Minutes of the 2023 annual meeting of the European network of paediatric research at the EMA (Enpr-EMA)

Date: Monday, 9 October 2023

The 2023 annual meeting of the member networks of Enpr-EMA was held on the 9th of October 2023 at the premises of the European Medicines Agency (EMA) in Amsterdam, and online via Webex. Enpr-EMA members and networks met face-to-face with the objective to facilitate interaction and communication to foster high-quality ethical research in children. The programme covered various aspects of the conduct of paediatric clinical trials such as the involvement of patients and young people advisory organisations, the work around finding commonly accepted definitions and how to identify quality standards for paediatric clinical trial sites and best practices for paediatric trial conduct, along with the evolution of Enpr-EMA's structure and objectives to adapt to a changing environment and the proposed new pharmaceutical legislation.

Chairpersons: Pirkko Lepola, Gunter Egger

Enpr-EMA in a changing environment

Gunter Egger, co-chair of Enpr-EMA's Coordinating Group (CG), presented an overview of the current structure of Enpr-EMA, including its membership criteria and categories, with the aim to evaluate how these requirements could be simplified to reduce the administrative burden while keeping the approriate amount of information to categorise the members and inform stakeholders about members' capacities via the public Enpr-EMA database.

Article 44 of the Paediatric Regulation provided the legal basis for the formation of Enpr-EMA, as a European network of existing national and European networks, investigators and centres with specific expertise in the performance of studies in the paediatric population. Enpr-EMA's current structure and governance were defined subsequently, with the creation of 6 membership criteria (research experience and ability, network organisation and processes, scientific competences and capacity to provide expert advice, quality management, training and educational capacity to build competences and public involvement), each of them defined by a list of minimum requirements. The grade of fulfilment of the minimum requirements, established by the evaluation of the information provided by the networks in a self-assessment form, designates the categorisation of the networks into: Category 1 networks that fulfil all minimum requirements, Category 2 networks that currently do not fulfil all minimum requirements and Category 3 networks that do not run paediatric clinical trials but have other expertise in clinical trial methodology or support clinical research infrastructure. Only Category 1 networks can be part of Enpr-EMA's CG which sets the network's long- and short-term strategy.

The adequacy of these criteria in the changing environment was explored together with the fact, that not all the database information has been updated regularly by the members. It was suggested that Enpr-EMA's organisation should be reviewed, also preparing the network for the changes envisaged by the proposed new pharmaceutical legislation.

The type and granularity of information that needs to be collected from the networks was discussed, considering that it should be balanced to provide relevant information for stakeholders to be recorded in the public database, to permit the structural organisation and management of Enpr-EMA and to serve as recognition of the networks, while allowing for simplification and reduction of administrative burden. The level of detail of the information and the timeframe for regular updates, the evidence to be provided, and opportunities to raise awareness about the database were highlighted as important discussion points.

Members expressed their interest to review membership criteria, categories, self-assessment forms and to contribute to proposals for further development of Enpr-EMA's governing structure. It was also suggested to revisit and refine the objectives of Enpr-EMA, which will help to define the criteria for the membership.

It was agreed that actions to raise stakeholders' awareness of Enpr-EMA and to reflect on the benefits of being a member of Enrp-EMA should be taken. Moreover, the database of Enpr-EMA's members should be kept up to date and made more easily accessible.

Presentation: Enpr-EMA in a changing environment (G. Egger, P. Lepola)

Young Persons Advisory Groups (YPAG)

The opportunities for and benefits of involvement of patients, the public, young persons, and children in clinical research was described using the examples of the European Young Persons Advisory Group Network (eYPAGnet) and the international Children's Advisory Network (iCAN) (with the example of TEDDY KIDS) by Segolene Gaillard and Donato Bonifazi, respectively.

eYPAGnet is a network of YPAGs that facilitates meaningful and ethical patient and public involvement (PPI) with children, young people, and families across Europe. This patient-centred organisation acts as a link between sponsors and patients, working with all stakeholders involved, to provide the young persons' perspective and advice on clinical trial design, recruitment, informed consent process and study procedures, along with other activities ranging from the development of training materials and the participation in international events.

eYPAGnet's working methodology starts with the creation of a patient and public involvement plan designed individually for each project, describing the activities and the kind of participants that are needed, the method to be applied, the expected impact of the plan and how to assess it.

