical trials for new treatments that are poorly designed and carried out. Several extensive surveys to identify expertise to generate research projects and identify potential gaps in the IMD field that need to be filled in the next couple of years have been developed and shared. Jean Michel made an analysis of the results of the research surveys and main outcomes have been fed into a report and this report provides recommendations on the priority setting for the Research Agenda in the area of IMDs.

Database reporting the Number of patients per diseases: the database has been created and shared.

Initially the MetabERN patient coverage was estimated form the data provided by each HCPs through the application form and it correspond to 42.427, 68% of which were paediatric patients.

Now, although the acquisition of data is not completed it appears clear that 50% of patients in follow up during this year are paediatric patients.

The fact that lots of new diagnoses are done in adults (late diagnosis) together with the consideration of the longer survival justify the increment of the % of adult patients with IMDs.

During the discussion it was ascertained that the possible duplication of patients belonging to more than one HCPs are really minimal since patients do not travel so much.

State of the Research; Research activity inside the network is high and highly performed also by physicians: High motivation and commitment to do research, 70% of HCPs have worked in a foreign country. Problem is the absence of research nurses: this is fundamental.

Facilities and conditions to do research are good

Outcomes form the survey for the departments show that 97% of them do research and are involved in at least 5 projects. Importantly they do research not just for funds but also to produce knowledge: they in fact publish and the publications are very often done in international collaboration. This also because they consider that contribution to international research almost improve attractiveness of the institution.

A positive impact of teaching and links with industry was revealed.

More competitive fields are:

- Genetic and pathophysiology
- Epidemiology, registries and cohorts
- Public heatlh, population screening and establishment of guidelines

Weak fields are:

  - Preclinical research
  - Research in technology
  - E-health research
- **The weakest field is social sciences**, with possible negative impact on interaction with patient representatives

Barriers to research are mainly lack of time due to clinical work burden and funding

Grant Office The structure for setting up a Grant Office have been set out at the end of 2017 and a mapping exercise has stared to be able to identify potential opportunities for MetabERN to apply for grants.

Main encountered problems

- Categorisation and inclusion of diseases into the different groups was not an easy task
- Delays in getting required information
- Huge amount of data to analyse
- Survey too long and sometimes not clear
- Discussion for the establishment of a grant office has not been easy to discuss via TC and it has been postponed several times

Main activities to be performed during the second year

WP6 will identify potential project grant sources to initiate research projects and forge partnerships, including through active participation in the EJP-RD Programme. The WP has a particular interest in generating projects devoted to the development of blood brain barrier crossing therapies for effective delivery of therapeutic molecules to the brain. Surveys will serve to collect information on the state of the art of development of innovative therapies. The results will feed into a detailed report and recommendations on the priority setting for the research agenda in the area of IMDs and will be used for the generation of a white book on the situation of clinical trials on IMDs.

Patients involvement in WP6

Patient could contribute to WP6 activities by:

- Contributing to the identification of the needs in research
- Helping us addressing important issue as
    - Delay of diagnosis
    - Limited availability of treatments
    - Design of CTs failing to generate reliable data
    - Paucity of reliable biomarkers for the evaluation of drug safety and efficacy
    - Funding problem

WP7 Capacity building and training Nadia Belmatoug

Main activities performed during the first year

MetabERN finds education and training one of its most important goals. Activities have therefore focused on the identification of teaching and training programmes already available to HCPs and patient organisations within the network in order to develop a comprehensive programme for the education and specialized training of participating HCPs, young PhD/medical students, professionals involved in metabolic patient care, as well as patients and their families, putting particular attention on capacity-building in those centres currently underdeveloped in certain areas. To this regard a special subwebsite dedicated to the education and training has been developed and it is available at http://metabern-educ.eu. This MetabERN library is a site dedicated to sharing information and documentation linked to training, education and capacity building.

As soon as the Website on education was online there have been a lot of contact with people that want to add material to the website. The contact details of learned societies and websites need to be added.

Of all the ERNs, only MetabERN and EpiCARE have a dedicated education website.

There is also an idea for a programme called "*Regards Croises*" which is a multidisciplinary approach aimed at the students and based on patient stories. The programme is dedicated to description of patient pathway by patients, doctors, nurses and expert patients. There was a Teleconference on 4/4/2018 with patient organisations to discuss this and to have their opinion about this programme.

There can be connections with DG Employment, DG Education. From MetabERN we want to draft a document in which we explain how we want to progress education and training. WP7 wants to start with students in biochemistry.

Margaret Giuliani: Member of French association of patients VML "Vaincre les Maladies Lysosomales" and EGA 'European

	GaucherAlliance' is the link between E-PAG, EURORDIS and WP7. She is charge of revision of education section of the website for English language. Link with SSIEM assures a useful dissemination and linkage in the organization of the different programme. Nadia is going to deeply discuss the collaboration with Andy Morris from the SSIEM. Shamima, senior advisor of SSIEM Academy, could help in the team up with MetabERN.
Encountered problems	• There have been good interactions with patient associations, but some of them are reluctant to give materials and then there are problems with the local language and translations. • Who is helping with Translation? Eurordis is doing it at its own expenses • The use of single companies for funding and input is not to be promoted. • Curricula/requirements; what level of knowledge do participants to the training course need to have? A sort of list of criteria for application should be set. NEXT STEPs TO BE DONE • The Subnetworks that have more diseases can help the ones with less experienced diseases. • It will be necessary to promote education and training in others learned societies paediatrics, haematology etc. • Important to establish training school for early stage researchers to present their work to patients and families • Important to establish partnership with industry, private company, programmes developed with the institutional partnership with pharmaceutical company
Main activities to be performed during the second year	WP7 will develop a survey on patient education programmes in close collaboration with patient organisations in order to get a clear understanding of the needs of IMD patients and to ultimately design and organise teaching and training programmes, particularly in countries where currently no such programmes exist. The same will be done for HCP education programmes. The CPMS will be used to organise multidisciplinary consultations and discussions of clinical cases. To achieve a better idea of what programmes currently exist, a mapping exercise will be undertaken. Once in place, the best practice programmes will be widely disseminated.
Patients involvement in WP7	• Good interaction and Collaboration with patients associations But some are reluctant to give materials • Problems of languages and translation • Avoid redundancy with the work of other associations and Eurordis

Work Package 8 -Continuity of Care Trine Tangeraas and Yngve Thomas Bliksrud

Main activities performed during the first year	Activities undertaken during the first year of the WP8 were intended to harmonise diagnosis, screening, prevention and treatment of IMDs across Europe, and improve longitudinal care of patients with IMDs, by building multinational cohorts of patients with rare disorders. Unfortunately some difficulties in producing concrete results in the first year were encountered due to personal problems of the previous WP leadership. The Coordination office decided to designate 2 new WP-leaders in order to rectify the situation and make immediate progress at the start of Year 2. The new leadership is now making progress with the deliverables that were set out; the collating of the list of certified diagnostic tools has started by reaching out to ERNDIM and Orphanet to see if collaboration is possible. It was highlighted the importance of making a general recognition in the IMDs field to take advantages of what is already existing and fill the gaps
Encountered problems	• Problem with the leadership • Possible overlapping: Avoid overlap on work activities in the different subnetworks that may intervene with the WP tasks • Lack of cooperation: Ensure cooperation to keep the number of survey monkeys acceptable to ensure compliance on participation from HCP
Main activities to be performed during the second year	In order to have access to the best diagnostics (biochemical/genetic) and to genome-wide genetic investigations for undiagnosed patients with complex disorders, a list of metabolic tests/diagnostics available at the 69 Centers involved in MetabERN will be drawn up. The idea is to create a web based map at MetabERN website with the 69 center-associated laboratories including : - Biochemical/enzyme diagnostics - Genetic services (incl exome sequencing/gene panels) - Participants of ERNDIM In a second step patient representative together with other WP-8 participants will start drafting a strategy to involve other potential non-MetabERN members in EU/EFTA.
Patients involvement in WP8	Patient representative included in the WP 8 participant mailing list/ WP8 subgoups-to provide opinions and inputs during the process Patient representative strongly involved in the group drafting the strategy to establish contact withother centers within the EU/EFTA as potential members of metabERN

7 parallel breakout sessions of the disease sub-groups

Participants were invited to participate in one of the the 7 parallel breakout sessions according to their interest and willingness to collaborate in the activities undertaken by the specific subnetwork.

Sub-networks reports in plenary

Sub-Network coordinators briefly reported main outcomes of the discussion undertaken during the parallel session. Detailed minutes containing main outcomes will be shared in separate documents by the subnetwork coordinators.

