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Short REPORT

ERN-EYE

6th GENERAL ANNUAL MEETING

NETWORK COORDINATOR

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This document includes :

- *The short report, published on the ERN-EYE website*
- *The results of the satisfaction survey as annex 1*
- *The program of the event as annex 2*

European Reference Network for rare or low prevalence complex diseases
Network Eye Diseases (ERN-EYE)

25th to 26th April 2022
Amsterdam, Netherlands

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ERN-EYE WORKSHOP ON EYE MODELLING

ERN-EYE Project Management Team

Introduction

General Annual Meeting– April 25th- 26th, 2022

ERN-EYE organized its 6th General Annual Meeting from April 25th to 26th in Amsterdam, Netherlands. It gathered nearly 80 people from the HCPs of 17 member countries of the network, as well as invited speakers. Opened by Pr Hélène Dollfus, coordinator of ERN-EYE and Pr Camiel Boon, our local host, representative of the Amsterdam University Medical Centers, member of ERN-EYE, the meeting started with a discussion on the goals of ERNs in the next years with representatives of the European Commission.

The central part of the meeting was dedicated to the governance board bringing together the representatives of ERN-EYE full members and patient representatives. During this board, a positive assessment of the actions of ERN-EYE in 2021 could be made: the main objectives have been achieved or are in progress and new projects will be launched. These projects are part of the 2023 objectives that the board has approved: among them to continue the production of guidelines, to use more the Clinical Patient Management System (CPMS) and to finalize the e-learning program.The rest of the meeting was devoted in particular to the question of the crucial need for collecting data from Rare disease patients in Europe: the importance of registries in Europe, the experience of ERN ERKnet and the presentation of the progress of the ERN-EYE registry (REDgistry). The Clinical Patient Management System CPMS was also discussed with the presence of Joao De Sousa and Michèle Foucart, from the European Commission, who gave a view of the new version of the system.

This meeting was also the opportunity to speak about national integration and ERN research projects (EJP-RD, ERICA). Finally, several ERN-EYE working groups had the chance to meet in parallel sessions.

ERNs in brief

European Reference Networks (ERNs) are unique and innovative cross-border cooperation platforms between specialists for the diagnosis and treatment of rare or low prevalence complex diseases.

ERNs are virtual networks bringing together healthcare providers across Europe to tackle complex or rare medical conditions that require highly specialized treatment and a concentration of knowledge and resources. They are being set up under the EU Directive on Patients' Rights in Healthcare (2011/24/EU), which also makes it easier for patients to access information on healthcare and thus increase their treatment options.

The ERNs are supported by European cross-border telemedicine tools, and can benefit from a range of EU funding mechanisms such as the "Health Program", the "Connecting Europe Facility" and the EU research program "Horizon 2020".

All the persons on the pictures of this report gave their authorization for ERN-EYE use their image for this event, in accordance with the European and local laws. The signed autorizations are available upon request.

DAY 1 -

General objectives of the meeting

Hélène Dollfus, ERN-EYE coordinator, Camiel Boon, host of this ERN-EYE workshop and representative of the Amsterdam University Medical Centers, member of ERN-EYE.

The workshop was opened by the organizing committee composed by Camiel Boon, host of this ERN-EYE workshop and Hélène Dollfus, ERN-EYE coordinator. They welcomed all attendees, for the first ERN-EYE in-person meeting since the beginning of the pandemic.

They introduced the topic of the meeting and highlighted the importance of ERNs for rare disease patients.

THE EUROPEAN COMMISSION OPENING ADDRESS

Why are ERNs important for Europe?

Andrzej Jan Rys, DG Sante, Director responsible for Health Systems, Medical Products and Innovation, European Commission, Brussels

ERNs are part of EU values of solidarity and equity. While it has been a long process of development, the strong political support has led to new opportunities. ERNs are now able to meet their goals of sharing knowledge, and through the Ukraine crisis have demonstrate their abilities to act in a crisis, organising help. Now, in line with their missions they are generating and sharing knowledge via the development of guidelines, the use of the Case Patient Management System (CPMS) and the implementation of registries. The EU tries to provide support with new financial systems, by reducing bureaucratic burden on ERNs for example through the new AMEQUIS evaluation platform, which will help improve the quality

of ERNs, through research opportunities or the implementation of a new partnership to help multinational clinical trials.

Main recent development and Challenge for ERNs

Martin Dorazil, DG santé Deputy Head of Unit, European Reference Networks and Digital Health Unit, European Commission, Brussels

The ERNs are still in development. Following their enlargement, they will have to consolidate the clinical collaborations and integrate their new members, ensure their financial stabilities, integrate the ERNs to the national healthcare systems and continue their actions of knowledge generation, training and dissemination as well as their research activities. They will also have to demonstrate their benefits through the new evaluation system. Regarding funding, the current situation involving three different types of grants created a

complex landscape that generated a heavy burden to manage. These activities will be integrated in 2023 in one direct grant under the EU4health program, streamlined by the FNLC tool and linked to achievement of objectives. Following an evaluation of the Cross-Border healthcare directive, it appears that one important challenges that ERNs will face is the ERNs integration to National Healthcare System. A joint action call was proposed with the support of the EU Commission. It would provide a methodology framework, with recommendations on governance, referrals, interface with ERNs, capacity building… The applications will open from Sept 2022 to Jan 2023, for a kick-off during 2023.

The new tool used for ERN evaluation, AMEQUIS, was also presented. Evaluation is a legal obligation, so AMEQUIS is an integrated process. After an initial assessment, there will be a continuous monitoring. The ERNs evaluation will start September 2022, for a final report around the summer of 2023

The Patient's expectations

Russel Wheeler, LHON Society, ePAG representative

Russell wheeler came to present the role of the European Patient Advisory Groups (ePAGs), who are an essential part of ERN governance. They are composed of volunteer patient and represent the interests of all patients whose conditions are covered by the ERNs. Patients bring to the table lived experience, a more holistic viewpoint of the entirety of the drug development process and can bring a fresh and pragmatic perspective to many discussions. They can also mobilise and move things along at a political level. Overall, ePAGs priorities are the implementation of registries, the development of better, more effective outcome measures as well as the development of guidelines and best practices, to work more closely with regulators

and payers and to support ERNs to become embedded into national health systems.

"The New ERN-EYE": setting the scene

Hélène Dollfus, ERN-EYE coordinator

As coordinator of the ERN-EYE, Pr Dollfus briefly recalled the missions of the ERN. The main upcoming challenge is the national integration. The ERN-EYE is currently in a transition phase, with many vacancies to fill, the addition of new members, the implementation of new funding and evaluation systems. The ERNcare4Ua action to provide support to rare disease patients from Ukraine through different actions (1) the creation of a website gathering all information for rare disease patients and doctors.

THE CPMS VIRTUAL CLINIC: SOLVING CASES BY EUROPEAN COOPERATION

CPMS current status and new compensation access

Hélène Dollfus, ERN-EYE coordinator

The Clinical Patient Management System (CPMS) will now implement a new financial system that will reimburse 50€ to the submitting HCP and 150€ to the panel lead once a case has been solved and the outcome posted in the CPMS. This will require organisation within the WGs who will have to pre-define panels for diseases (composed of 3 to 5 experts max) and to ensure regular turnovers of the panel lead. The legal framework of the reimbursement procedure will be covered by the network agreement and a financial annex. Reimbursement will follow invoices,

which will be requested every 6 months

The Grand Round ERN-EYE Transnational meetings (GREET)

Bart Leroy, Ghent University Hospital, Belgium

The GREET meetings are virtual case presentations of Rare Eye Disease cases (6 per GREET). Anyone from member-HCPs or affiliated partners can present interesting cases or request diagnostic input. The cases need to be uploaded on CPMS beforehand, and the discussion are led by Prof Holz, University Hospital of Bonn, and Prof Leroy, Ghent University Hospital. These meetings are scheduled three to four times annually, on Friday afternoons at 16.30hrs CET and last at most one hour and a half. Future GREET Meetings will be on the 3rd of June 2022 and the 2nd of December 2022.

Rare Eye Diseases-Variant Revue (RED-VAR) meetings

Elfride De Baere, Ghent University Hospital, Belgium

The RED-VAR meetings are virtual case presentation focused on variant validation for trials, particularly in case of Variants of Unknown Significance in actionable genes (RPE65). Anyone from member-HCPs or affiliated partners can participate. The cases need to be uploaded on CPMS beforehand, and submitted using a given template. The information needed are the genetic testing, medical and family history. These meetings are scheduled four times annually, and the next meetings will be on the 17th of May 2022.

