Minutes of the 2024 annual meeting of the European network of paediatric research at the EMA (Enpr-EMA)

Date: Tuesday, 1 October 2024

The 2024 annual meeting of the member networks of Enpr-EMA was held on the 1st of October 2024 at the premises of the European Medicines Agency (EMA) in Amsterdam, with online participation available via Webex. The agenda featured updates from Enpr-EMA working groups, as well as progress on major initiatives like data standardisation and a facilitation framework. Additionally, members engaged in discussions on proposed priority activities for the coming year and explored strategies for further network development.

Chairpersons: Pirkko Lepola, Gunter Egger

Update from Enpr-EMA working groups:

Working group on paediatric clinical trial site quality criteria

Pernille Skovby and Ricardo Fernandes presented the progress of the Enpr-EMA working group on quality criteria for paediatric clinical trial sites.

Recognising the unique challenges of conducting paediatric clinical trials, Enpr-EMA and connect4children (c4c) hosted a 2022 workshop focused on quality requirements for paediatric clinical trial sites. Building on insights from this event, the working group developed a shared understanding of "quality" for these sites and mapped existing standards, and produced a report addressing key questions, including the definition and quality criteria for paediatric sites.

A core definition of paediatric trial site has been established as a location for evaluating therapies in participants under 18 years of age. Quality requirements can be used as a specified standards or criteria covering areas like staff expertise, infrastructure, quality management, and patient engagement. The group's recommendations provide a baseline standard and an aspirational development pathway for excellence. They are meant to reflect the quality of paediatric sites, facilitating site selection while supporting the development of paediatric research infrastructure without adding regulatory burdens.

Key examples highlighted the need for paediatric-trained teams, child and family friendly environments, and age-appropriate facilities and equipment. While ICH Good Clinical Practice (GCP)

and other regulatory requirements set general standards, the group concluded that additional criteria are essential to address the complexities of paediatric trials.

The final report, following review by Enpr-EMA members and a one-month public consultation, will be published on the Enpr-EMA website, accompanied by the publication of a scientific article.

Presentation*: Quality criteria for paediatric clinical trial sites - an Enpr-EMA initiative (R.Fernandez, P.Skovby)*

Working group on international collaboration

The working group on international collaboration includes representatives from networks and regulatory agencies across the EU, US, Canada, Japan, Australia and the UK. Its primary objective is to foster international collaboration and to facilitate the development of paediatric medicines.

To support global paediatric clinical trials, the group has developed two manuscripts detailing the clinical trial authorisation and ethics review processes for paediatric clinical trials within each of the six represented jurisdictions. These manuscripts draw on findings from a comprehensive questionnaire distributed to relevant regulatory authorities and networks within each region.

Following the necessary clearance from each jurisdiction, the manuscripts are scheduled for submission in November 2024, for the collection "Paediatric Drug Development" as part of the Regulatory Science Section of the Journal "Frontiers in Medicine".

Working group on cross-border clinical trials

Begonya Nafria presented the progress of the working group on cross-border access to paediatric clinical trials.

In Europe, the diversity of 24 official languages and cultural backgrounds poses challenges for patients to be involved in clinical trials. Eligibility criteria based on language or country of residence can lead to unintentional exclusion of patients, raising ethical concerns.

This working group aims to develop guidance for more inclusive paediatric cross-border clinical trials in Europe by addressing language, cultural, and residency barriers.

Recommendations will be informed by studying various data:

- An analysis of trials on clinicaltrials.gov assessing language and residency requirements, specific needs for technologies as eligibility criteria or as part of the study criteria.
- Survey data on discrimination cases from clinical trial sites across Europe.
- Patient feedback on trial participation experiences and digital preferences.

Results so far highlighted language barriers as a significant reason for patient exclusion from trials.

Next steps include analysing the rest of the collected data, surveying medicine developers on managing language-related issues, and conducting interviews with researchers and parents willing to share their experiences.

The final guidance with potential solutions will be made available on the Enpr-EMA website, following a public consultation period to refine and enhance the document.

Presentation: *Language discrimination and cross border access to paediatric clinical trials working group (B.Nafria)*

Working group on patient and public involvement (PPI)

The working group on patient and public involvement (PI) was established to address the growing need for developing and enhancing PPI capabilities. It also aims to standardise processes that ensure consistent engagement of paediatric patients and their parents across Europe.

The group has outlined clear objectives: to map existing PPI capabilities in paediatrics, assess current groups based on their development level, expertise, and available resources, evaluate their training and resource needs, and, ultimately, to establish a robust framework for engaging children, young people, and parents in the research process.