Amino and organic acids-related disorders (AOA)	**Stefan Kölker** The Subnetwork has divided itself in disease groups and have distributed the activities linked to WPs. Some of the activities that were done in the first year have been to create a list of AOA-specific disorders (done), inventory of AO landscape (done), Evaluation and implementation of European recommendations, evidence based recommendations, long-term safety study on Orfadin. For the Second Year the activities have been set out and planned.
Disorder of pyruvate metabolism, Krebs cycle defects, mitochondrial oxidative phosphorylation disorders, disorders of thiamine transport and metabolism (PM-MD)	**Shamima Rahman, Manuel Schiff, Enrico Bertini** This SNW has focused on the survey, dissemination, and coordination with other mitochondrial groups. The survey on mitochondrial diseases was send out but could do with more respondents (it was a short survey). This SNW has about 2046 patients in total. The Neuromuscular ERN also has a mitochondrial network. CPMS is being explored and WP-6 Clinical trials are finally on the horizon. The plans for the second year are to complete the survey, draft a classification of mitochondrial disorders, consolidate activities of work packages, involve Patient Organisations, continue to link with other ERNs & other international groups, work actively with CPMS and link to U-IMD.
Carbohydrate, fatty acid oxidation and ketone bodies disorders (C-FAO)	**Terry Derks** Terry explains that there are practical issues in doing work for MetabERN such as money, time and the lack of support from within the hospitals. WP-2, 3 and 7 are not represen. WP-4 is proceeding with long-chain + MTP deficiency. There is the question of the governance structure for Guidelines production: what is the optimum number to be included and should we include specialists from outside MetabERN.

	WP-5 CPMS opportunities like consulting for patients within CPMS. The SNW feels it is important to appoint patient advocates at the HCP-level. WP-6; discussions on how transparent one can be with regard to clinical trials and how to inform patients: this requires communication with patients. Making use of the infrastructure that we already have for communication; what should be used for this?
Lysosomal storage disorders (LSD)	**Ans van der Ploeg** For the coordination this SNW has a monthly teleconference of the steering committee and include WP-representatives in this. This SNW developed the template for the MetabERN-wide data collection. For WP-4 there are five diseases selected that will be worked on; Pompe will be the first.
Peroxisomal Lipid related Disorders (PD)	**Francois Eyskens** In the PD SNW they realized that in the Netherlands there are more than 100 patients and one of the reasons that diagnosis is good is the fact that the clinics and labs facilities are centralized. The SNW is working on a Guideline for X-ALD They also want to invite the PD and lipid-related disorders to participate in MetabERN.
Congenital disorders of glycosylation and disorders of intracellular trafficking (CDG)	**Peter Witters** This network follows 1350 known patients. The idea of establishing guidelines for diagnosis and treatment for PMM2-CDG was initiated on the last International Scientific CDG Symposium which was held in July 2017 in Leuven. They are using the knowledge of the international CDG community where experts were gathering. There are often delays in diagnosis of PMM2-CDG and the absence of standardized diagnostic and treatment protocols. They are doing evaluation of the published knowledge and outlining of guidelines for diagnosis and treatment of this rare disorder are highly demanded. They are working on Guidelines: As for the most of the rare disorders, most of the existing studies and reports are non-systematic, observational studies, case series or case reports, which are generally considered to be low quality evidence. However, collation of the available evidence along the expert opinions will help in establishing the guidelines. European grants are necessary to carry out research.
Disorders of Neuromodulators and Other Small Molecules (NOMS)	**Angeles Garcia-Cazorla** Angeles gave a brief description of the NOMS activity and achievements in the different WPs: **WP1** Definition of HCP participation in WP5 is still pending. Diseases to work on: Biogenic amines neurotransmitter (BH4, TH); Porphyrias (Erythropoietic, Acute Intermittent); TO WORK DURING THE FOLLOWING YEAR: Lesch-Nyhan, GLUT-1, NKH Current HCP participation in existing professional NOMPS networks: I-NTD, European Porhyria Network (EPNET)

Pending - Inventory on which NOMS are treated at each participating HCP including patients numbers (2 HCP are pending-)

WP2 Press release : Newsletters from the I-NTD group (http://www.intd-online.org)
Monthly/weekly publications about brain metabolism and neuroscience at : www.connectingthegrowingbrain.com

Recordati Foundation course “Synaptic Metabolism and Brain Circuitries in IEM”, Nov, at: www.rrd-foundation.org/en/course/synaptic-metabolism-and-brain-circuitries-iem-exploring-old-and-new-disorders/93

Lesch-Nyhan research in therapies (Genova, Sept)
International Porphyria Congress (ICPP) (Bordeaux, June)
Presentation: Rockefeller University, NY, March2018 (Conference Neurotransmitter related disorders

ACTIVITIES DURING THE FOLLOWING YEAR: -June GLUT-1 (London), I-NTD meeting (SSIEM, Athens 2018), -Next ICPP (Italy, 2019)

WP4 Inventory on existing guidelines/protocols (published, international and local) for NOMPS diseases

Guidelines for the porphyrias are currently revised and will be published at the EPNET webpage

WP6

- Research projects ongoing I-NTD: CSF proteomic studies in NT deficiencies; iPSc development in TH and BH4 defects, Brain Mapping.
- Grant applications ITN-Marie Curie submitted (resolution in May 2018), E-Rare(1° step June)
- U-IMD (iNTD registry as pilot)
- Purines research (animal model Lesch-Nyhan, ADSL new drug (patent), clinical trial in France)
- 2 clinical trials going on in acute porphyrias (EXPLORE and ENVISION)
- Glut-1 : new drug under development, clinical-biochemical-response to treatment study CIBERER, Spain; APP for ketogenic diet monitoring, Santiago de Compostela, Spain)

Wp7

- Pediatric Movement Disorders Course, Barcelona Feb 2019
- Yearly: iNTD meeting ; Ketogenic diet courses
- MDs and Students TRAINING: DU in metabolic diseases (France), Online Master in Metabolic Diseases (Santiago de Compostela, www.mastermh.es), Fellowship in Neurometabolic Diseases (online and practical training in 2019, Barcelona)
- Patients’ associations: Lesch-Nyhan action French association, Spanish and Italian Lesch-Nyhan association, European Lesch-Nyhan association, AFMAP (porphyrias in France), DeNeu (Spanish NT), SSDAH German Association, German NT Association, AsGLUTdiece (GLUT-1 Spanish)

Wp8

- ERNDIM participation of several HCPs involved in NOMS
- National accreditation completed

No activity for WP 3 and 5.

MetabERN involvement in EU projects

Maurizio Scarpa

MetabERN participation in EU programmes and projects were discussed.

Consumers, Health, Agriculture and Food Executive Agency (CHAFEA) Grant agreement	APPLICATION FOR THE 1° YEAR submitted on January 27th 2017, 17:00 h Luxembourg APPLICATION FOR THE 2° YEAR submitted on January 9th 2018, 17:00 h Luxembourg
3rd Public Health Programme - Unified European Registry for Inherited Metabolic Disorders (U-IMD)	Call for applications for Rare diseases –in support of the setup of new registries. The call is based on the Third Programme for the Union's action in the field of Health (2014-2020) and its 2016 Work Programme. Application submitted on March 21st 2017 The 400k € Grant has given the possibility to launch the U-IMD registry
Proposal Collaborative Network for European Clinical Trials For Children, (conect4children, c4c) within the 10th call of IMI2	The first stage deadline for the call was 28 March 2017 – submission of a short proposal via the electronic submission system of the H2020 participant portal. The second state deadline was be 14 September 2017 Launch of the c4c project by May 1st, 2018, The c4c Kick-off-meeting will take place in Berlin 23-25 May 2018. Grant: 400.000€
Call AIFA 2017 study protocol	Another application was sent on 31 January 2018 by the MetabERN Italian group of HCPs entitled “Information Technology approach to explore the impact of therapies and the cost of rare inherited metabolic disorders”. Partner: all the MetabERN Italy HCPs Expected result: summer 2018
Horizon 2020 - MSCA-ITN-2018: Innovative Training Networks	Collaboration Horizon 2020 -MSCA-ITN-2018 proposal NEUROTRANSMIT! (Fundació Sant Joan de Déu, SP) Collaboration Horizon 2020 -MSCA-ITN-2018 proposal on the topic of liver-related GSDs and mFAO defects (University of Groningen, NL)
The 2017 CEF Telecom Work Programme for grants managed by INEA in the area of Generic Services	Preparation of the Grant agreement, grant 125.000€ for personnel This includes activities such as: • Provision of IT technical support (e.g. helpdesk, coding support, upload of data, maintenance of ERN-related webpage, etc.) to ensure the appropriate use of the ERN Core Services • Training necessary for the use of ERN Core Services • Purchase of hardware and software necessary for the use of ERN Core Services (e.g. hardware, high definition cameras,

	webcams, specific software related to the area of expertise and appropriate licenses)
European Joint Programme	This is the last programme for the RDs in HORIZON 2020, programme for 5 years, part of the funding will be devoted to competitive proposals (there will be budget). All ERNs are on board: little money, but possibility to participate to competitive calls and to dedicated proposal to assess methodologies for clinical trials
EU-China Health Synergies in Health Research & Innovation	SC1-HCO-11-2018: Strategic collaboration in health research and innovation between EU and China Coordination & support action [CSA] RDs as a model to develop different strategies to translate models for dissemination in China since unfortunately in China patients do not have access to many therapies. our experience in creating network could be useful to connect physicians and we can meet with them and create some projects in order to have retrospective and prospective studies in China
TOPIC : Rare 2030 - a participatory foresight study for policy-making rare diseases PPPA-AG-Pilot Project & Preparation Action Grant	PARTNERSHIP UNDER CONSTRUCTION: GRANT 1.2M€ • The methodological steps and timeline for Rare 2030 will include different work packages: • Base research, including literature reviews and exploratory interviews to identify drivers of change and current and future challenges; - establishment of an expert / multi-stakeholder panel; • Consensus building methods will be used to define the main drivers (political, scientific, etc.) for scenario building and will be open to large groups of stakeholders on a European level; • An interdisciplinary and forward-looking workshop for scenario building will be used as a tool to reveal available choices and their potential consequences; the scenarios developed will take into account resources at EU level, and include options to use the existing structures better, in particular the framework of the European Reference Networks (ERN) and the Steering Group on Promotion and Prevention (SGPP). • EU added value will be defined in options for action at EU level, both as theoretical concept and in terms of practical scenarios, with a clear distinction from actions recommended at national level. • Extended patient consultation (survey) on the identified scenarios; • A European 'consensus conference' ('conférence de citoyens') to present, discuss and review results, engaging society to shape and take ownership of the outcomes; • Identification of sustainable options for future action, bringing together the results of the scenarios and conference; • Final report, in English, outlining the options for future action and outcomes of the project and measuring its impact; the executive summary of the report will be translated into various EU languages;