The new CPMS: future challenges and opportunities

Joao De Sousa & Michèle Foucart, Directorate general for Health and Food safety, European Reference Networks and Digital Health, European Commission

Following clinicians' feedback that they needed a tool easier to access and to use, a call was open to design new CPMS from scratch and focused on clinicians.

Offers are currently under review, for an estimated start of the project in Sept 2022 and a Go-Live of the first version towards the end of 2023, followed by a progressive, one-year phase-out of the current CPMS starting 2024. In order to be closer to the actual needs of the user, the development cycle will see the involvement of user-representatives throughout the process. These URs (ideally at least one clinician from the network), will have to help define and validate requirements at regular intervals, perform user acceptance tests and participate in demos and pilot phases. The objectives are to make the CPMS more flexible, easier to use and to search (depending on GDPR compliance approval).

COLLECTING DATA FROM RED PATIENTS IN EUROPE: A CRUCIAL NEED

REDgistry: the ERN-EYE registry

Dorothée Leroux, ERN-EYE project manager, standing for Yann Brelivet, REDgistry Project Manager

Sharing of knowledge and data is crucial to the ERNs' mission. Registries are necessary infrastructure for the implementation of the ERNs' mission, which makes them a priority for the RD community at a National, European and International level. Registries are a major determinant for successful translational research in the field of RD, as they connect data from multiple HCPs and reinforce research capabilities and knowledge. REDgistry will be composed of 2 datasets, the JRC Common Dataset (16 items) which is common to all RD registries and ensure the interoperability of all ERDRI-based registry and the REDgistry Eye Dataset, composed of 60 items. It will be interoperable, secured through pseudonymisation,

GDPR-compliant and FAIR (Findable, Accessible, Interoperable and Re-usable). Each centre owns their data, and patient consent will have to be obtained.

REDgistry in practice – Pilot centres

Dorothée Leroux, ERN-EYE project manager

REDgistry requires a fairly long implementation process that requires the validation of the HCP legal and ethics committees. To account for this, a new financial compensation system has been set up, using the network agreement and a financial annex. To start, 5 HCP will be pilots, and more centres can be opened later, on a voluntary basis. 100 000€ over 18 months were dedicated, meaning 10€ per patient with a total objective of 10 000 patients entered (2000 per HCP). The system will be interoperable, and programmed to check whether patients were already entered, to avoid duplicates. Whether patients who are already entered in another registry will have to sign an informed consent form again will depend on local regulations.

EMA & Real world evidence

Alexandra Pacurariu, Pharmacovigilance and Epidemiology Department at the European Medicines Agency (EMA), Task Force in Data Analyis Methods

Real-World Data (RWD): routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials eal-World Evidence (RWE): information derived from analysis of real-world data. In the regulatory process, RWE is mostly used in phase 4 for safety monitoring, but it can be involved at any stage of the regulatory process. The main issue is the fragmentation of data collection between countries and the skills and technologies involved in data collection. For their studies, the EMA uses in-houses databases, but has also set up a new framework contract with eight research organisations and is launching the Darwin EU, expected to be fully operational in 2025. It is a federated network of data, expertise and services that will support better decision-making throughout the product lifecycle, by generating reliable evidence from real world healthcare data. The data will stay local and the use of Common Data Model will help perform studies in a timely manner and increase consistency of results. RWD is particularly useful for rare diseases due to their small numbers and the potentially different clinical presentations. Finally, the EMA has

produced a guideline to provide recommendations on key methodological aspects of registry-based studies, and to highlight relevant legal bases and regulatory requirements. The role of the ERNs has to be included by the EMA, which will come, and in the meantime, it is important to have a strong collaboration and dialogues with partners and countries.

COLLECTING DATA FROM RED PATIENTS IN EUROPE: A CRUCIAL NEED

Building ERN registries: the ERKnet experience and beyond

Franz Schaefer, Heidelberg University, Germany.

Frank Schaefer, ERNKnet Coordinator, came to describe the implementation of the ERNKnet registry: ERKReg. As a reminder, the first registries were started in 2018, with five ERNs pilot that were funded through the EU Health Program 2018. In 2019, the program was extended to the 19 remaining ERNs. Currently, 50% of registries are approved. There are two ways to do a registry: by using centralised , which is the classical way, using human input, and the federated way, with uses local data, interrogated by queries, which increases data security but decreases precision. ERKReg is a single core registry for all rare kidney diseases. It contains demographic information, allows for identification of patient cohorts for clinical research and deep phenotyping and natural history tracking in disease-specific sub-registries and allow a monitoring of clinical management performances and outcomes. It is divided in two datasets, one core and one disease-specific, with two type of data collection: one basic, containing JCR core data element, diagnostic information, genetic diagnostics… and a longitudinal data collection, with annual updates, and entering treatment modality kidney function, blood pressure… as well as KPIs for treatment efficacy . It allows the existence of individual registries more focused on details industries are very interested in sub-registries. The KPI monitoring allows harmonising and optimising patient management to produce useful statistics. The registry includes 200 items, but not all are filled. Usually, around 30 to 40 items are filled per patients. Registries increases clinical research, which means that centres develop relations with industries for use of data, with clear contracts. The political side remains reluctant though, while this issue is crucial. Some issues to consider with registries: have a lean data

collection, with all information gathered in one place; define the rules of authorship, ownership and data sharing. The harmonisation with ERICA and EJP-RD, define the details and requirements from data holders but overall benefits for all users.

ERN registries, what for? The Commission's vision

Hélène Le Borgne, Policy and programme officer – Research programmes, DG Research and Innovation, European Commission

Rare diseases are a priority for the EU, who has recognised the need for pooling data that is currently very fragmented. Registries are a high priority for ERNs, as integrated patient registration and follow-up will demonstrate the added value of Networks. Registries objectives are the collection of epidemiological data on rare diseases, the identification of current RD cohorts for clinical research as well as the monitoring of natural disease history, adherence to best-practice treatment protocols and outcomes of therapeutic interventions. The main challenges include data fragmentation & duplication, insufficient geographical coverage, the wide range of expertise needed (medical, biostatisticians, IT….), the availability of funding required setting up and maintaining a sustainable registry. The disparity in ethical and legal aspects: consent of patients, ethics approval… is also an issue. Non or insufficient involvement of patients and patients groups in the development of registries can be a hindrance. In conclusion, ERN registries have a true and growing potential to gather real-world evidence, to achieve generalizable results based on patient cohorts and overall, to help structuring the rare disease field (healthcare and research) and improving interoperability. To achieve these goals, support is available through programs such as EJP RD, ERICA, future Partnership on Rare Diseases under EU, R&I programme Horizon Europe and can take the form of tools, webinars, fora for discussion, exchange and consensus building, funding…

MEETING WITHIN WORKING GROUPS: ORGANISING THE ROADMAP FOR THE COMING YEAR

Guidelines: the process for guidelines and related documents production

Amélie Gavard, ERN-EYE medical writer

The production of high quality guidance is an important aspect of ERNs activity. Clinical consensus statements reflect opinions drafted by subject matter experts for which consensus is sought using explicit methodology to identify areas of agreement and disagreement. Several guidelines have been identified as priority (RPE65, LHON, RP and Aniridia), one consensus is ongoing for Bardet-Biedl syndrome.

CPMS use (standard, GREET and RED-VAR): how to make it through?

Francesco Rotolo, ERN-EYE IT Specialist

The CPMS (Clinical Patient Management System) can be used to discuss patient cases at an European level. Prior to any consent must be signed by the patient (). Should the ophthalmologist wishes to consult with other experts, they can do so via the CPMS. First, he will enrol the patient (with his consent, prior to any enrolment. Versions are available directly on the application) and fill in the dataset with all relevant information (e.g. OCT, ERG…). An e-mail is sent to invited experts all over Europe to discuss the case. The case is discussed and a recommendation will be produced for diagnosis, treatment or management. The ERN-EYE also organises different type of meetings using the Clinical Patient Management System: the GREET meetings (Grand Rounds ERN-EYE Transnational), every two months, which is a unique opportunity to discuss challenging cases and to share the knowledge of various European experts; and the

RED-VAR meeting (Rare Eye Diseases VARiants), four times a year, where RPE65 cases for which treatment by Luxturna® may be considered an option but where a concertation of ERN-EYE experts might be necessary to reach an treatment decision are discussed.

Training & Education per disease

Dorothée Leroux, ERN-EYE project manager

Training and education are a key part of the ERN activities. It can take different forms and aim at different audiences, but the sharing of knowledge is very important and valorise the expertise within the network.

ERN-EYE Webinars for professionals are short (usually 1h) and focused on a specific subject. They are open to all and free, but there are no official recognition for the attendees. They are however recognised as ERN activities in the monitoring. An accreditation by a scientific society could be an opportunity to increase visibility and recognition. The objective is to produce at least three webinars per WG.