The group's activities are expected to result in the creation of guidance documents, development of training materials, and the publication and dissemination of key findings. Patient representatives will review all outcomes to ensure they align with the needs and perspectives of the intended audience.

Presentation: *Patient and Public Involvement (PPI) working group (S.Gaillard)*

Working group on paediatric research nurses

The working group on paediatric research nurses has been established to analyse the current status of research nurses, focusing on career pathways, professional development opportunities, employment conditions, and training needs, as well as to identify key challenges within this role. The group's primary objective is to advocate for and elevate the role of paediatric research nurses across Europe.

To assess the current landscape, two surveys were conducted among paediatric research nurses and their managers. The findings from these surveys were presented during the meeting. Responses, largely from publicly funded institutions and tertiary care hospitals involved primarily in Phase III studies, highlighted major concerns such as limited career advancement opportunities, insufficient recognition of the specialisation, issues related to contracts and salary, and language barriers.

Following this analysis, the group has set core objectives: to increase recognition of paediatric research nurses and related roles, to establish a European Forum for research nursing professionals to advocate for the profession, promote education, and exchange best practices.

The next steps involve preparing a detailed report of the analysis, to be published on the Enpr-EMA website in 2025. Further opportunities for dissemination, such as sharing the report with relevant professional bodies or through other platforms, may also be explored to maximise its impact.

Presentation: *Enpr-EMA- Paediatric Research Nurse Working Group (P.Dicks)*

Enpr-EMA activities and networks' & stakeholder proposals for 2024/25

During the meeting, potential priority activities for Enpr-EMA in 2025 were discussed.

In addition to ongoing working group initiatives, several critical challenges in paediatric clinical research were highlighted, including rare and ultra-rare diseases, the inclusion of adolescents in adult trials, the use of real-world data and registries (particularly for rare diseases and single-arm studies), decentralized trial elements such as e-consent, platform trials, and trials conducted in emergency settings.

Enpr-EMA evaluated its potential contributions in these areas, emphasising an educational role by enhancing existing guidance, addressing paediatric-specific needs, and offering practical

recommendations. Members noted that several ongoing initiatives and focus groups are already addressing some of these topics, with clinical trials in emergency settings identified as a key area for Enpr-EMA's future engagement.

It was also acknowledged that Enpr-EMA would continue monitoring developments as the EU Health Technology Assessment Regulation (Regulation (EU) 2021/2282) is implemented.

Further discussions will define Enpr-EMA's roles, objectives, and potential actions for future engagement or working groups dedicated to these priorities.

Presentation: *Enpr-EMA activities, proposals for 2024-2025 (P.Lepola, G.Egger)*

Further development of Enpr-EMA

An overview of Enpr-EMA's current structure and network organisation was presented, highlighting the role and composition of the Coordinating Group (CG). The CG acts as the network's governing body and is responsible for addressing both operational and scientific matters while developing Enpr-EMA's short- and long-term strategy.

The CG consists of 18 members representing Category 1 Enpr-EMA member networks, alongside 2 members from the Paediatric Committee and up to 4 additional members who may be appointed by the CG for specialised expertise. CG membership is limited to a three-year term to ensure adequate renewal and involvement of various individuals. The current CG will be reconstituted this year, with the new membership announced in February 2025.

Members interested in joining the CG were advised of the responsibilities and requirements for candidacy and encouraged to apply by November 30, 2024. Applications should include a brief résumé, a statement of motivation, and an updated self-assessment form if their latest submission is from 2022 or earlier. Candidacies will be evaluated based on criteria outlined in the CG mandate, aiming for balance of skills, expertise, active participation, and regional representation.

Furthermore, it was confirmed that the next CG Chair will be elected from within the group during the 2025 Enpr-EMA annual meeting.

Presentation: *Further development of Enpr-EMA (P.Lepola)*

The conect4children initiative on paediatric data standardisation

Rebecca Leary presented the conect4children (c4c) initiative's efforts to harmonise and standardise data in paediatric clinical trials. The primary goal of these initiatives is to improve the usability of the data, facilitate sharing, expand knowledge, and promote clinical development for children while avoiding unnecessary repetitions.

Several initiatives have been established to create tools and resources that support data reuse and encourage standardisation and harmonisation. Central to these initiatives is the implementation of data standards that bring structure and meaning, enabling future data reuse and sharing.