In alignment with the objective to involve children in the decision-making processes within clinical trials, **iCAN,** with the example of TEDDY KIDS as part of the iCAN community, is a consortium of children and young persons advisory groups dedicated to providing a voice for children and families in medicine, research, and innovation, in a progressive process adapted to their evolving capacities.

These groups provide advice to sponsors for paediatric clinical trials in activities that range from contributing to study designs and treatment plans, to creating age-appropriate tools and materials, adapting the trial methodology, providing training, participating in workshops, and interacting with stakeholders, creating a recognition certificate of their deliverables to recognise the involvement of children in these activities.

During the discussion, consensus was expressed regarding the benefits of involving patients, carers and young people in the decision-making process for the designing of clinical trials. It ensures that trial methodologies are less burdensome for patients and their families, and that outcome measures are indeed of relevance to the patients. It increases patients' and their families' satisfaction and their trust in the clinical trial and health care.

During the discussion it was agreed that it would be important to identify and map all the different PPI communities and YPAGs that already exist in Europe. This would also facilitate their involvement in the trial design by sponsors.

Presentation: Patient and public involvement in paediatric research within eYPAGnet (S. Gaillard)

Presentation: Promoting children participation in decision making process (D. Bonifazi)

Paediatric clinical trial site standards

Following the workshop on paediatric trial site suitability criteria co-organised in 2022 by Enpr-EMA and conect4children (c4c) with the objective to reach a common understanding of the definition, need and recognition of site suitability criteria, two workstreams were created to follow the topics of (1) agreeing on a definition of quality of paediatric trial sites, identification and mapping of existing quality standards, and (2) implementation of the recommendations for quality criteria.

An update on the progress of both workstreams was presented during the meeting.

Workstream 1 has aimed to establish a common understanding of what quality of paediatric sites means, the reasons why paediatric site standards are needed and how to identify them across different jurisdictions, paediatric age ranges and sponsors, building upon previous knowledge, consensus guidelines and regulations.

With the aim of creating a common framework regarding paediatric clinical sites, and quality categories or domains, two categories of site standards have been proposed: (1) a basic category of quality criteria that provides minimum criteria that all clinical trial sites that enrol children and young people should meet to ensure the delivery of high-quality regulatory grade clinical trials and (2) an aspirational category to provide improvement requirements and a developmental pathway across the established domains of qualifications, experience, facilities, site performance, quality management and patient engagement.

Workstream 2 has worked on identifying existing quality criteria and standards for paediatric clinical sites and has mapped how these criteria apply to different types of trials. For this purpose, a global literature search was conducted in the categories of staff experience, requirements, documentation, infrastructure, cycle times and patient engagement, concluding that it is possible to identify common areas for performing clinical trials across countries and multiple specialties. Furthermore, the findings demonstrated that clinical trials conducted in children introduce additional complexities compared to adult clinical trials, requiring that stakeholders and clinical sites involved in paediatric clinical research meet unique requirements.

The presented results of both workstreams are considered the first step to define and identify general quality criteria, that could then be further investigated for specific cases, considering young adults, de-centralised clinical trial elements, innovation and digitalisation, and international collaboration. The publication of these recommendations on the Enpr-EMA website and as an article in a scientific journal is envisaged for 2024, along with the creation of a plan for dissemination and implementation.