Sustainability of the Network/Stakeholder Meeting/establishment of MetabERN grant office

Maurizio Scarpa & Ans van der Ploeg

Although MEtabERN is not a funding agency, busgdet should be raised to sustain the activities of the Work Pakages and Substerworks tasks .

To this aim, the discussion for the establishment of a grant office has been initiated but it has not been easy to discuss via TC and it has been postponed several times. This morning

Maurizio Scarpa discussed with Ines Hernando (Eurordis) about this issue and also EC is starting to think about the global budget for health. Maurizio is going to write to all the coordinators requiring to have an idea about the cost of the ERN in terms of running cost includes the amount of money necessary to sustain the network activities (GL, registry and patients empowerment, virtual counselling and CPMS) in order to see the amount to be funded per year (e.g. how much is for each physician an hour cost devoted to the CPMS in order to be reimbursed by the hospital and be able to do the CPMS during the normal activities).

Grant office

AIM: To get all the providers aware of any kind of grant and proposals
The major role of the MetabERN Grant Office should be to

(1) Contact policy makers in order to discuss suitable future calls,

(2) Identify suitable calls (mostly on a European level) that could help to support the activities of MetabERN members and

(3) To support grant application for MetabERN activities

The grant office it is not meant to control the amount of money that is being granted but to evaluate the different opportunities available in each country and to compare how the people inside the country are exploiting these opportunities

It will not be involved in the administration of the grant and will be run by totally independent personal

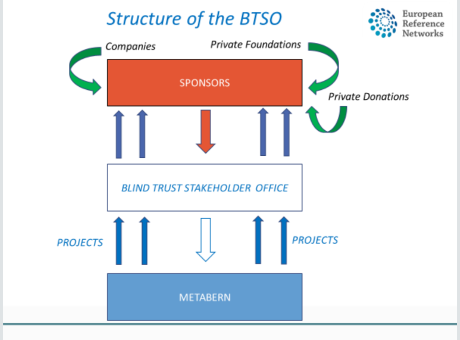
Interaction with third parties

The legal WG of the coordinators is developing a legal document under approval, in order to define how to legally interact with companies and third parties in general.

Since ERNs must not have private contact with companies and considering that all the diseases and all the patients are equal in the ERNs, the idea is that, in order to separate in a very solid way the sponsor money and the MetabERN providers, Maurizio launches a proposal that he would like to discuss with the Board. The proposal sets out the creation of a blind trust stakeholder office that will be the interim among the private money and the ERNs that will look the availability of producing money (a sort of fundraising entity that will take care to fund the projects that HCPs want to do for the MetabERN) .

The main concept is that Sponsors will have a contract with the blind trust and the blind trust will have a contract with MetabERN

THE GRANT OFFICE could be included in a Blind Trust Stakeholder Office (BTSO) as a way to directly interact with stakeholders and finance research projects.



The BTSO will provide opportunities to facilitate the interface and collaboration putting providers in contact with third parties. The BTSO will contract with the HCPs and it will take care about the final financial report.

The BTSO will not be involved in the administration of EU grants.

The BTSO will be run by an independent blind body of external members not involved in MetabERN. The BTSO reports to the Coordinator, who will not have any financial involvement. (TBD)

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The MetabERN Stakeholders Meeting

As soon as the conflict of interest policy will be approved we can start thinking to organize a meeting with the stakeholders (companies, associations, and everybody else with whom MetabERN could work for projects)

All stakeholders will be invited to participate at their own cost

The program would be planned together with Dr. Nathalie Moll who is the president of EFPIA.

Meeting could be held in Autumn 2018.

Questions and emerged issues

- It would be preferable to not give to the Sponsor the power to decide about individual projects

- Relationship with companies is still too strong

- EC will not be happy about it

- Money should not come only from companies, we will have for sure also private funding, private donors, and other foundation

- The Blind office will need to be controlled according to transparent code that we will be defined

- Management of the network should be an EU duty, we cannot raise the money for the constitution of the network, we find 5-6 private sponsors to maintain the registry for everything. ERNs should not be involved in this issues, they should just provide assistance to the patient need in term of clinical needs

- Maurizio explains that there has been a meeting organised by Eurordis in which 70 companies participated, the companies are asking for transparency, regulation, etc. so he was thinking to start planning a meeting in collaboration with EFPIA and have a representation of the people to interact with them

- Why don’t we create a foundation to sustain the patients data base and the activities? The problem with a foundation is that we will need to find the money to establish it, we need to find the way to start paying somebody

- No matter who is providing money as soon as we follow the rules that we set out, it should not be a problem.
- Few HCPs representatives declared “My research is independent from companies, they have insidious way to push the way to proceed!”
- MetabERN is the first ERN thinking on sustainability and third parties
- EC should launch call for ERNs but it is still not enough, we are a bit in a trap, ERNs should address their issues sitting together and seeing what the EC can do for them. The issue should be addressed with the EC and the members states in order to avoid any kind of legal issue

To run an ERN we roughly need 1.2 million per year

Vote

Who is in favour of discussing with EC, lawyers and having better third parties money? Out of the 52 present participants 32 people are in favour of further discussion.

A final consensus was not achieved and participants were invited to come up with suggestions to modify the proposal in order to be able to achieve a consensus

Maurizio will check with the other coordinators and will ask to the legal office of the EC whether ERNs are allowed to receive money from companies.

Getting ready for the annual IAB Assessment
Maurizio Scarpa

DG SANTE and CHAFEA are about to sign the contract with the Independent Assessment Body (IAB) to carry out the technical assessment of a sample of ERN members' applications. In the audit 79 ERN members will be selected to undergo the documentation assessment against the specific criteria of the self-assessment checklist for healthcare providers. 23 of them will also receive the IAB on-site visits (audit).

As it has been the case in 2016, the sample is identified respecting objective criteria such as geographical balance and the size of the ERNs.

To be done for getting ready

- You will need to have ready the documentation that justifies compliance with the specific operational criteria (compliance for each rating expressed in the self assessment).
- Ensure that all supporting documentation and English summaries are ready
- As coordination office we will need to have them at hand when the Independent Assessment Body takes initial contact with you.

