European network of paediatric research at the European Medicines Agency

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Last updated: March 2021
EMA/493016/2013

Mandate of Enpr-EMA working groups

Contents

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000

1. Introduction

At the open meeting of Enpr-EMA in June 2013 it was agreed to set up ad-hoc working groups (WG) tasked with addressing some of the most important needs identified. The needs relate to making the best use of paediatric research networks to develop medicines for children.

The number, composition and tasks of the WGs are reviewed every year following the annual face to face meeting.

2. Purpose and composition of working groups

The purpose of the WGs is to develop pragmatic responses to some of the needs relating to paediatric medicines research that can be implemented within a reasonably short period of six to twelve months. The focus is on stating what networks can do, or what networks need to do, rather than developing comprehensive guidance. There is already good practice in many of these areas so that Enpr-EMA needs to focus on disseminating good practice rather than developing new solutions.

Each WG is responsible for defining its role and working practices, including identifying a spokesperson, preparing meeting minutes and drafting outcomes/deliverables.

Members of the WGs, who represent a network, are required to lodge a declaration of interests with the EMA[1].

Participant numbers of WGs are to be decided on a case by case basis. However, in order to ensure efficiency of the WGs they should generally not consist of more than 10 core members. A maximum of one core member should be nominated by organisation. Further interested parties could support a respective WG as co-members, e.g. by reviewing draft documents.

3. Work methods of working groups

1. Each WG sets up communication by e-mail or teleconference/videoconference to discuss:
    a. Terms of reference;
    b. Chair / contact person;
    c. Tasks and timelines;
    d. Ways of working;
    e. Outputs.
2. Each WG sends a plan to the Secretariat for discussion by the Coordinating Group.
3. Each WG works on their tasks.
4. Each WG sends an update to the Secretariat in time for discussion at the regular Coordinating Group meetings.
5. EMA support consists of secretarial support, distributing documents or other resources at the disposal of WG members. EMA staff members may not be able to participate or attend all WG meetings.

[1] See Policy on transparency and the handling of potential conflicts of interests of members of the European Network of Paediatric Research at the European Medicines Agency(Enpr-EMA) Coordinating Group and working groups

4. List of working groups

4.1. Active working groups

4.1.1. WG on international collaboration

WG topic	Collaboration between regulators and paediatric clinical trial networks across Europe, the US, Canada, Japan, and Australia
Objectives	To identify, understand, and address cross-jurisdiction challenges in order to boost international collaboration
Chair(s)	Thierry Lacaze (MICYRN)
Members	Regulatory Authorities: • EU (EMA): Koen Norga, Gunter Egger • US (FDA): Jean Temeck, Susan McCune • Canada (Health Canada): Pauline Kerr, Agnes Klein, Alysha Croker, Megan Bettle • Japan (PMDA): Michiyo Sakiyama, Junko Sato • Australia (TGA): Monique Stone Paediatric clinical networks: • EU: Pirkko Lepola (Enpr-EMA), Mark Turner (c4c) • US: Collin Hovinga (i-ACT), Christoph Hornik (Duke) • Canada: Thierry Lacaze, Breanne Stewart (MICYRN) • Japan: Hidefumi Nakamura (Japanese Children Trials Network) • Australia: Andrew Davidson (Paediatric Trials Network Australia (PTNA))

2018-2019 activities:

- Nomination of representatives for each NCA; NCAs identified max 2 relevant and representative paediatric clinical trial networks in their regions
- First meeting via teleconference in December 2018 to agree scope and activities
- Agreement on first task: to do an environmental scan comparing the regulatory and ethics requirements for paediatric clinical trials, as well as submission and review processes in the five regions in order to assist investigators and industry involved in conducting these studies and to identify regulatory challenges in conducting these trials on an international scale.
- A survey based environmental scan was developed to be answered by both the regulators and the networks.
- Compilation and summary of the answers and data to be published in tabulated form on the Enpr-EMA website and in more detail in a manuscript for publication in a scientific journal.

2020-2021 activities:

- A need for an update of the environmental scan was identified due to several reasons: i) in some jurisdictions modernisation approaches are ongoing, looking at risk-based approaches related to the conduct of clinical trials, ii) some jurisdictions developed streamlined regulatory and ethics submission processes (i.e. submission of the regulatory as well as the ethics applications at the same time), iii) because of the pandemic, some processes have been adapted to expedite clinical trial authorisations.
- The WG considers conducting another survey among its international members in order to update the initial results before publishing them, also with the intention to advocate implementation of some of the interim orders on a more permanent basis.