The eLearning program for professionals aims to bring the best care to all EU citizen affected by a RED and to establish a reference educational program dedicated to Rare Eye Diseases. Students are expected to come from a wide range of backgrounds.

The ERN academy is for now a pilot project that will feature a Moodle-based platform and will provide integrated support for virtual classes, online testing and evaluation, discussion fora, Web conferences…. The pilot phase is expected Q3 of 2022, and two modules (retina and anterior segment) are being developed.

National Integration

The national integration challenge

Holm Graessner, Institute of Medical Genetics and Applied Genomics, Germany.

ERNs are developed on three levels: structures, processes and outputs. National integration can be defined as national healthcare providers adopting ERNs' structures and processes, and using ERNs' outputs. However, the fact remains that there are 24 ERNs, 27 countries, and that one size most certainly does not fit all. Member states are at different stages of rare disease care organisation and implementation. They can have different reimbursement politics. Furthermore, integration of process would interfere with national responsibility for healthcare, and ERN services includes healthcare systems with different resources, which would require a reorganisation of health care services in member states. Other challenges include the differences of priorities of ERNs and the need for

national decision makers to be involved. The easiest way to start would involve with structures and d outcomes, as Eurodris made a publication to help with this, and call for member states to get involved

National integration of ERNs seen from the Board of Member States' perspective

Till Voigtländer, MedUni Vienna, Austria

The board of Member states (BoMS) does not have a unified opinion on national integration. However, they understand the need for national integration and are planning a joint working group with the ERN committee to develop papers on guidance for member states. They plan a joint action, which would aims to be repository of recommendation, examples, and successful implementation concepts and to serve as an initiator of first action at national level joint action. It would focus on five working areas governance framework for national integration, particularly at the level of national reference framework, patient care pathway, referral systems to ERNs Education and national awareness raising on ERNs sustainability of the ERNs model at national level. Challenges come mainly from the huge diversity of national healthcare systems.

ERN Enlargement: New member states represented as full members in ERN-EYE

Finland

Joni Turunen, Helsinki University Hospital

Helsinki concentrates 40% of the Finnish population, and Helsinki University Hospital Department of Ophthalmology has a special clinic dedicated to inherited ocular diseases. The department also serves as a tertiary referral center for several subspecialties e.g. ocular oncology, rare anterior segment, and rare pediatric ophthalmology diseases. Clinicians in the HUH Department of Ophthalmology are

carrying out research on several trajectories of rare eye diseases, e.g., ocular oncology, retinal dystrophies, inherited glaucoma, inherited corneal dystrophies, and inflammatory conditions. The clinic also provides facilities for gene therapy of retinal dystrophies. Rare disease patient societies' representatives participate in the rare disease centers. Consultants involved in the rare eye diseases clinics are also actively available for the patient societies.

Ireland

David Keegan, ERN-EYE Ireland Consortium (EEIC), Dublin

The ERN-EYE Ireland Consortium is composed of the Mater Misericordia Hospital (Lead HCP), the Royal Victoria Eye and Ear Hospital and Children's Health Ireland, all located in Dublin. Their field of expertise for are retinal diseases, neuro-ophthalmology, paediatric rare eye diseases and anterior segment diseases. Patients associations are very active.

Romania

Adela Chirita-Emandi & Flora Stoica & Victor Babes, University of Medecine and Pharmacy, Timisoara*

The team is coordinated by Dr Florina Stoica and is situated in th Romanian Centrul De Expertiză Pentru Boli Oculare Rare (CEBOR), which is the only centre in the country in the field of rare eye diseases. The team includes three ophthalmologists, four geneticists, one specialist in Information Technology and one nurse. They have extensive experience medical management for people with rare eye diseases. They provide equitable access to diagnosis and treatment for patients (children and adults) with rare diseases of the retina, anterior segment of the eye, neuro-ophthalmology or syndromic. They also provide genetic testing, in collaboration with the Center for Genomic Medicine in the University of Medicine Timisoara, genetic counseling, support for the patients and their family for access to integrated care programs, early intervention, recovery and social services

CEBOR, in the field of Rare Eye Diseases, organize education and training, are involved in various research projects and clinical trials,

publish articles in internationally recognized medical journals and collaborate with patient association. As a new member in the ERN-EYE, their hope is to keep the team updated in offer medical care for people with rare eye diseases - at the highest European standards and to enable collaborative research.

Slovenia

Marko Hawlina, Eye Hospital, University Medical Centre, Ljubljana

The Eye Hospital, University Medical Centre Ljubljana, is represented by Prof. Marko Hawlina and Assist. Prof. Ana Fakin, MD.

The majority of patients with rare eye diseases are seen at the Ljubljana Eye Hospital, UMC, the only tertiary Eye Hospital in Slovenia, serving 2M people. Their field of expertise for rare eye diseases are retinal Rare Eye Diseases, Neuro-Ophthalmology Rare Diseases, Pediatric Ophthalmology Rare Diseases, Anterior Segment Rare Eye Diseases,. They bring active research in the field of genetic eye disease, a registry already including over 1000 patients with genetic eye disease and lectures about retinal dystrophies and hereditary optic

neuropathies, available online for all the members. They also have long follow-up of patients, with electrophysiology results and autofluorescence images, as well as interesting, specific genetic results (i.e. in LHON additional new mutations were found besides three most common mitochondrial mutations).

Spain

José Maria Herreras & Lidia Cocho, Hospital Clinico Universitario de Valladolid

In Spain, a royal Decree on Reference Centres, Services and Units (CSUR), prioritized the definition of the criteria, accreditation and designation of reference centres for rare diseases. The seven full members for ERN-EYE are selected from these centres, each with their specialities.

The University Hospital Cruces, Bilbao, is a CSUR since 2008 and focus on ocular Surface Reconstruction (keratoprosthesis), orbit and oculoplasty. They look forward to share expertise help for some cases in panels or in a sub-workgroup on KPro to share experience, help define guidelines for KPro, participate in exchanges and unify data collection.

Sant Joan de Déu Hospital, Barcelona is a CSUR for paediatric eye diseases and have expertise in retinoblastoma, hereditary retinal dystrophy, paediatric vitreoretinal diseases, congenital and infantile glaucoma, paediatric penetrating keratoplasty, complex paediatric cataracts, paediatric orbital and eyelid misdevelopment, paediatric orbital tumours.

University Clinical Hospital and IOBA, Valladolid, is a CSUR for complex reconstruction of ocular surface and for brachytherapy for uveal tumours in adults. IOBA - University of Valladolid focus on hereditary retinal dystrophy, low vision and visual rehabilitation, neuro-ophthalmology, genetic counselling. It has a large experience in cell therapy in humans (stem cells for limbal insufficiency syndromes) and is used to collaboration in EU granted projects.

Hospital Universitario de Bellvitge, Barcelona, is the national referral centre in inherited retinal diseases (IRD) in Spain and is a Luxturna treating centre. Combined with Children's Hospital (H. Sant Joan de Deu), it sees over 850 IRD patients and realises over 600 genetic tests.

Hospital La Paz, Madrid, is the national referral centre for congenital cataract, paediatric intraocular tumours, paediatric orbital tumour, and developmental anomalies of the eye, paediatric keratoplasty, ocular melanoma and paediatric VR surgery.

Hospital Clinico San Carlos, Madrid, is a national reference centre for childhood glaucoma and for ocular surface disease and anterior segment reconstruction research. They also have several collaborations in genetics and research.

Hospital Clinic, Barcelona, is focused on Neuro-ophthalmology rare disorders and is a national reference centre for hereditary optic nerve disorders (LHON, DOA), optic neuromyelitis and MOG disease, multiple sclerosis, ataxias, paraneoplastic disorders, autoimmune diseases, other neuro-ophthalmological anomalies.

Sweden

Stefan Lögren, St Erik Eye Hospital, Stockholm

The St. Erik Eye Hospital is represented by Stefan Löfgren, MD PhD Assoc Prof and Kristina Teär Fahnehjelm, MD PhD Assoc Prof. It is strong of 440 personnel and over 100+ ophthalmologists and is the national center for paediatric cataract, paediatric glaucoma and ocular oncology, and has a field of expertise in rare eye disease.

They bring a strong expertise in paediatric eye disease, clinical expertise in a broad spectrum of diseases, experience on quality registers and research capacities on, amongst others, optic nerve diseases and metabolic diseases. In return, they hope to benefit from other members' expertise for individual patient cases and to participate in multicenter studies on rare diseases and European registers.