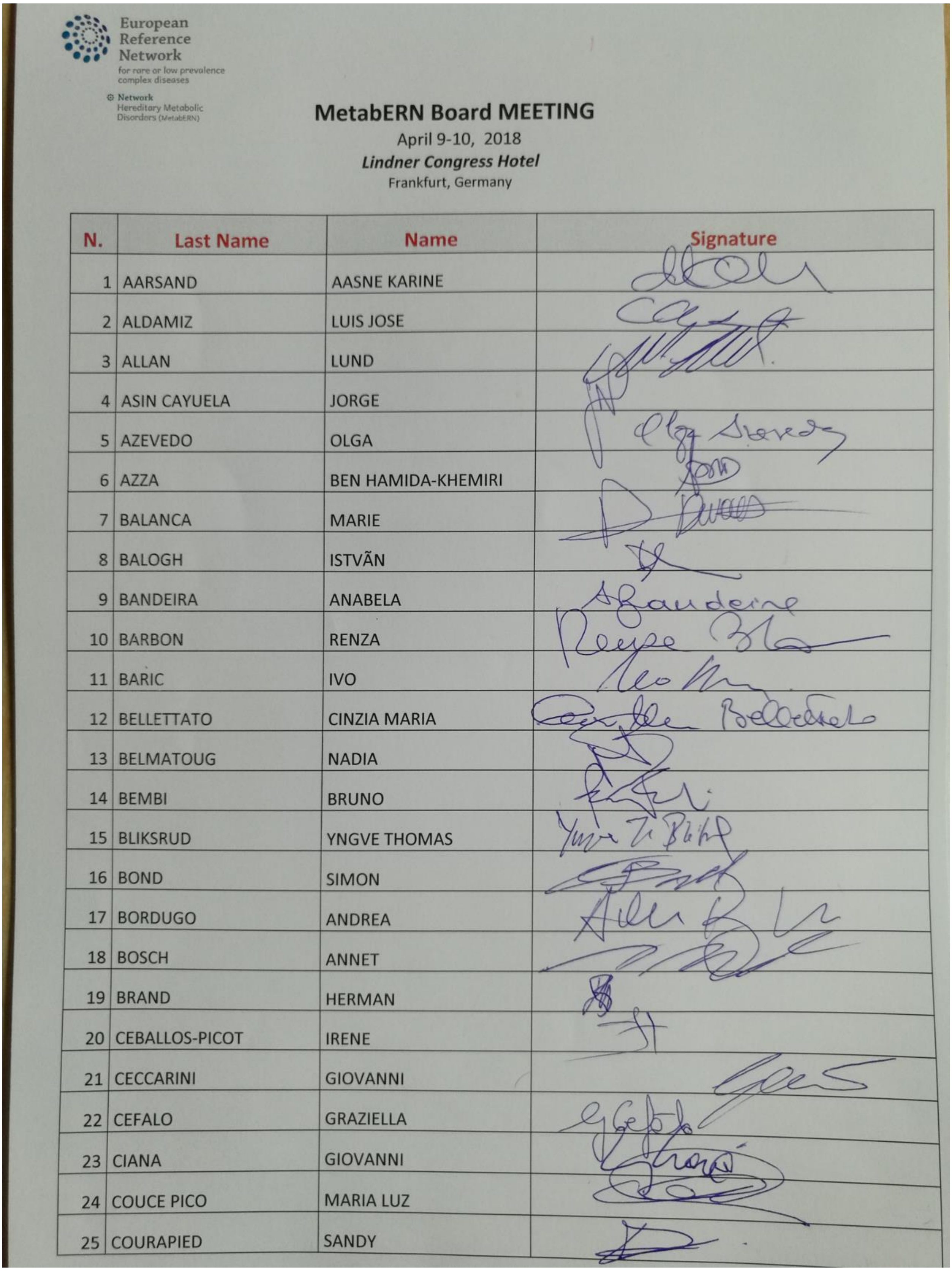
Next steps
Maurizio Scarpa

Maurizio Scarpa gave a detailed overview of the Institutional and internal activities of both HCPs and POs. After having reviewed all work plans in the framework of the overarching MetabERN objectives, the group approved the consolidated plan of work as developed by the team and presented at the meeting.

It was agreed that the **next meeting of the Board will be held on APRIL 4th starting at 14 and will finish on April 6 (Saturday) by 15,00**

From next year in order to cover the cost of POs the contribution of 250 Euro will be used to cover the POs in order to enlarge the participation: the physician should be here paid by their hospital.

If an HCP has a problem with general directors that are not in favour of letting HCPs representatives participating in the network meeting: Maurizio will write an e-mail to sort this out.



European Reference Network
for rare or low prevalence complex diseases

Network Hereditary Metabolic Disorders (MetabERN)