4.1.2. WG on paediatric research staff / nurses

WG topic	Good clinical practice (GCP) training across multispecialty and countries
Objectives	To help connect research nurses across Europe who conduct clinical trials, facilitate access to training resources: models, needs and current gaps across different specialties and countries
Chair(s) Members	Pamela Dicks (ScotCRN) Pirkko Lepola (Enpr-EMA, FINPEDMED), Catherine Cornu (PDCO), Adriana Ceci (TEDDY), Mary Costello (IPCRN), Susan Macfarlane (ScotCRN), Florence Bosco (Clinicobru), Vincent O'Mahony (IPCRN)

Agreed actions:

- Identify target organisations in countries under-represented in the database for circulation of a questionnaire on nurses' roles and needs, training gaps etc.
- Collect new data, analyse them and publish results.

2017-2018 activities:

The publication of the results of the group's survey investigating the roles and training of paediatric research nurses across Europe in BMJ Paediatric Open (https://bmjpaedsopen.bmj.com/content/1/1/e000170) in 2017 raised relevant points for discussion, such as different roles and funding of research nurses across countries.

About 40 European paediatric research nurse networks and groups have expressed interest in working together with Enpr-EMA, considering it as a central resource where to find and share information. To this end, information on paediatric research nurse networks and groups was published on the Enpr-EMA website: Table of European Paediatric Research Nurse Networks and Groups.

Next action point: Facilitation of connection between the various groups and networks.

2019-2020 activities:

- An inaugural teleconference of an Enpr-EMA research nurse group with nurses from more than 10 European countries took place. The following topics of mutual interest were identified:
  - Training needs and access to training resources across Europe

- Standardisation of research nurse practices across Europe
- Investigation into cultural differences in the role of the research nurse across Europe
- Need to raise awareness about Enpr-EMA and its initiatives among research nurses.
- In some European countries dedicated associations for research nurses are needed as they do not yet exist.

The group will work on providing potential solutions for these issues. However, due to the COVID-19 pandemic, work has been significantly impacted and delayed.

4.1.3. WG on off-label evidence

WG topic	To increase paediatric information in the product information (label) based on "best available" evidence
Objectives	To search and propose new ways to enable updating the product information for products already having valid Marketing Authorisation in EU/EEA by using published clinical and other data evidence supporting medicine safety and efficacy when these are used off-label in the paediatric population.
Chair(s) Members	Saskia de Wildt (Pedmed-NL), Ivan Foeldvari (JSWG of PRES) Lucia Ruggieri (TEDDY), Hide Nakamura (Japanese paediatric research network), Berit Kristrom (Umea University), Pirkko Lepola (Enpr-EMA), Gunter Egger (Enpr-EMA, EMA)

2019-2020 activities:

For several medicines not authorised for use in children, paediatric data have been generated, providing some evidence of safe and efficacious use from clinical practice, yet are not reflected in the labelling or are reflected differently across countries/regions. Most of these medicines are no longer covered by a patent. Frequently, a paediatric indication for these medicines is of no commercial interest for marketing authorisation holders and consequently, there is no interest in using existing or generating new data to obtain such an indication.

The aim of the WG is to increase labelling information based on 'best available' evidence, including practice experience.

A manuscript for publication in a scientific journal is being prepared to present selected medicinal products as examples with high unmet medical need, 2. to present existing data sources to support risk-benefit risk analyses, and 3. to discuss potential solutions to provide physicians with best-evidence dosing information while striving for the highest possible level of evidence to support uptake of paediatric indications in the product information.