DAY 2 –

ERNs & RESEARCH SESSION

Introduction & Context

Hélène Dollfus, ERN-EYE coordinator

While the ERNs are care-orientated, research is of critical importance in Rare Diseases and ERNs evolve in a research-orientated environment, where many research opportunities are available. ERN-EYE needs to make a full use of these opportunities and be more involved in research.

The future Rare Diseases Partnership initiative for research

Birute Tumiene, Vilnius University, Lithuania

While a lot has been done already in the European Rare Disease ecosystem, a lot remains to be done. This is why the Rare Diseases Partnership has been created. Its missions are (1) to bring support to Research and Innovation, (2) to ensure that every RD patient is contactable and can be enrolled in suitable clinical studies and (3) to make EU a global leader in rare diseases research. The partnership will have several activities, such as coordination; strategy and governance activities, but also a research funding support activities, clinical research network for rare diseases and transversal support services. They will also support patient engagement. Funding increases for research opportunities, the ERN are encouraged to participate to joint calls and to associate underrepresented

countries. The RDP should start in 2024, and represents a huge opportunity for research within the ERN.

The EJP-RD general presentation & future Clinical Research Networks

Yan Mimouni, EJP-RD

Building up on the Rare disease partnership, Yan Mimouni came to present the European Joint Program for Rare Diseases (EJD-RD). This program aims to gather and develop structures, funding programs; tools… to create a research and innovation pipeline that ensure a rapid translation of research results into clinical applications. Opportunities include joint transnational calls, research mobility, Network support scheme, Research training workshops… and can be found at https://www.ejprarediseases.org/our-actions-and-services/funding-opportunities/

The EJP-RD is also developing a virtual platform that aims to assess needs and address them, for example by harmonising patient consent forms across EU or helping find the relevant resources at https://resourcemap.ejprarediseases.org/

In conclusion, this will provide an improved ecosystem for ERNs' research needs.

Flash example of ERN collaborations: EJP SeeMyLife

Hélène Dollfus, ERN-EYE coordinator

SeeMyLife is a project that tries to capture the quantitative and qualitative impact of Rare Eye diseases on affected European Children. SeeMyLife is a multinational and multilevel project that uses Mixed Methods Research to provide a holistic approach to child-centred evaluation of QoL and a better understanding of young RED patients' own experience. It also aims to create the European standards for VR-QoL and PROMS in children, as well as a unique, robust framework to evaluate the socio-anthropological consequences of poor vision and blindness in European children.

ERICA project and related WGs

Alberto Pereira Arias, Endo-ERN and ERICA coordinator, UMC Amsterdam, Netherlands

ERICA is a research coordination and support action serving the ERNs. The aim of ERICA is to strengthen ERN's research and innovation capacity, through facilitating inter-ERN collaboration and increasing the visibility and impact of ERNs. ERNs engagement is crucial, particularly in the Data collection, Integration and Sharing work package. ERICA has set up several resources such as the ERICA research wall, which is a centralised location that serves as a matchmaking tool to announce any new project and search for collaborators. Any new inter-ERN collaborative project can be advertised via this research wall, and it provides basic information about open calls for collaboration as well as contact details of the project PI. ERICA also provides workshops, webinars, and catalogues of services. They can be found at http://www.erica-rd.eu/

Presentation of the ERNs access to various programmes & opportunities via ERNs: in practice

ERN-EYE team

Within the different programmes, especially the EJP-RD, ERN members can apply to funding opportunities regular calls.
The ERN-EYE and ECORYS exchange programme has been extended to December 2022 and now allows group exchanges.
On top of several joint transnational calls, the EJP-RD has other specific opportunities:
ERN Research Training workshops: aims to train researchers and clinicians affiliated to ERN on relevant topics on research in rare diseases and offers up to 25 000€ for a 2-day workshop

Networking Support Scheme Call: encourage sharing of knowledge on RD, and aims to increase the participation of underrepresented countries in Europe. It is funded quarterly, with a maximum of 30,000 € per event.
Mentoring for Translational Research (partnership with EATRIS): a mentoring service for researchers planning a project that has translational potential for RD, in order to increase the impact of projects by providing tailored expertise along each step of the translational pathway. EJP-RD Support office: provides support for

the preparation of clinical studies into rare diseases.
EJP-RD Rare Diseases Clinical Trials is a practical and guided toolbox to help clinical trialists and R&D managers understand the regulations and requirements for conducting trials, with special focus on investigator-initiated trials for rare diseases.

WRAP-UP FROM THE WG LEADS

WG 1: Retinal Rare Eye Diseases

Introduction: The working groups were to propose and settle on action regarding the following topics: CPMS, Webinars, e-learning and guidelines.

Bart Leroy, Ghent University Hospital, Belgium

CPMS: the CPMS was an extra, as the WG1 uses regularly the CPMS due to the GREET and RED-VAR meeting. Several webinars have been proposed on CMO in IRDs, CSCR, Usher Syndromes, Deferoxamine retinopathy, Pseudoxanthoma elasticum and FEVR.Regarding the eLearning, a module on Retinal diseases is already being finalise. Considering the guidelines, the WG is already involved in Bardet-Biedl Syndrome, RPE65 and RP guidelines. Other suggestions have been made. As Pr Audo and Pr Leroy are current board members of Euretina, an endorsement of the guidelines produced by the ERN-EYE might be envisaged.

WG 2: Neuro-Ophthalmology Rare Diseases

Steffen Haman, Righospitalet, Denmark

Regarding the use of the CPMS, WG2 is probably going to stick to the classical format for the time being, eagerly waiting for the new version to arrive. However, in NO due to often challenging and tricky cases, GREET sessions may be a possibility, as experts from this group are used to grand rounds already. A webinar were on ODD-AION, the optic disc drusen associated anterior ischemic optic neuropathy was suggested. For eLearning, Valladolid, a new working group member, has developed for neuro-ophthalmology eLearning programme and but it was agreed that it should not be a huge undertaking to translate these materials to English, subject to the necessary approvals from and acknowledgement of the work undertaken by Valladolid.

A guideline on MOGad (myelin oligodendrocyte glycoprotein antibody disease) was suggested, as MOGad is a hot topic in neuroophthalmology and a place where consensus guidelines are needed, as this is a disease that is actually being treated, and where recent studies suggest that maintenance intravenous immunoglobulin may be an effective treatment to prevent relapses. Names for who could / would be potential leads for this guideline can be brought up at the next meeting, which should also identify

appropriate centres for leading on LHON guidelines.

It was was agreed to arrange a Zoom call in June for the group both to continue the discussion and also to allow new members to contribute to the discussion. In addition to the zoom meeting, a hybrid follow-up meeting in Berlin in September 2022, endorsed by ERN-EYE.

Finally, it was mentioned that this WG would need to find a co-chair.

WG 3: Paediatric Ophthalmology Rare Diseases

Dominique Brémond-Gignac, Necker Hospital, Paris, France

For the CPMS, WG3 decided to split in four groups: anterior segment, paediatrics, early diagnostics and neonatal, panocular and syndromic forms. For eLearning, the Spanish members have produced several webinars that the group would like to have translated. They also suggested that the GREET could have special paediatrics cases. Regarding the guidelines, the Aniridia guideline is beginning under the coordination of Pr Brémond-Gignac. The group also raised the wish to be included in other groups' guidelines, as many of the diseases considered often appear in paediatric patients. They also suggested an inter-ERN initiative on neonatal patients.

WG 4: Anterior Segment Rare Eye Diseases

Daniel Böhringer, Eye Center, University Hospital Freiburg, Germany

The WG mentionned that they had, so far, no GREET cases. They decided to implement 4 groups of experts to reply to any requests: corneodystrophies, tumors of the eye, Advanced therapies and inflammation. Regarding the webinars, they proposed four topics, on corneal dystrophies, stem cells replpacement, keratocones in children. They also raised the idea of a MOOC, to build up interest in their area. This sparked a discussion on the aims of the training and

education goals of the ERN-EYE. These goals are first focused on normal, non-specialist HCP, but the idea of different levels, ranging from basic to advanced, has merit. The possible implementation of an ERN-Academy, with synchrone sessions roughly three times per year. Pr Leroy also raised the possibility of short clinical "pills", small snippets of knowledge (10-20min max) on specific cases and topics, and to create a repository to host them.