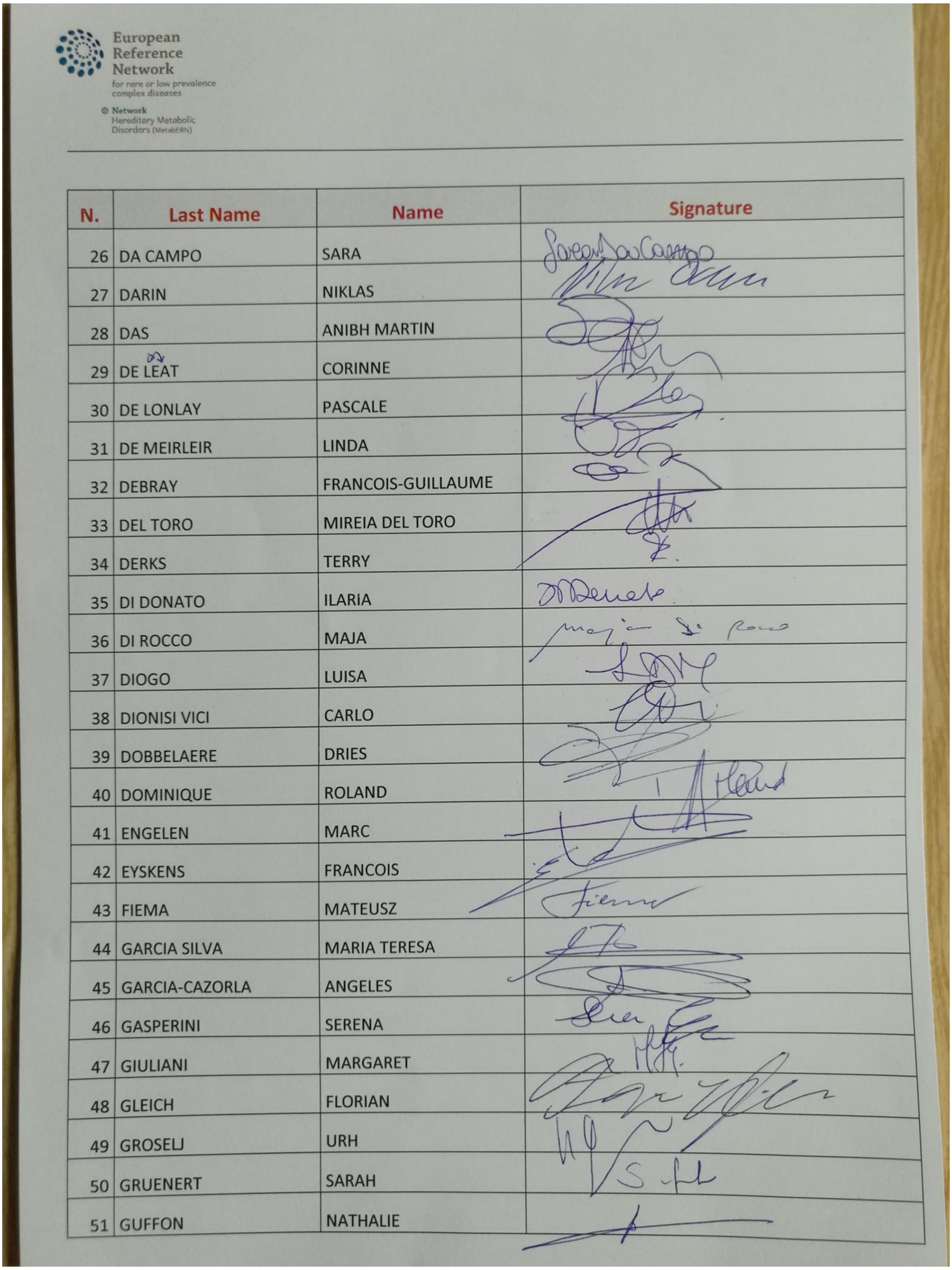
MetabERN Board MEETING

April 9-10, 2018

Lindner Congress Hotel

Frankfurt, Germany

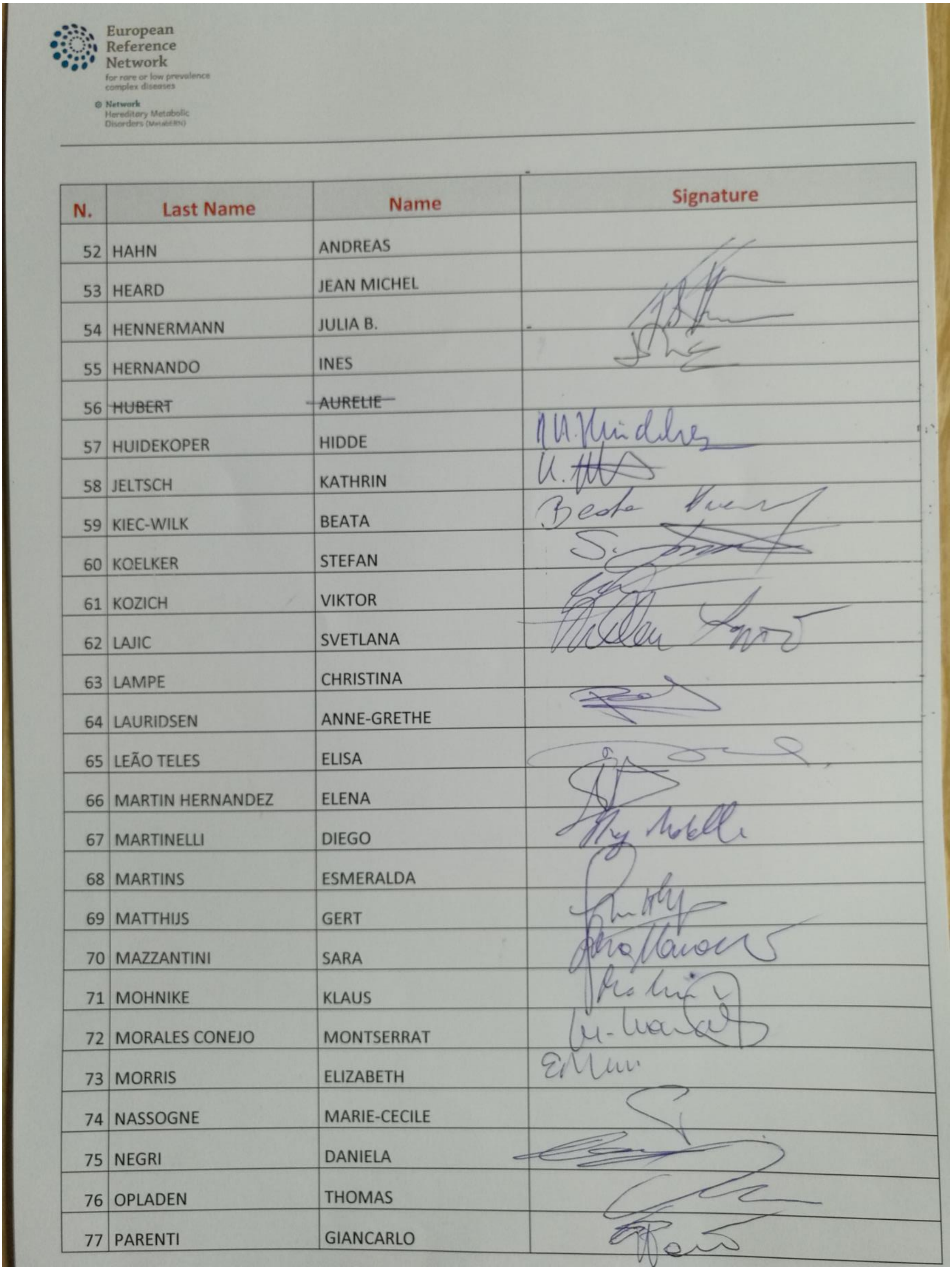
N.	Last Name	Name	Signature
1	AARSAND	AASNE KARINE	
2	ALDAMIZ	LUIS JOSE	
3	ALLAN	LUND	
4	ASIN CAYUELA	JORGE	
5	AZEVEDO	OLGA	Olga Azevedo
6	AZZA	BEN HAMIDA-KHEMIRI	
7	BALANCA	MARIE	
8	BALOGH	ISTVÃN	
9	BANDEIRA	ANABELA	ABandeira
10	BARBON	RENZA	
11	BARIC	IVO	
12	BELLETTATO	CINZIA MARIA	
13	BELMATOUG	NADIA	
14	BEMBI	BRUNO	
15	BLIKSRUD	YNGVE THOMAS	
16	BOND	SIMON	
17	BORDUGO	ANDREA	
18	BOSCH	ANNET	
19	BRAND	HERMAN	
20	CEBALLOS-PICOT	IRENE	
21	CECCARINI	GIOVANNI	
22	CEFALO	GRAZIELLA	
23	CIANA	GIOVANNI	
24	COUCE PICO	MARIA LUZ	
25	COURAPIED	SANDY	



European Reference Network
for rare or low prevalence complex diseases

Network
Hereditary Metabolic Disorders (MetabERN)

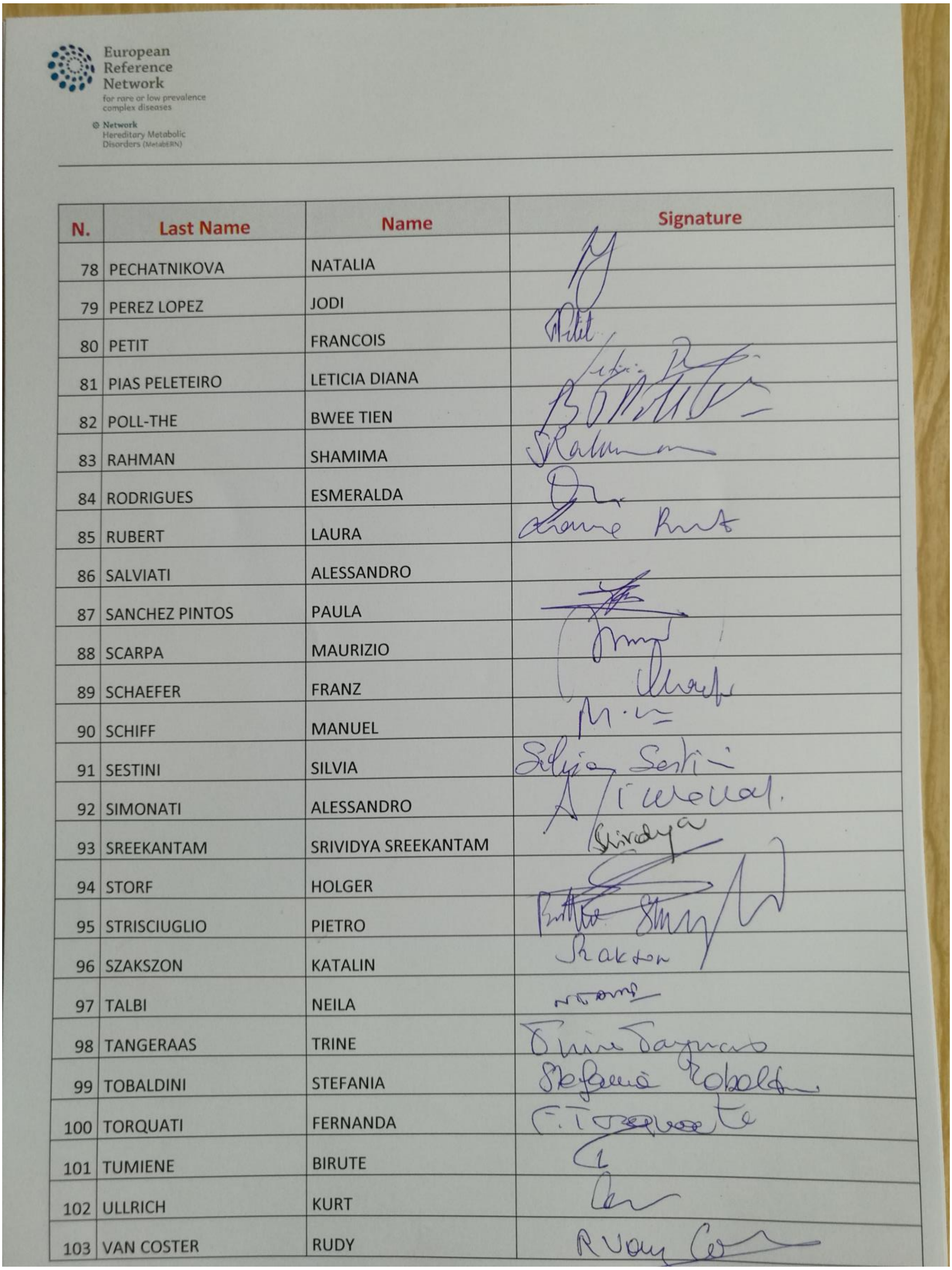
N.	Last Name	Name	Signature
26	DA CAMPO	SARA	Sara Da Campo
27	DARIN	NIKLAS	Nikl Darin
28	DAS	ANIBH MARTIN	
29	DE LEAT	CORINNE	
30	DE LONLAY	PASCALE	
31	DE MEIRLEIR	LINDA	
32	DEBRAY	FRANCOIS-GUILLAUME	
33	DEL TORO	MIREIA DEL TORO	
34	DERKS	TERRY	
35	DI DONATO	ILARIA	IDonato
36	DI ROCCO	MAJA	maja di rocco
37	DIOGO	LUISA	
38	DIONISI VICI	CARLO	
39	DOBBELAERE	DRIES	
40	DOMINIQUE	ROLAND	
41	ENGELEN	MARC	
42	EYSKENS	FRANCOIS	
43	FIEMA	MATEUSZ	Fiema
44	GARCIA SILVA	MARIA TERESA	
45	GARCIA-CAZORLA	ANGELES	
46	GASPERINI	SERENA	
47	GIULIANI	MARGARET	
48	GLEICH	FLORIAN	
49	GROSELJ	URH	
50	GRUENERT	SARAH	
51	GUFFON	NATHALIE	



European Reference Network
for rare or low prevalence complex diseases

Network Hereditary Metabolic Disorders (MetabERN)