4.2. Historical working groups

4.2.1. WG on clinical trial preparedness

WG topic	Facilitation of paediatric clinical trials by focusing on identification and resolution of feasibility barriers at the planning stage
Objectives	To develop preparedness-orientated strategic guidance to facilitate paediatric study development and implementation
Chair(s) Members	Angeliki Siapkara (PDCO), Ruth Ladenstein (OKIDS) Roberto de Lisa (EMA), Donato Bonifazi (Enpr-EMA), Segolene Galliard (Enpr-EMA), Geraldine Boylan (Enpr-EMA), Carmelo Rizzari (Enpr-EMA), Samantha Scarlett (Enpr-EMA), Cristina Seren Trasorras (Enpr-EMA), Mark Turner (Enpr-EMA), Dimitrios Athanasiou (PDCO), Siri Wang (PDCO), Jame Barnes (EUCOPE-Vertex), Claudio Fracasso (EuropaBIO-Pfizer), Tillmann Taube (EFPIA (Boehringer Ingelhiem)), Loic Notelet (Vaccines Europe (Sanofi)), Sabine Scherer (PDCO), Marek Migdal (PDCO), Nicola Ruperto (Enpr-EMA), Ivan Foeldvari (Enpr-EMA), Margaret Patton (EUCOPE-Novartis), Niyati Prasad (EUCOPE (Vertex)), Ensio Norjavaara (EBE (AstraZeneca)), [Solange Rohou (EBE-AstraZeneca)], [Jackie O'Leary (Enpr-EMA)]

Agreed actions:

- To promote dialogue among different parties to consolidate proposals
- To agree on factors recognised by all parties to have critical impact on clinical trial recruitment
- To gather examples of good as well as suboptimal practice for the development and conduction of clinical trials in the paediatric population
- To develop preparedness-orientated strategic guidance to facilitate paediatric study development and implementation

2017-2018 activities:

- The WG reviewed the current regulatory guidance and academic publications in relation to the conduct of trials in the paediatric population to identify discussion on preparedness.
- A prompt guide/questionnaire was developed to be used in interviews and brainstorming sessions on trial preparedness with stakeholder groups.
- A first draft of a preparedness-orientated guidance document was produced.

2019-2020 activities:

- Recommendations on clinical trial preparedness, for sponsors, principal investigators and triallists involved in paediatric clinical trials were published on the Enpr-EMA website: Preparedness of medicines' clinical trials in paediatrics: Recommendations by the Enpr-EMA working group on trial preparedness

The WG was closed because its objective has been fulfilled.

4.2.2. WG on public-private partnership

WG topic	How to establish communication between Enpr-EMA, networks and industry Sharing good practices within Enpr-EMA and with industry partners
Objectives	To develop recommendations for how Enpr-EMA can: • facilitate communication between industry and networks, • provide industry with easy access to information about capacities of individual Enpr-EMA networks, • increase the visibility of individual networks, • make contact with a range of industry partners (big Pharma, SMEs, biotech, CROs etc.), • gather examples of network involvement in good practice for the development and implementation of clinical trials in children and young people, • develop proposals to disseminate examples of good practice to Enpr-EMA members and industry partners.
Chair(s) Members	Susan Tansey (Quintiles); Pirkko Lepola (FIINPEDMED) Pamela Dicks (ScotCRN), Martine Dehlinger-Kremer (EUCROF), Jenny Preston, Stefanie Breitenstein (Bayer), Colin Hayward (Premier-research-CRO), Enrico Bosone (Celgene), Chris Walker (Amgen), Andrea Wassmuth (Gruenenthal), Mark Sorrentino (PRA)

2014-2015 activities:

- A survey was run to collect good practice examples from both network members and Industry colleagues.
- Proposals were developed to disseminate examples of good practice to Enpr-EMA members and industry partners.
- Publication of results:
  Pharmaceutical Industry and Pediatric Clinical Trial Networks in Europe – How Do They Communicate?

2016-2018 activities:

- Development of a consultation model how industry can best engage with Enpr-EMA networks and the benefit from such consultations.

2019-2020 activities:

- Publication of guidance to pharmaceutical industry stakeholders on Enpr-EMA website outlining the recommended model for consulting paediatric research networks, particularly on developing and conducting paediatric investigation plans.

The WG was closed because its objective has been fulfilled.

4.2.3. WG on ethics

WG topic	Dialogue and interaction with Ethics Committees (ECs)
Objectives	• To gather examples of good practice when ECs consider trials relating to children and young people. • To develop proposals to disseminate examples of good practice to ECs. • Contributing work to support the implementation of the Regulation with the view that these efforts will create a more favourable environment to speed up high quality Paediatric Research.
Chair(s) Members	Pirkko Lepola (FINPEDMED) Primary members (drafting documents): Peter Sallabank (RegulinX, UK, CRO), David Neubauer (Chairman of the Ethics WG of European Academy of Paediatrics), Martine Dehlinger-Kremer (EUCROF), Viviana Giannuzzi (Gianni Benzi Pharmacological Research Foundation), Heidi Glosli (NorPedMed, Oslo University), Geraldine Boylan (INFANT), Maxine Kindred (Janssen R&D, UK), Harris Dalrymple (PRA HealthSciences, UK) Co-members (reviewing documents): Christina Manfredi (CVBF-Consorzio per Valutazioni Biologiche e Farmacologiche, Pavia, Italy), Jo Mendum (PRA HealthSciences, UK), Diane Hoffman (retired?)