WG 5: Low vision, Daily Life and Patients Groups

David Keegan, ERN-EYE Ireland Consortium (EEIC), Dublin

The group confirmed the Low Vision Services Survey prior to circulation, checked the acknowledgement of all TWG5 members on Care plan paper, which is finished and ready to submit.Regarding the guidelines (CCS), two guidelines were proposed: Paediatric Vision Assessment Consensus statement and Adult Vision Assessment Consensus statement. A meeting was set up for the end of May.For the new CPMS Representative, a volunteer (clinician with interest in registry / IT / CPMS) will be designed if one has not manifested themselves by May 7th. Three themes, split over 5 sessions done over 18 months, were suggested . One on Paediatric Vision Assessment, including General Testing in paediatric, and Examining and Diagnosing Child with CVI / Multi-Disability; one on Adult Vision Assessment, divided in Assessment and Management; and finally on PROMs, for paediatrics, adults and ULV.Last, for the education modules, the group proposed post webinar lectures (all invitees will be informed that they will be recorded), multiple videos on testing techniques, for example looking for "ideal" and "real world" examples, PROM deployment… and a "Practical Pearls" Section (1-3 tips).

WG 6: Genetic Diagnostics

Elfride De Baere, Ghent University Hospital, Belgium

The group was presented the genetic testing and variant classification RED as well as the RED-VAR meetings.
The matter of genetic testing and reporting in the context of carrier screening (pilot ABCA4) was discussed. It was agreed that a follow-up by ERN-EYE/TWG6 was needed regarding the practice of clinical genetic testing and counselling. The group identified several challenges to address: Preconceptual carrier screening of ABCA4 in partners of patients ; Preconceptual carrier screening of ABCA4 in healthy carriers (expanded carrier screening).
Several questions were asked: 1. Technically: which test is recommended? Targeted testing, coding region, entire gene? 2. What variants to report? All variants (class 3-5) or just 4/5 ACMG variants? 3. What to do with known class 3 variants (e.g. in LOVD)? To report? 4. How to deal with requests for PND or PGT? 5. Do you report low penetrance variants? How? 6. What about variants that are often seen in cis? How does one approach segregation here? 7. If you only report level 4/5 variants, how does

this reduce risk for partners (i.e. what proportion of pathogenic alleles in ABCA4 are 4/5?).
For the Fall meeting 2022, the aim is to share survey with TWG6/ERN-EYE, which the core team will analyse and use to draft guideline, then share that draft with the TWG6 members in order to deliver an ERN-EYE guideline for testing and reporting of (mild) variants in

REDgenes in a preconceptual context (partners) – ABCA4 as an example.
Several webinars were planned: Genetic Testing Strategies for RED, Whole genome sequencing for diagnostics of IRD, Interpretation of Sequence Variants in RED, Collection and classification of variants associated with IRD. The following topics were suggested: Counselling strategies for genetic diagnostics in RED, Genetic testing and variant reporting in preconceptual screening - survey on ABCA4, Genetic testing and variant reporting of hypomorphic alleles - example of albinism, Expanded carrier screening: feedback about RED from pilot projects, Opsin genes, Policy actions for genetic testing. The recording of webinars, followed by Q&A sessions should be done around fall 2022

ANNEX 1

ERN-EYE GENERAL ANNUAL MEETING

Satisfaction Survey- Results

ERN-EYE organized its 6th General Annual Meeting from April 25th to 26th 2022 in Amsterdam, Netherlands. It gathered nearly 80 people from the HCPs of 17 member countries of the network, as well as invited speakers.

The central part of the meeting was dedicated to the governance board bringing together the representatives of ERN-EYE full members and patient representatives. The rest of the meeting was devoted in particular to the question of the crucial need for collecting data from Rare disease patients in Europe: the importance of registries in Europe, the experience of ERN ERKnet and the presentation of the progress of the ERN-EYE registry (REDgistry). The Clinical Patient Management System CPMS was also discussed.

This meeting was also the opportunity to speak about national integration and ERN research projects (EJP-RD, ERICA). Finally, several ERN-EYE working groups had the chance to meet in parallel sessions.

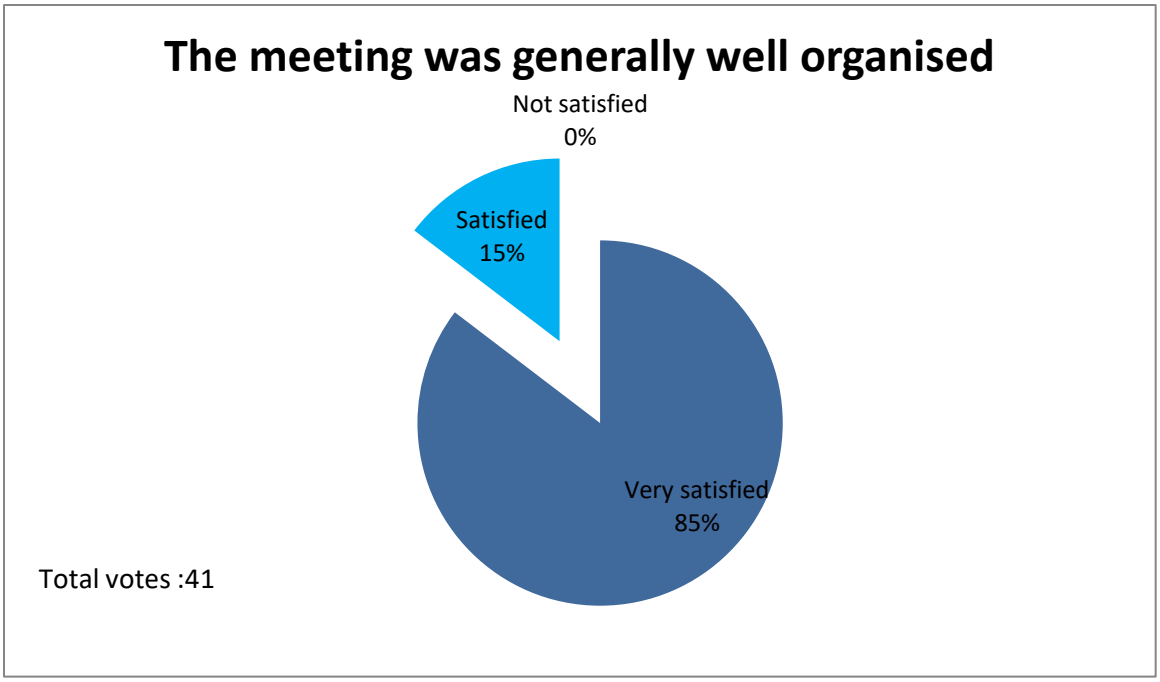
Above all, this meeting made it possible for the 28 new ERN-EYE members to introduce themselves and to meet (finally in person!) the rest of the network.

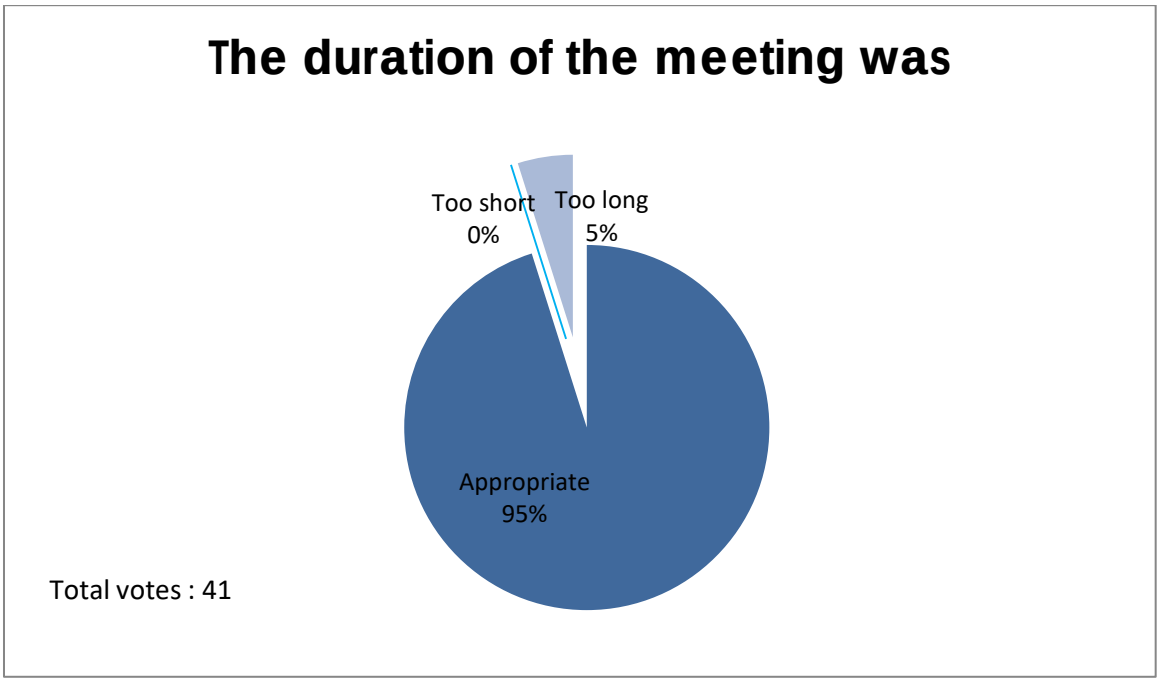
41 people answered the survey, representing half of the participants at the meeting.