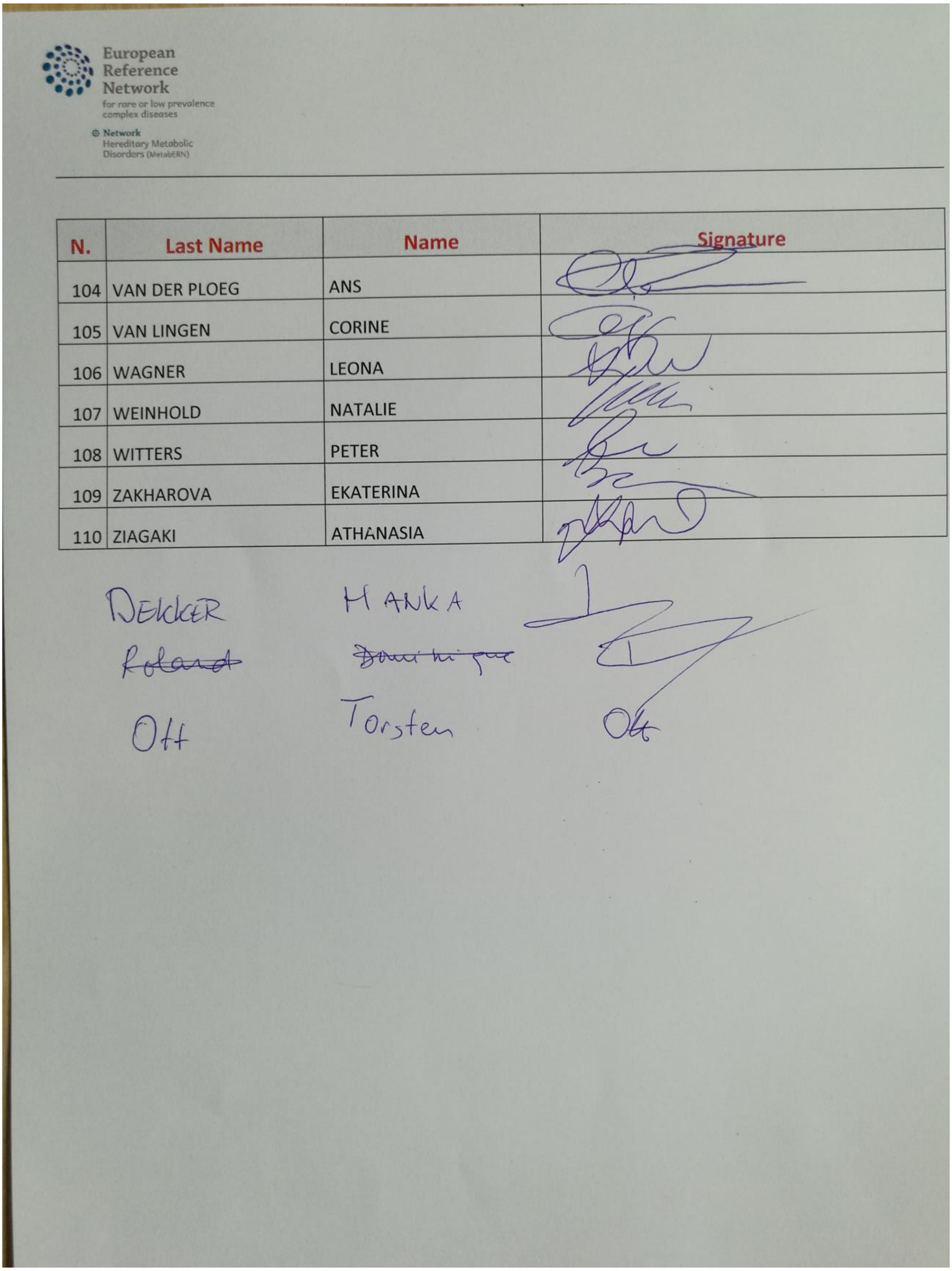
N.	Last Name	Name	Signature
52	HAHN	ANDREAS	
53	HEARD	JEAN MICHEL	
54	HENNERMANN	JULIA B.	
55	HERNANDO	INES	
56	~~HUBERT~~	~~AURELIE~~	
57	HUIDEKOPER	HIDDE	
58	JELTSCH	KATHRIN	
59	KIEC-WILK	BEATA	Beata
60	KOELKER	STEFAN	
61	KOZICH	VIKTOR	
62	LAJIC	SVETLANA	
63	LAMPE	CHRISTINA	
64	LAURIDSEN	ANNE-GRETHE	
65	LEÃO TELES	ELISA	
66	MARTIN HERNANDEZ	ELENA	
67	MARTINELLI	DIEGO	
68	MARTINS	ESMERALDA	
69	MATTHIJS	GERT	
70	MAZZANTINI	SARA	
71	MOHNIKE	KLAUS	
72	MORALES CONEJO	MONTSERRAT	
73	MORRIS	ELIZABETH	
74	NASSOGNE	MARIE-CECILE	
75	NEGRI	DANIELA	
76	OPLADEN	THOMAS	
77	PARENTI	GIANCARLO	



European
Reference
Network
for rare or low prevalence
complex diseases

Network
Hereditary Metabolic
Disorders (MetabERN)

N.	Last Name	Name	Signature
78	PECHATNIKOVA	NATALIA	
79	PEREZ LOPEZ	JODI	
80	PETIT	FRANCOIS	Petit
81	PIAS PELETEIRO	LETICIA DIANA	
82	POLL-THE	BWEE TIEN	
83	RAHMAN	SHAMIMA	SRahman
84	RODRIGUES	ESMERALDA	
85	RUBERT	LAURA	
86	SALVIATI	ALESSANDRO	
87	SANCHEZ PINTOS	PAULA	
88	SCARPA	MAURIZIO	
89	SCHAEFER	FRANZ	
90	SCHIFF	MANUEL	
91	SESTINI	SILVIA	Silvia Sestini
92	SIMONATI	ALESSANDRO	A Simonati.
93	SREEKANTAM	SRIVIDYA SREEKANTAM	Srividya
94	STORF	HOLGER	
95	STRISCIUGLIO	PIETRO	
96	SZAKSZON	KATALIN	Szakszon
97	TALBI	NEILA	
98	TANGERAAS	TRINE	Trine Tangeraas
99	TOBALDINI	STEFANIA	Stefania Tobaldini
100	TORQUATI	FERNANDA	F. Torquati
101	TUMIENE	BIRUTE	
102	ULLRICH	KURT	
103	VAN COSTER	RUDY	R Van Co



European Reference Network
for rare or low prevalence complex diseases

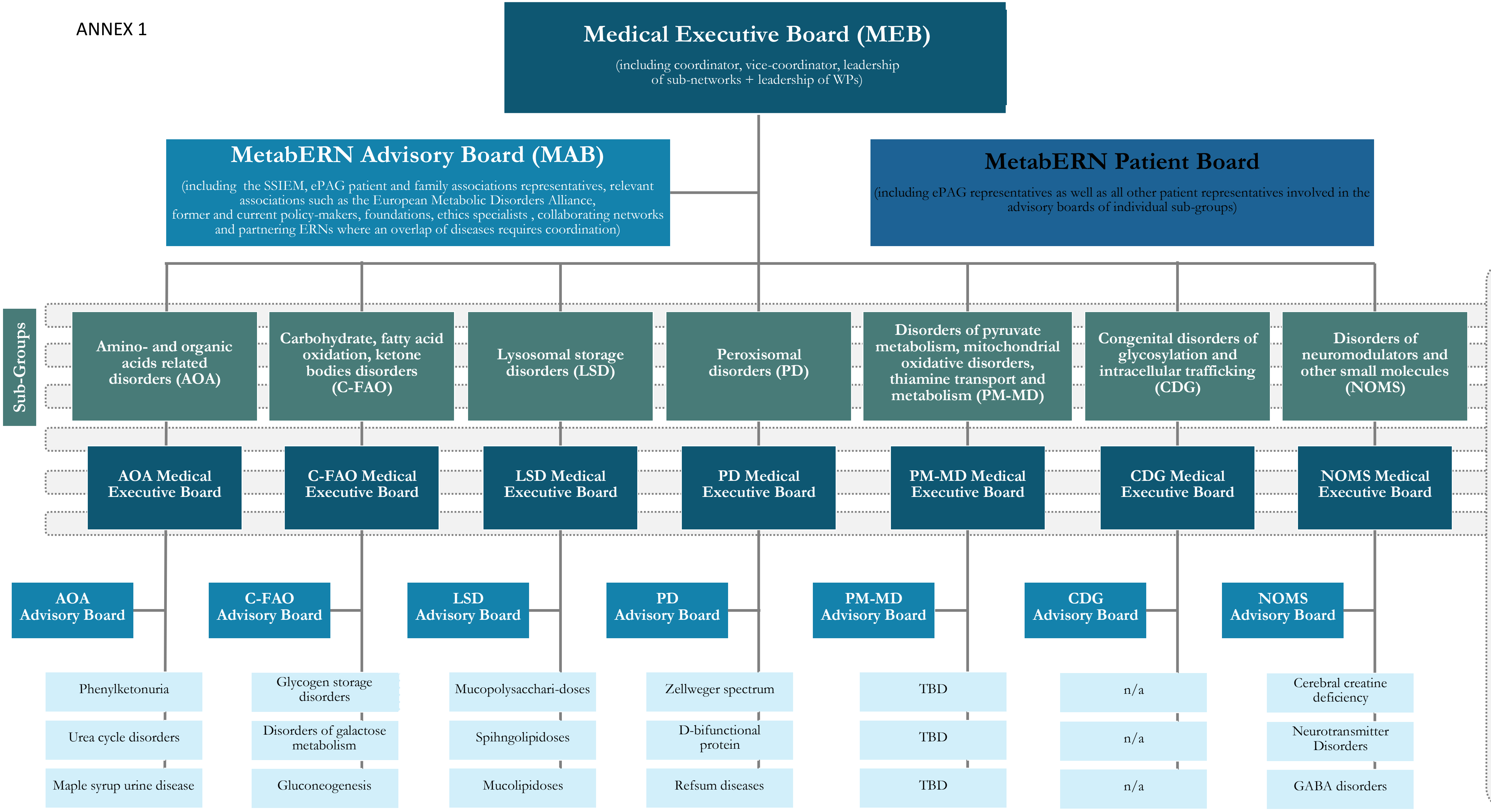
Network
Hereditary Metabolic Disorders (MetabERN)