Presentation: Paediatric clinical trial site standards, workstream 1 (R. Fernandes, S. Corriol-Rohou)

Presentation: Paediatric clinical trial site standards, workstream 2 (P. Skovby)

Draft Enpr-EMA work plan for 2023/2024

Pirkko Lepola, chair of Enpr-EMA's CG, presented the currently ongoing activities of Enpr-EMA working groups, which are expected to be continued during the next year, including the publications on the requirements for clinical trial applications and ethics reviews in different jurisdictions; the analysis of the data collected regarding the role and current situation of the paediatric clinical study nurse; the data collection, analysis and future guidance to facilitate cross-border clinical trials; the recommendations on paediatric clinical trial site standards; and the possibility to further advance the repurposing of medicines due to opportunities that the new pharmaceutical legislation may bring.

Several new topics were discussed during the meeting. Members expressed interest in the revision of the membership criteria and the adaptation of Enpr-EMA to the current environment, the need for raising awareness and mapping of existing YPAGs, the use of real-world-data in the paediatric environment, clinical trials in special circumstances such as emergency settings and acute diseases, data sharing, the inclusion of adolescents in adult trials and paediatric elements in de-centralised clinical trials.

Based on the suggestions during this discussion, the CG will decide which topics should be prioritised next year and concretise the activities to address them at their first meeting in 2024.

Presentation: Draft Enpr-EMA work plan for 2023-2024 (P. Lepola)

Networks' practical experiences regarding trial conduct

Early dialogue – essential for better trials

Bernhard Sandner presented the network of paediatricians for clinical studies in ambulant patients (NETSTAP) as an example of how early dialogue between sponsors and networks can facilitate the conduct of paediatric clinical trials and improve their quality by assessing medical needs, impacting on trial designs, facilitating site feasibility, and optimising patient recruitment.

It was highlighted that early dialogue across different stakeholders involved in paediatric clinical trials is paramount, with the network being the centre of communication between sponsor, contract research organisation (CRO) and sites, in order to avoid delays and pitfalls in the trial conduct.

During the discussion, the benefits of early dialogue between sponsors and networks and the need to increase awareness of the existence and purposes of the networks were acknowledged. It was highlighted that the involvement of networks leads to better communication between stakeholders, helps reduce administrative burden and improves relationships with the clinical sites based on trust.

Presentation: Early dialogue – essential for better trials (B. Sandner)

Supporting paediatric trials: learnings and insights from conect4children (c4c)

Ricardo Fernandes presented the activities, experiences and lessons learned from conect4children (c4c), a collaborative network for European clinical trials for children, that provides among other services strategic feasibility advice, patient and parent involvement, standardised training materials/courses for all study sites and site personnel trough the c4c training academy, and a single point of contact for the local networks and trial sites for queries, service delivery and quality control.

The c4c services have been designed by academic and industry partners across the project work packages under the principles of collaboration and co-development, taking into account local knowledge and memory, combined with a shared vision for new approaches. As part of the

infrastructure built by c4c, national hubs have been established as academic institutions that support trials at national level, who have the local knowledge of the country and the local stakeholders. This has shown to speed up study set-up, and recruitment, and increase feasibility.

The network's activities are developed under a quality and measurable performance framework built upon early engagement, local knowledge, flexibility, learning points and lessons learnt.

Presentation: Learnings and insights from conect4children (R. Fernandes)

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 10th of October 2023, where Enpr-EMA members were joined by other stakeholders involved in paediatric clinical research, including patient and parents organisations, healthcare professionals, academia, industry representatives and international regulators.

Speakers:

- Bonifazi, Donato. TEDDY European Network of Excellence for Paediatric Research
- Egger, Gunter. Co-chair of Enrpr-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)*
- *Lepola, Pirkko. Chair of Enpr-EMA, Finpedmed (Finnish paediatric research network)*
- *Rohou, Solange. AstraZeneca*
- *Sandner, Bernhard. NETSTAP, NETwork of pediatricians for clinical STudies in Ambulant Pediatrics*
- *Sherman Cervati, Kirsten. ICON plc contract research organisation*
- *Skovby, Pernille. Conect4children National HUB, Denmark*