Connect4children has focused on developing paediatric data standards. As a first step, a paediatric data dictionary was created. This resource provided recommendations on essential data elements like demographics, vital signs, and pubertal status. Following this, the CDISC Paediatric User Guide was developed, specifying how data should be structured in clinical trials to ensure standardisation. This work applied the FAIRPLUS initiative tools for the disease specific data. Additionally, the CDISC User Network was established as a collaborative platform for users, facilitating discussions regarding the

implementation of CDISC standards, sharing experiences with paediatric data, and identifying missing paediatric data elements within the CDISC standards. This network also aims to support the development of new standards and training modules for effective implementation.

Other global initiatives were also highlighted, as well as future steps aimed at strengthening collaboration and minimising duplication of efforts in this area.

Presentation: *The connect4children paediatric data harmonisation journey (R.Leary)*

Considerations for a PIP facilitation framework

Ensuring timely access to safe and effective treatments for children with unmet medical needs is a shared common goal among regulators involved in paediatric drug development. However, achieving this goal is challenging due to the limited number of patients available to be included in clinical trials and the increasing number of innovative products in development.

To address these challenges and explore the feasibility of a PIP facilitation framework that could support the companies with the development of products meeting paediatric unmet medical needs, efforts are currently underway to assess its potential for future implementation. This framework aims to foster an innovative research and development environment that accommodates the evolution of scientific knowledge and considers changing evidence and unmet needs. It aims to facilitate science-focused feasibility discussions, helping set realistic objectives and generate robust, timely evidence that enables innovation.

The regulatory landscape already includes tools and processes to facilitate scientific discussions. This foundation allows for the development of a framework proposal that provides a safe space for discussions with the pharmaceutical companies, setting a clear scientific focus, supported by regulators that would observe the meetings and help to connect the outcomes to regulatory process as appropriate.

For such a facilitation framework to succeed, it is essential to recognise the benefits, challenges, and unintended consequences associated with its implementation.

Presentation: *Reflections on the concept of a facilitation framework (D.Karres*)

New projects and infrastructures:

EPTRI AISBL

The European Paediatric Translational Research Infrastructure (EPTRI) AISBL (Association Internationale Sans But Lucratif) was presented as a new pan-European initiative designed to strengthen paediatric research and provide services to private and public stakeholders. EPTRI focuses on translational science to bridge the gap between basic research and clinical application for children's health. It aims to support the development of high-quality, safe medicines, technologies and devices for children by fostering stakeholders engagement and knowledge translation, with input from young patients and families, policymakers, payers, regulators, researchers, academia and industry.

Presentation: *European PaediatricTranslational Research Infrastructure (EPTRI) (D.Bonifazi*)

OrphaDev4Kids

OrphaDev4Kids is an ongoing collaborative initiative focused on advancing orphan medical devices (MDs) for paediatric use. The project aims to establish a robust innovation ecosystem for orphan and paediatric MDs, maximising patient benefit from research and development efforts. This initiative will support academic institutions, scientific societies, device developers - particularly small and medium-sized enterprises (SMEs) - and non-governmental organisations (NGOs) throughout all phases of development, from concept to market access.

Presentation: *OrphaDev4Kids (M.Migdal)*

A.O.B. and wrap-up

The meeting was concluded by the chairs thanking all participants for their contributions. The Annual Meeting was followed by the Annual Workshop of the European network of paediatric research at EMA (Enpr-EMA) conducted on the 2nd of October 2024.

Speakers:

- Bonifazi, Donato. TEDDY European Network of Excellence for Paediatric Research
- Dicks, Pamela. ScotCRN (Scottish Children's Research Network)
- Egger, Gunter. Co-chair of Enpr-EMA, European Medicines Agency
- Fernandes, Ricardo. conect4children National HUB lead and STAND4kids (Portuguese paediatric research network)
- Gaillard, Segolene. RIPPS (Paediatric Investigation into Health Products Network, France)
- Karres, Dominik. European Medicines Agency
- Lacaze, Thierry. MICYRN (Maternal Infant Child and Youth Research Network, Canada)
- Leary, Rebecca. TREAT-NMD - Neuromuscular Network
- Lepola, Pirkko. Chair of Enpr-EMA, FINPEDMED (Finnish Investigators Network for Pediatric Medicines)
- Migdal, Marek. PDCO (Paediatric Committee) at EMA, conect4children National HUB, Poland
- Nafria, Begonya. eYPAGnet (European Young Persons Advisory Groups Network)
- Rohou, Solange. Astra Zeneca
- Sherman Cervati, Kirsten. ICON plc contract research organisation
- Skovby, Pernille. conect4children National HUB, Denmark