N.	Last Name	Name	Signature
104	VAN DER PLOEG	ANS	
105	VAN LINGEN	CORINE	
106	WAGNER	LEONA	
107	WEINHOLD	NATALIE	
108	WITTERS	PETER	
109	ZAKHAROVA	EKATERINA	
110	ZIAGAKI	ATHANASIA	
	DEKKER	HANKA	
	~~Roland~~	~~Dominique~~	
	Ott	Torsten	Ott

ANNEX 1

MetabERN Board

(General assembly of representatives from all HCPs, patient groups and other third party stakeholders involved in the activities of the MetabERN)



Medical Executive Board (MEB)

(including coordinator, vice-coordinator, leadership of sub-networks + leadership of WPs)

MetabERN Advisory Board (MAB)

(including the SSIEM, ePAG patient and family associations representatives, relevant associations such as the European Metabolic Disorders Alliance, former and current policy-makers, foundations, ethics specialists , collaborating networks and partnering ERNs where an overlap of diseases requires coordination)

MetabERN Patient Board

(including ePAG representatives as well as all other patient representatives involved in the advisory boards of individual sub-groups)

Sub-Groups

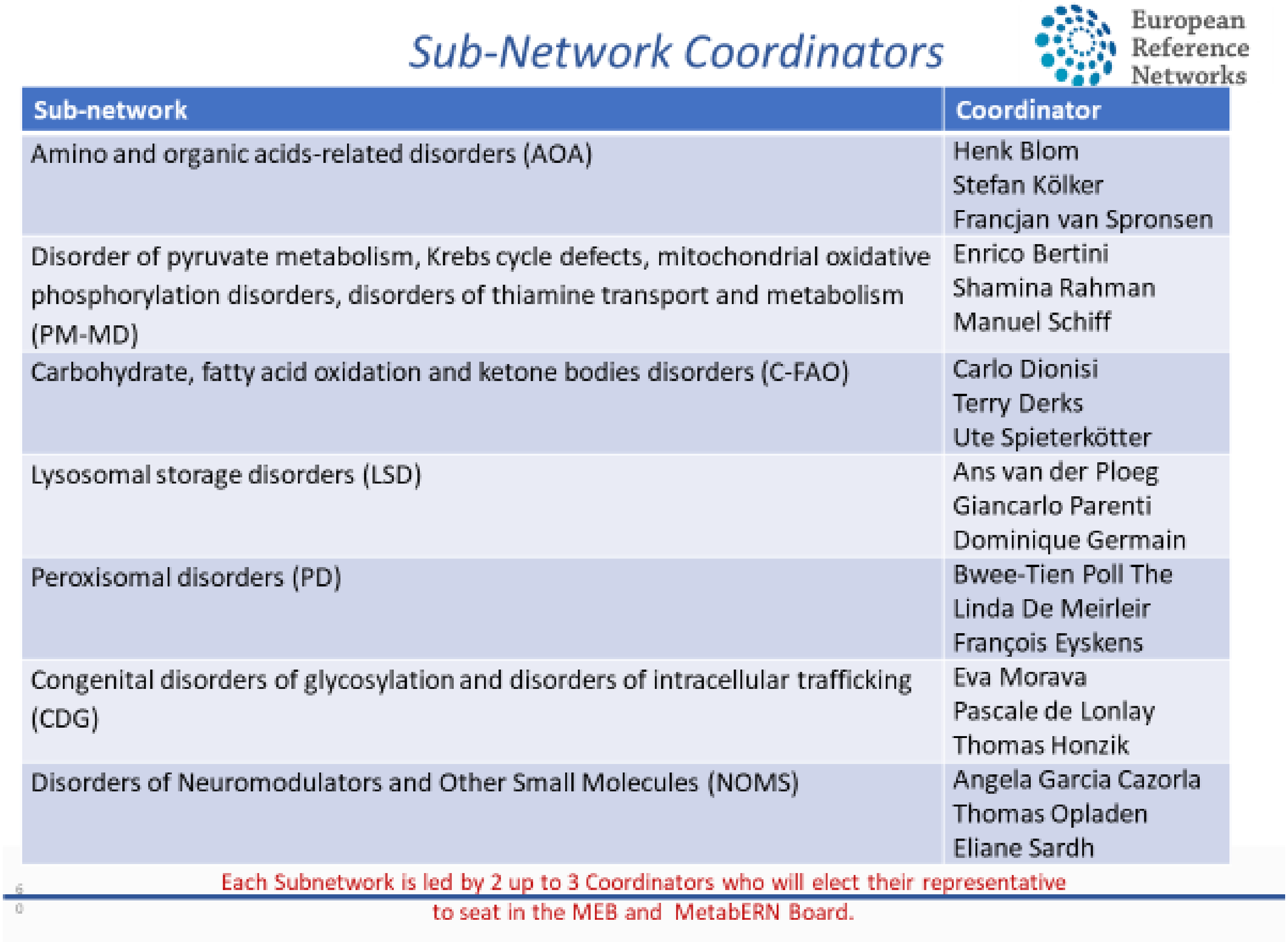
Amino- and organic acids related disorders (AOA)	Carbohydrate, fatty acid oxidation, ketone bodies disorders (C-FAO)	Lysosomal storage disorders (LSD)	Peroxisomal disorders (PD)	Disorders of pyruvate metabolism, mitochondrial oxidative disorders, thiamine transport and metabolism (PM-MD)	Congenital disorders of glycosylation and intracellular trafficking (CDG)	Disorders of neuromodulators and other small molecules (NOMS)
AOA Medical Executive Board	C-FAO Medical Executive Board	LSD Medical Executive Board	PD Medical Executive Board	PM-MD Medical Executive Board	CDG Medical Executive Board	NOMS Medical Executive Board
AOA Advisory Board	C-FAO Advisory Board	LSD Advisory Board	PD Advisory Board	PM-MD Advisory Board	CDG Advisory Board	NOMS Advisory Board
Phenylketonuria	Glycogen storage disorders	Mucopolysacchari-doses	Zellweger spectrum	TBD	n/a	Cerebral creatine deficiency
Urea cycle disorders	Disorders of galactose metabolism	Spihngolipidoses	D-bifunctional protein	TBD	n/a	Neurotransmitter Disorders
Maple syrup urine disease	Gluconeogenesis	Mucolipidoses	Refsum diseases	TBD	n/a	GABA disorders

ANNEX 2

MetabERN Coordinator and Vice-coordinators Roles and Responsibilities

MetabERN	Coordinator
COORDINATOR: Maurizio Scarpa; HSK Germany. Moving/ VOTING NEEDED	The Network Coordinator is the legal representative of MetabERN. The Coordinator, assisted by the Medical Executive Board, supports and facilitates coordination within and outside of the network. • Coordinate activities within the network and with core network coordinators • Act as contact point for European Commission and external stakeholders
VICE-COORDINATORS • Stefan Koelker, University of Heidelberg, DE • Ans van der Ploeg, Erasmus MC, University Medical Center, Rotterdam, NL	The Vice-Coordinators support the Coordinator, and, in the event of the Coordinator's absence, the Vice-Coordinators will carry out the Coordinator's duties on his/her behalf. The Vice Coordinators will be generally responsible for: a) the coordination of the HCPs, b) the coordination of the Patients Associations and stakeholders c) the coordination of the Communication/ Information Technology Platform.
COORDINATION OFFICERS • Cinzia Maria Bellettato Project Manager • Corine van Lingen Stakeholder manager	The coordination officers support the coordinator in his role and take care of the internal communication between the different bodies.