In view of the 41 answers of the satisfaction survey, it seems that, generally speaking, this meeting met the expectations of the participants.

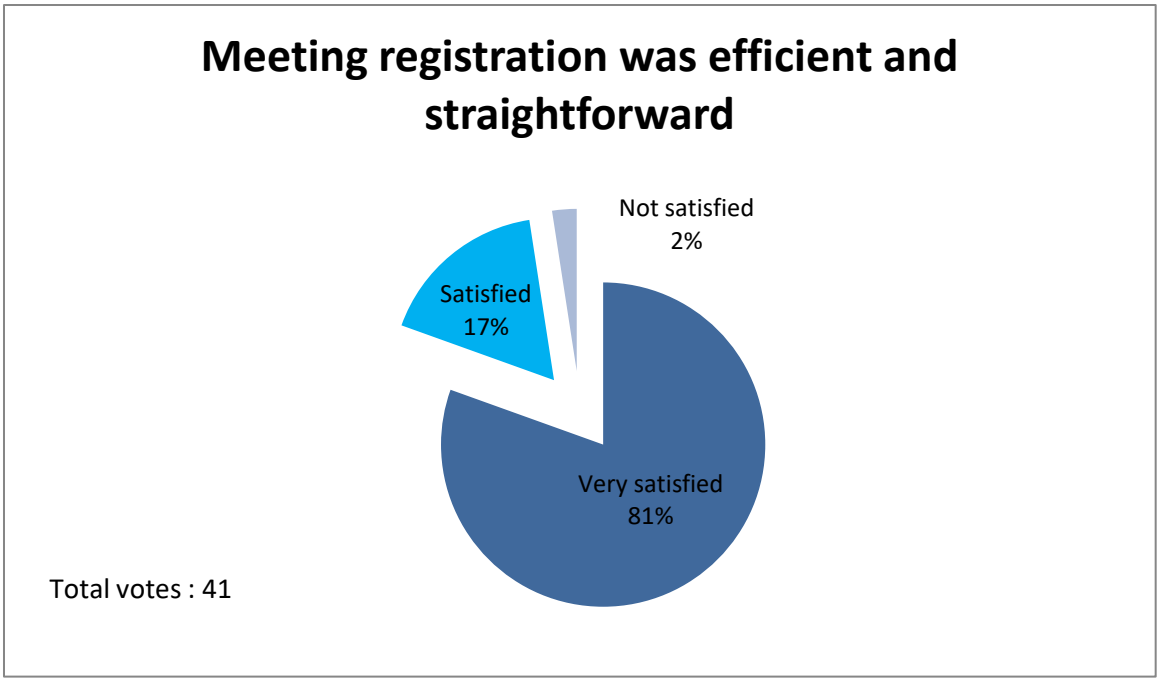
The only weakness in the organisation of this meeting was perhaps that the documentation (programme) was sent too late. Otherwise, the organization in general suited the participants.

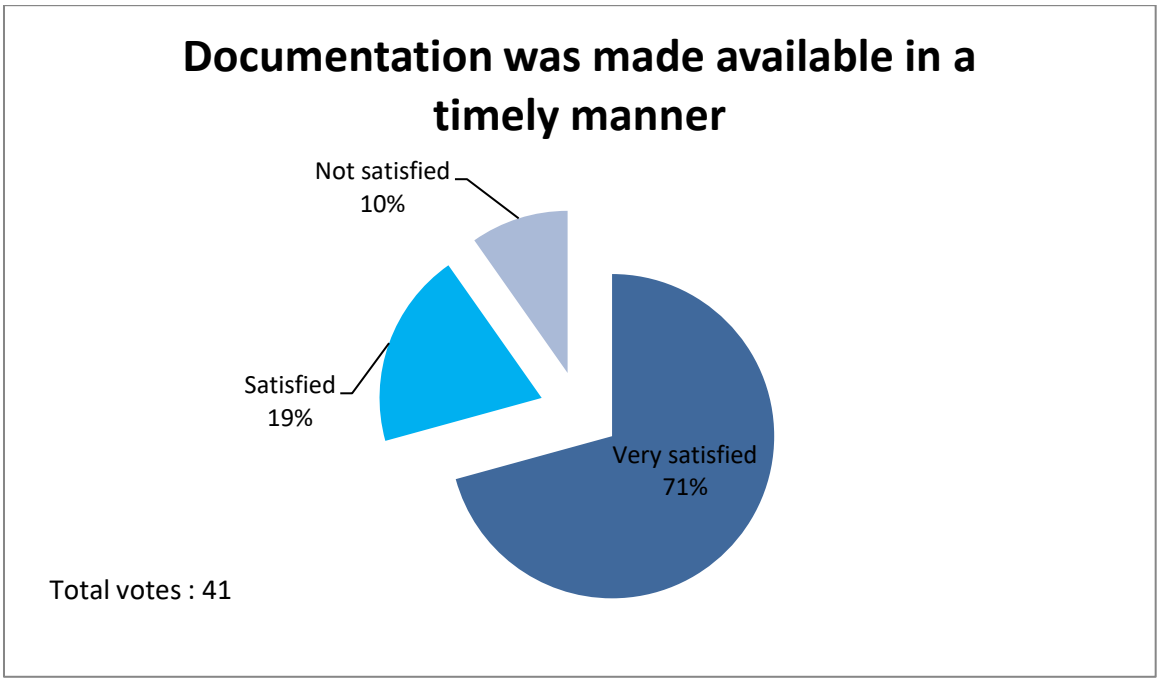
The results are presented below, question by question, with the percentages of responses.





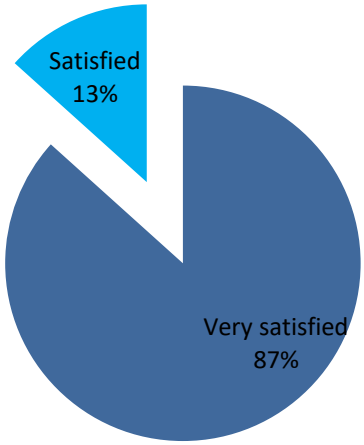
We noted that the participants were generally satisfied with the progress and organization of the meeting. This time, the duration of two days seemed to be good, a little too long for some of them.





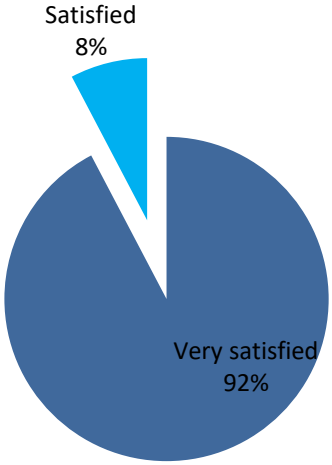
The registration was efficient for the participants but some of them would receive the documentation earlier.