ANNEX 3



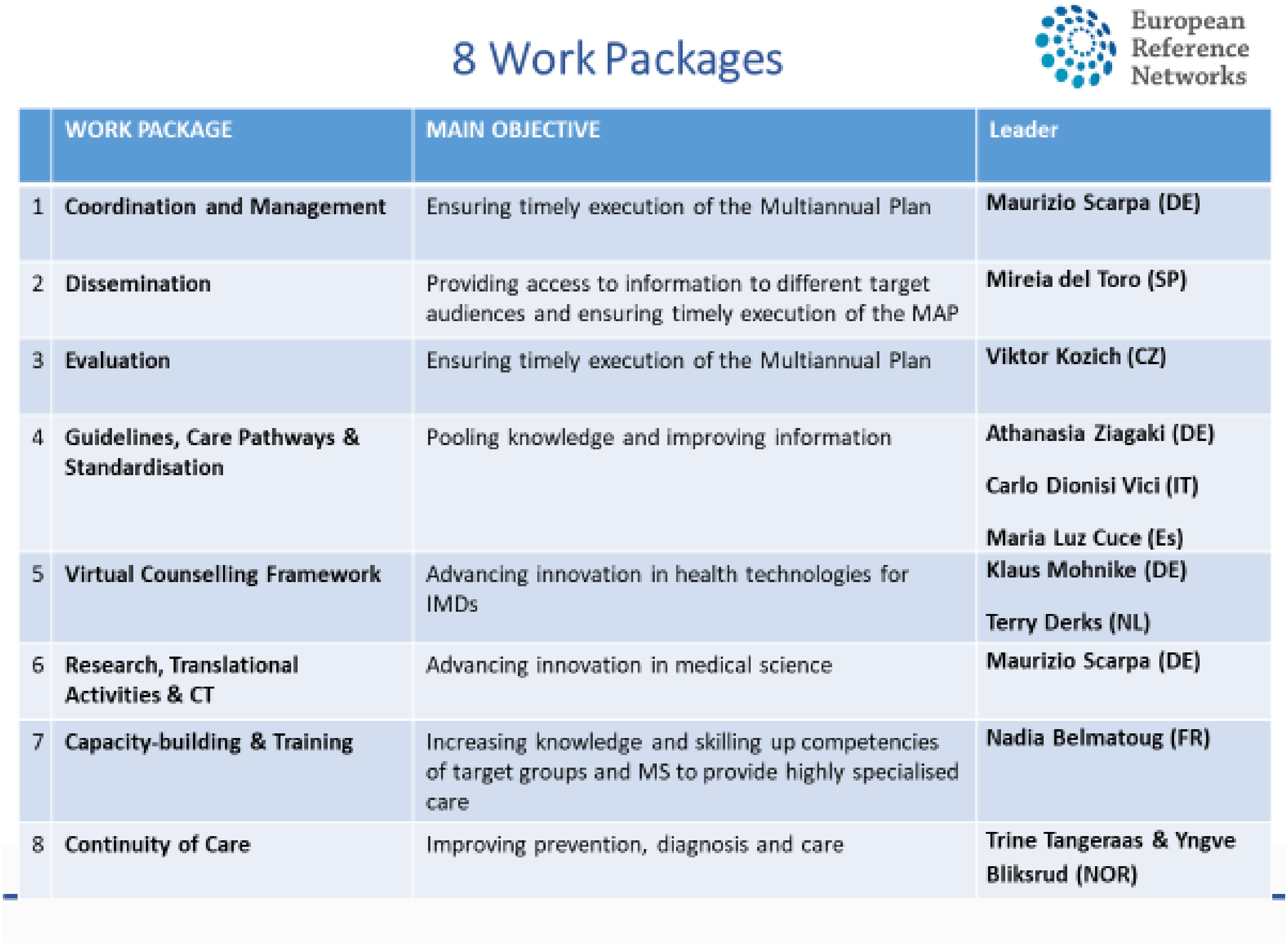
Sub-Network Coordinators

European
Reference
Networks

Sub-network	Coordinator
Amino and organic acids-related disorders (AOA)	Henk Blom Stefan Kölker Francjan van Spronsen
Disorder of pyruvate metabolism, Krebs cycle defects, mitochondrial oxidative phosphorylation disorders, disorders of thiamine transport and metabolism (PM-MD)	Enrico Bertini Shamina Rahman Manuel Schiff
Carbohydrate, fatty acid oxidation and ketone bodies disorders (C-FAO)	Carlo Dionisi Terry Derks Ute Spieterkötter
Lysosomal storage disorders (LSD)	Ans van der Ploeg Giancarlo Parenti Dominique Germain
Peroxisomal disorders (PD)	Bwee-Tien Poll The Linda De Meirleir François Eyskens
Congenital disorders of glycosylation and disorders of intracellular trafficking (CDG)	Eva Morava Pascale de Lonlay Thomas Honzik
Disorders of Neuromodulators and Other Small Molecules (NOMS)	Angela Garcia Cazorla Thomas Opladen Eliane Sardh

Each Subnetwork is led by 2 up to 3 Coordinators who will elect their representative
to seat in the MEB and MetabERN Board.

ANNEX 4

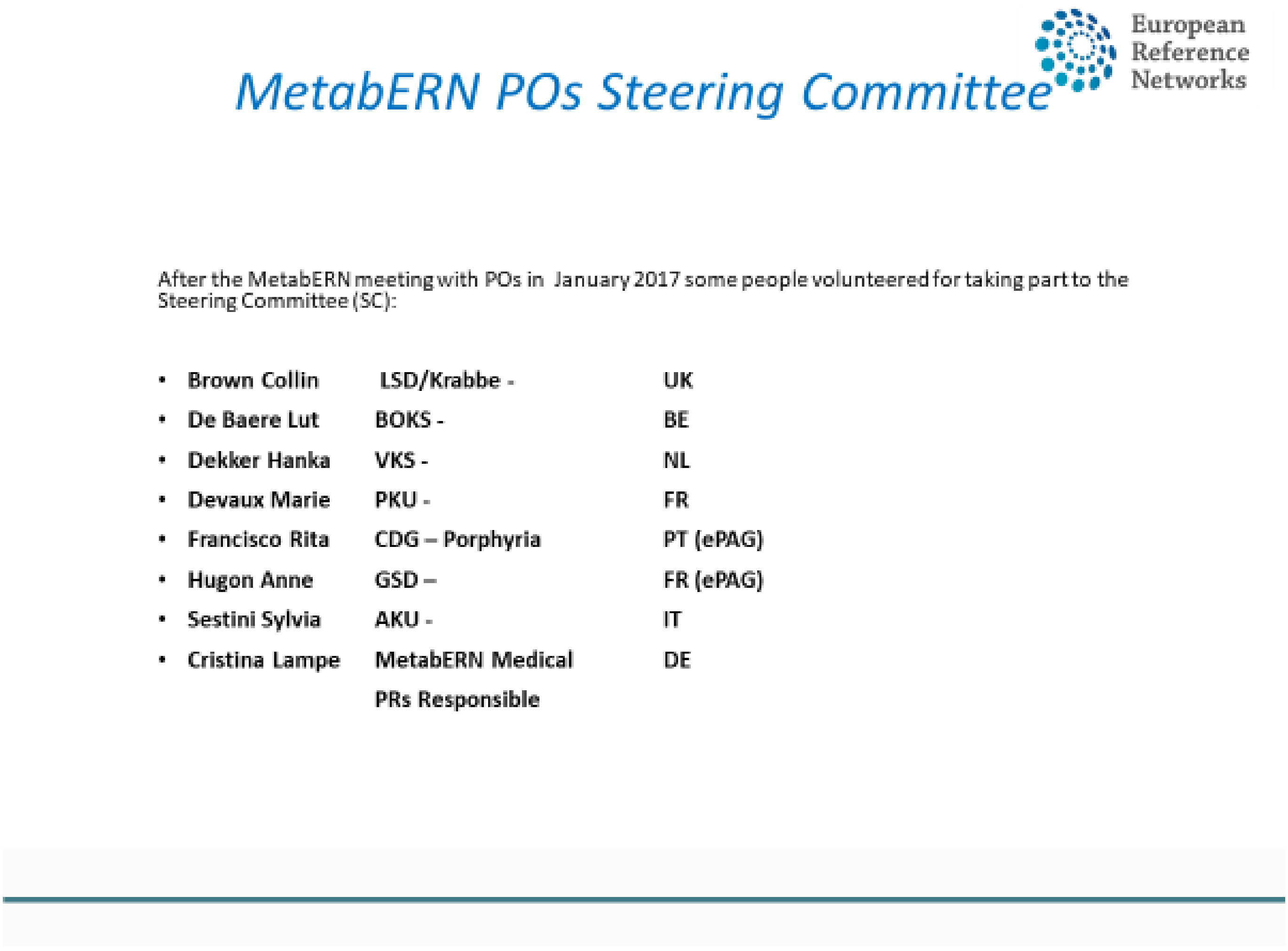


8 Work Packages

European Reference Networks

	WORK PACKAGE	MAIN OBJECTIVE	Leader
1	**Coordination and Management**	Ensuring timely execution of the Multiannual Plan	**Maurizio Scarpa (DE)**
2	**Dissemination**	Providing access to information to different target audiences and ensuring timely execution of the MAP	**Mireia del Toro (SP)**
3	**Evaluation**	Ensuring timely execution of the Multiannual Plan	**Viktor Kozich (CZ)**
4	**Guidelines, Care Pathways & Standardisation**	Pooling knowledge and improving information	**Athanasia Ziagaki (DE)** **Carlo Dionisi Vici (IT)** **Maria Luz Cuce (Es)**
5	**Virtual Counselling Framework**	Advancing innovation in health technologies for IMDs	**Klaus Mohnike (DE)** **Terry Derks (NL)**
6	**Research, Translational Activities & CT**	Advancing innovation in medical science	**Maurizio Scarpa (DE)**
7	**Capacity-building & Training**	Increasing knowledge and skilling up competencies of target groups and MS to provide highly specialised care	**Nadia Belmatoug (FR)**
8	**Continuity of Care**	Improving prevention, diagnosis and care	**Trine Tangeraas & Yngve Bliksrud (NOR)**

ANNEX 5



MetabERN POs Steering Committee

After the MetabERN meeting with POs in January 2017 some people volunteered for taking part to the Steering Committee (SC):

• Brown Collin	LSD/Krabbe -	UK
• De Baere Lut	BOKS -	BE
• Dekker Hanka	VKS -	NL
• Devaux Marie	PKU -	FR
• Francisco Rita	CDG – Porphyria	PT (ePAG)
• Hugon Anne	GSD –	FR (ePAG)
• Sestini Sylvia	AKU -	IT
• Cristina Lampe	MetabERN Medical PRs Responsible	DE

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