The venue and its location met my expectations

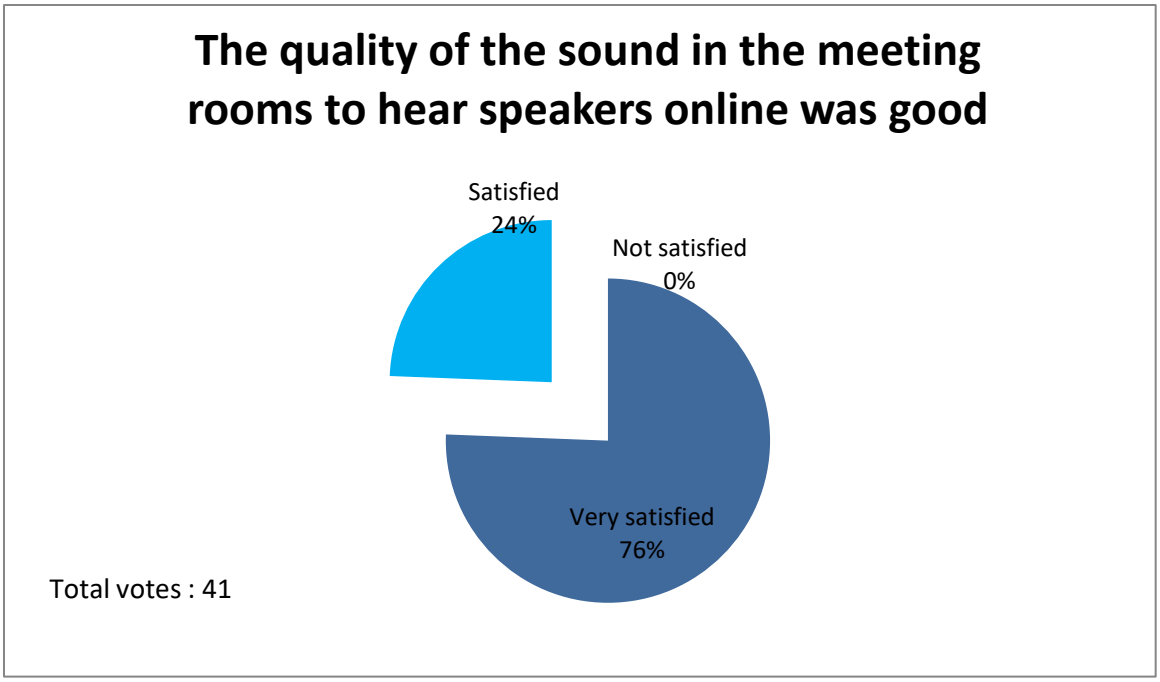


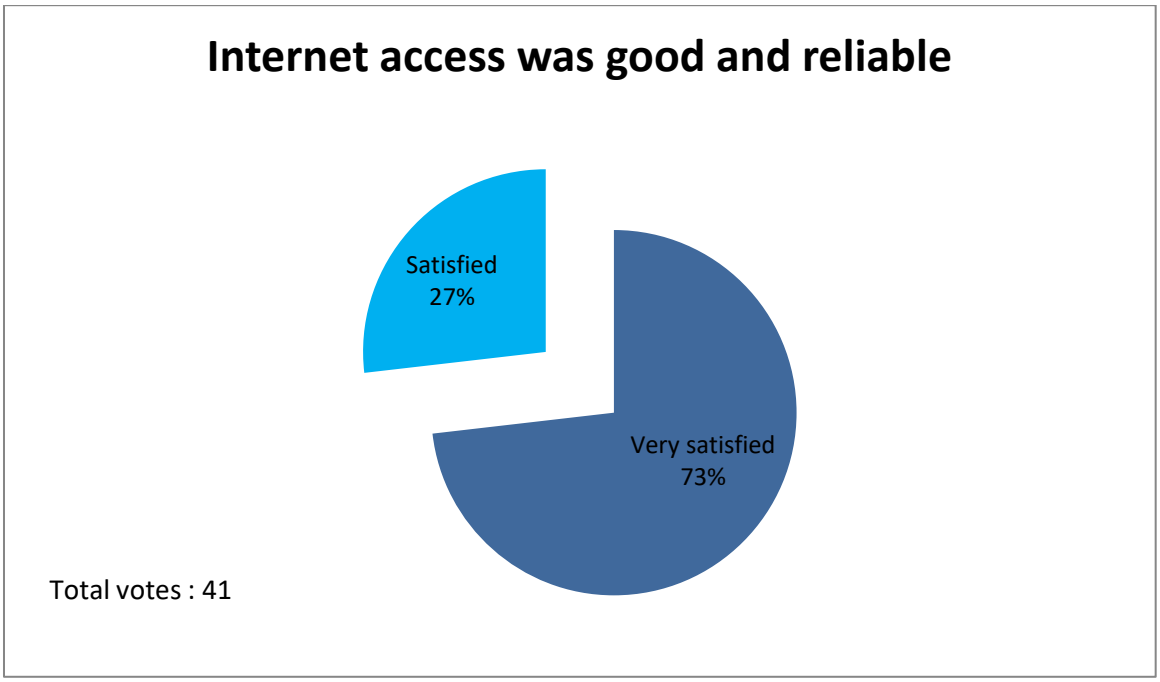
Total votes : 41

The quality of the sound in the meeting rooms to hear speaker on site was good



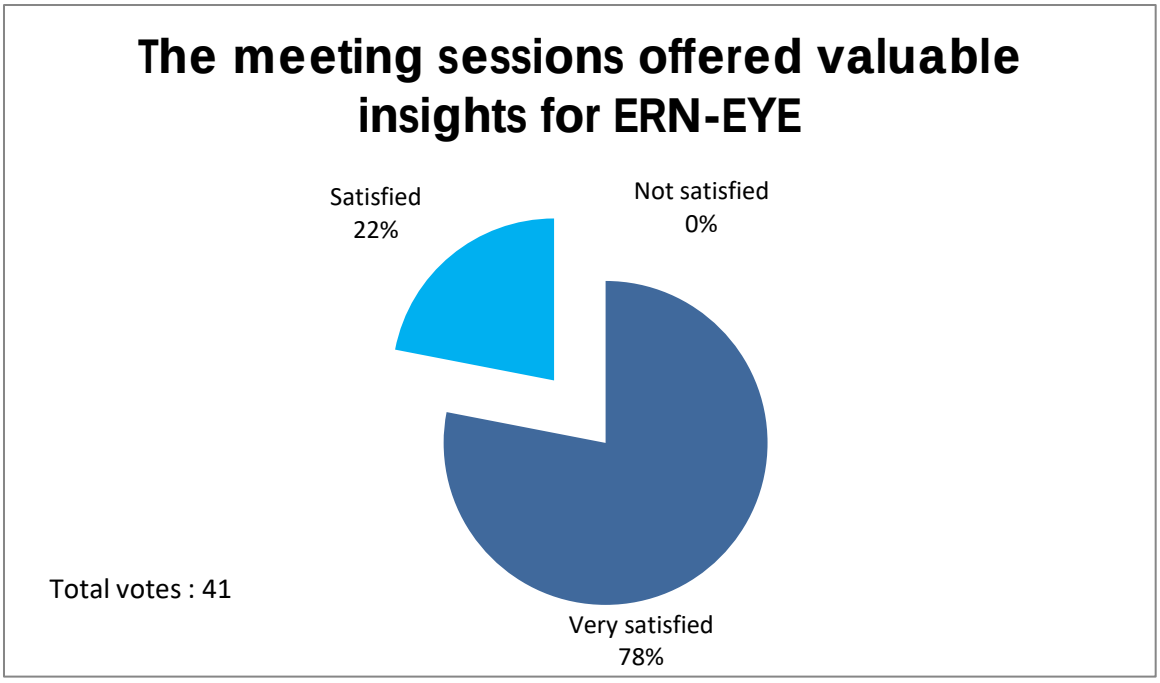
Total votes : 41

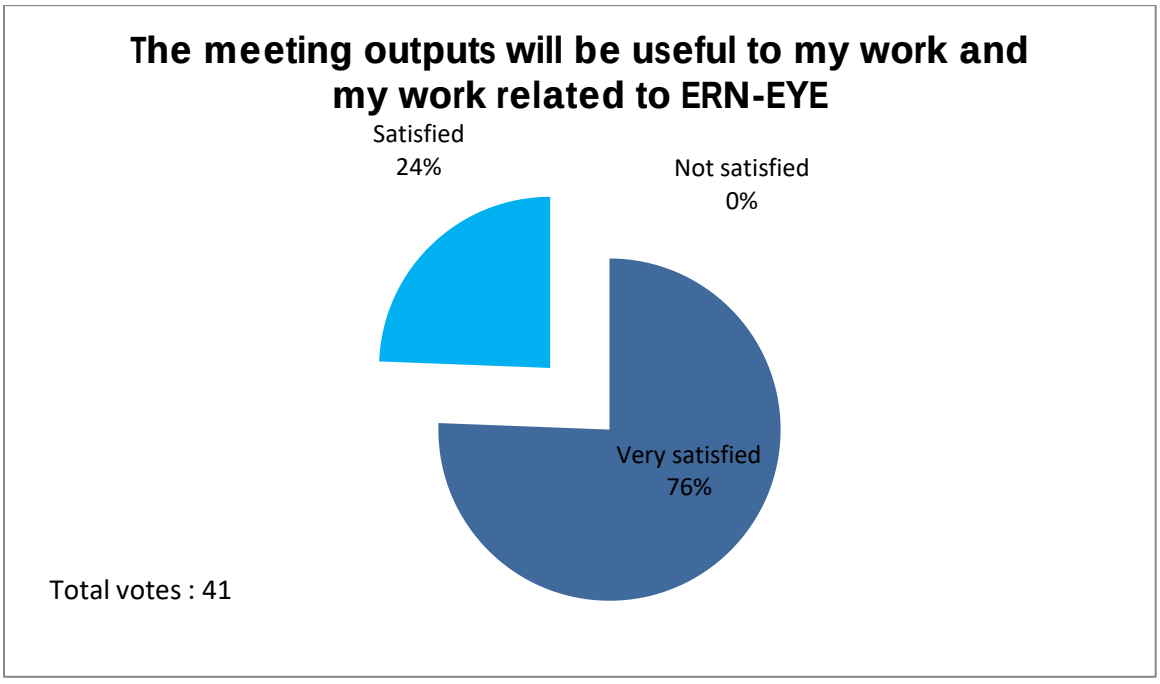




The event's format made it possible to satisfy almost all the participants.

The quality of the sound and Internet was good.





The goals of the General Annual Meeting were to draw the situation of the ERN-EYE projects, as well as the next issues for ERN-EYE in the coming months. It was also a good opportunity to welcome the new members. In view of the results mentioned above, it seems that the objective has been achieved.

ANNEX 2

PROGRAM

6th ERN-EYE GENERAL ANNUAL MEETING

April 25th - 26th 2022

Venue: Koninklijke Industrieele Groote Club, Dam 27, 1012 JS, AMSTERDAM

MONDAY – 25th OF APRIL 2022

08.30 – 09.00 Registration

09.00 – 09.40 WELCOME SESSION

09.00 – 09.05 Welcome and program of the 2 days
Hélène DOLLFUS (ERN-EYE Coordinator) & Camiel BOON (Local host, Academic Medical Center Amsterdam)

09.05 – 09.20 **THE EUROPEAN COMMISSION OPENING ADDRESS**

1) Why are ERNs important for Europe?
Andrzej Jan RYS, DG SANTE, Director responsible for Health Systems, Medical Products and Innovation, European Commission, Brussels

2) Main recent development and challenges for ERNs
Martin DORAZIL, DG SANTE, Deputy Head of Unit, European Reference Networks and Digital Health Unit, European Commission, Brussels

09.20 – 09.30 The patients' expectations
Russell Wheeler, LHON Society, ePAG representative

09.30 – 09.40 "The NEW ERN-EYE": setting the scene
Hélène DOLLFUS, ERN-EYE coordinator

09.40 – 10.30 THE CPMS VIRTUAL CLINIC: SOLVING CASES BY THE EUROPEAN COOPERATION

09.40 – 09.45 CPMS current status and new compensation access
Hélène DOLLFUS, ERN-EYE coordinator

09.45 – 09.50 The Grand Rounds ERN-EYE Transnational meetings (GREET)
Bart LEROY, Ghent University Hospital, Belgium

09.50– 09.55 Rare Eye Diseases-Variant Revue (RED-VAR) meetings
Elfride DE BAERE, Ghent University Hospital, Belgium

Guest speaker

09.55 – 10.20 The New CPMS: future Challenges and Opportunities
Joao DE SOUSA & Michèle FOUCART, Directorate-General for Health and Food Safety, European Reference Networks and Digital Health, European Commission

Funded by the European Union

MONDAY – 25th OF APRIL 2022

10.20 – 10.30 Q&A, CPMS: how to use it within WGs?: a road map
Francesco ROTOLO & Dorothée LEROUX

10.30-11.00 COFFEE BREAK

11.00 – 12.30 COLLECTING DATA FROM RED PATIENTS IN EUROPE: A CRUCIAL NEED

11.00 – 11.30 TEHDAS towards a European Health data space: what place for rare diseases?
Markus KALLIOLA, Project Director in Sitra's Health data 2030 project, The Finnish Innovation Fund Sitra

11.30 – 11.40 REDgistry: the ERN-EYE registry
Yann BRELIVET, REDgistry Project Manager

11.40 – 11.50 REDgistry in practice – Pilot centres
Dorothée LEROUX, ERN-EYE Project Manager

Guest speakers

11.50 – 12.30 EMA & real world evidence
Alexandra PACURARIU, Pharmacovigilance and Epidemiology Department at the European Medicines Agency (EMA), Task Force in Data Analysis Methods

12.45 – 14.00 LUNCH PAUSE

14.00 – 16.00 MEETING WITHIN WORKING GROUPS: ORGANISING THE ROADMAP FOR THE COMING YEAR

WG1- Retinal Rare Eye Diseases, *Bart Leroy (Ghent University Hospital, Belgium) & Michael Larsen (Rigshospitalet, Denmark)*

WG2- Neuro-Ophthalmology Rare Diseases, *Steffen Hamann (Rigshospitalet, Denmark)*

WG3- Paediatric Ophthalmology Rare Diseases, *Birgit Lorenz (Universitäts-Augenklinik Bonn, Germany), Dominique Brémond-Gignac (Necker Hospital, Paris, France) & Susana Noval (Hospital Universitario La Paz, Spain)*

WG4- Anterior Segment Rare Eye Diseases, *Daniel Böhringer (Eye Center, University Hospital Freiburg, Germany) & Petra Lišková (General University Hospital in Prague, Czech Republic)*

MONDAY – 25th OF APRIL 2022

14.00 – 15.00 3 presentations for all working groups

PRESENTATION 1: GUIDELINES: the process for guidelines and related documents production
Amélie GAVARD, ERN-EYE medical writer

PRESENTATION 2: CPMS use (standard, GREET and RED-VAR): how to make it through?
Francesco ROTOLO, ERN-EYE IT specialist

PRESENTATION 3: TRAINING & EDUCATION per disease
Dorothée LEROUX, ERN-EYE Project Manager

15.00 – 16.00 **4 WORKING GROUPS INTERNAL MEETINGS**

16.00 – 16.30 COFFEE BREAK

16.30 – 17.00 Building ERN registries: the ERKnet experience and beyond
Franz SCHAEFER, Heidelberg University, Germany

17.00 – 17.15 ERN registries what for? The Commission's vision
Hélène LE BORGNE, Policy and programme officer – Research programmes
DG Research and Innovation, European Commission

17.15 – 17.35 NATIONAL INTEGRATION

17.15 – 17.35 The national integration challenge
Holm GRAESSNER, Institute of Medical Genetics and Applied Genomics, Germany

17.35 – 17.45 National integration of ERNs seen from the Board of Member States perspective
Till VOIGTLÄNDER, MedUni Vienna, Austria

17.45 – 17.50 National integration group
Hélène DOLLFUS, ERN-EYE coordinator

17.50 – 18.30 ERN-EYE ENLARGEMENT: NEW MEMBER STATES REPRESENTED AS FULL MEMBERS IN ERN-EYE

- Finland: Joni TURUNEN, Helsinki University Hospital
- Ireland: David KEEGAN, ERN-EYE Ireland Consortium (EEIC), Dublin
- Romania: Adela CHIRITA-EMANDI & Florina STOICA, Victor Babes University of Medicine and Pharmacy, Timisoara
- Slovenia: Marko HAWLINA, Eye Hospital, University Medical Centre Ljubljana
- Spain: José María HERRERAS & Lidia COCHO, Hospital Clinico Universitario de Valladolid
- Sweden: Stefan LÖFGREN, St. Erik Eye Hospital, Stockholm

20.00 JOINT DINNER

TUESDAY – 26th OF APRIL 2022

08.30 – 10.00 ERN-EYE GOVERNANCE BOARD

10.00 – 10.30 COFFEE BREAK

10.30 – 11.30 TRANSVERSAL WORKING GROUPS SESSIONS: TWG 5, 6 & 8

Session 1: Low Vision, Daily Life and Patients Groups, *David KEEGAN (ERN-EYE Ireland Consortium (EEIC), Dublin)*

Session 2: Genetic Diagnostics, *Elfride DE BAERE (Ghent University hospital, Belgium) & Susanne KOHL (University Eye Hospital, Tübingen, Germany)*

Session 3: Data collection/registries/IT tools, *Christina FASSER (patient representative) & Hélène DOLLFUS (ERN-EYE coordinator)*

11.30 – 13.00 ERNs & RESEARCH SESSION

11.30 – 11.35 Introduction & Context
Hélène DOLLFUS, ERN-EYE coordinator

Guest speakers

11.35 – 11.55 The future Rare Diseases Partnership initiative for research
Birute TUMIENE, Vilnius University, Lithuania

11.55 – 12.15 The EJP-RD general presentation & future Clinical Research Networks
Yanis MIMOUNI, EJP-RD

12.15 – 12.25 Flash example of ERN collaborations: EJP SeeMyLife
Hélène DOLLFUS, ERN-EYE coordinator

General discussion

12.25 – 12.45 General debate on the needs within ERN-EYE
Hélène DOLLFUS, ERN-EYE coordinator

13.00 – 14.00 LUNCH PAUSE

14.00 – 14.20 ERICA project and related WGs
Alberto PEREIRA ARIAS, Leiden University, Netherlands

14.20 – 14.50 Presentation of the ERN access to various programmes & opportunities *via* ERNs: in practice
ERN-EYE team

14.50 – 16.20 Wrap up from the WG leads
Presentation of each Working Group's Workplan (10' per WG)

16.30 END OF THE MEETING