2014-2015 activities:

- Table of EU EC details for informed consent for paediatric trials: legislative surroundings of the informed consent requirements for pediatric clinical trials, listed by country: Informed consent for paediatric clinical trials in Europe 2015
- Publication of this work in a scientific journal and thereafter on Enpr-EMA webpage Informed consent for paediatric clinical trials in Europe

2015-2016 activities:

- Take part in the revision of the Ethical considerations for clinical trials on medicinal products conducted with the paediatric population (2008) opened from June to September 2016 in collaboration with EFGCP CMWP (European Forum for Good Clinical Practice, Children's Medicines Working Party) and EMA.
- Work on the development of partly harmonised templates of inform consent / assent, in the context of the harmonisation of the application process, that will be implemented with the Clinical Trial Regulation.
- Improve dissemination of information through industry associations in order to face the major challenge of the lack of information regarding the different national requirements for informed consent.

2016-2018 activities:

- Collaboration with EUREC for the planning of a paediatric training course for research ethics committees

- Review of assent/consent template model by eYPAGnet, and by ethics expert
- The Consent / Assent guidance document was published on Enpr-EMA website: Informed consent for paediatric clinical trials in Europe (europa.eu)

2019-2021 activities:

- Recommendations regarding the contents of the various subject elements of consent / assent forms for each paediatric age group on the Enpr-EMA website: Informed consent / assent content recommendations for paediatric clinical trials in Europe

The WG was closed because its objective has been fulfilled. If the need for further work on ethics arises the group might be reopened.

4.2.4. WG on young people advisory groups

WG topic	Best Practices to address issues with EU multi-languages of Young Persons Advisory Groups
Objectives	• To design a survey on Google Groups to scope what YPAGS's were now running in the member networks of Enpr-EMA, to identify the structure of the groups, their contact details, the services they provided, some examples of projects they had been involved in, their funding etc. The European, Canadian and US groups will be included. • To collate the information and ask Enpr-EMA to host it on the Enpr-EMA webpages. • To determine if the groups would like a platform where they could access and share resources such as training materials. • To review platforms such as Google Groups where that could be hosted.
Chair(s) Members	Pamela Dicks (ScotCRN) Anne Junker, Jenny Preston, Joanna Claverol, Segolene Gaillard, Gareth Veal, Begonya Nafria Escalera (Hospital Sant Joan de Deu), Veerle Buteel

Agreed actions:

- To draft a report of the completed survey targeting Enpr-EMA networks.
- To complete the second survey by finding other non Enpr-EMA members to participate.
- To build a network of young advisory group across Europe, similarly to the initiatives in North America, starting by collecting information from the already existing advisory groups and develop a standardised procedure for a more European-oriented approach.
- To develop training packages for the other parties involved (cross-population approach).
- To reflect on the proposal to create a funding group to sustain the database and keep it updated.

2017-2018 activities:

- Informed groups: Create and maintain informed groups of young experts
- Training in clinical research: Develop a common curriculum for the European environment

- Participation at Scientific meetings: national, European, international
- Establish single point of contact and coordination at European level
- Business model for sustainability

2019-2020 activities:

- The network had substantially grown with 9 new YPAGs established in 8 European countries.
- Implementation of standard operating procedures for financial management, membership and communications
- Launch of a website (www.eypagnet.eu)
- Establishment of an advisory board
- eYPAGnet was successfully established and became operational as a member network of Enpr-EMA.

The WG was closed because its objective has been fulfilled.

4.2.5. WG on network funding, sustainability and FP7 projects

WG topic	Strategies for funding and maintaining a paediatric research network FP7 Projects
Objectives	To gather experience and elaborate key requirements for how to develop and maintain a national or specialty network from a business perspective, and share these with other networks which are being established/have just been established. Bring together all principal investigators of agreed FP7 programmes to discuss how to carry out research in off patent medicines funded by EC (FP7) and how to work with PDCO/EMA on this topic. This group intends to come up with a list of identified hurdles and proposals how to tackle them and to discuss directly with PDCO, once this list has been established and proposals are drafted.
Chair(s) Members	Mark Turner (Enpr-EMA, NIHR CRN) Kalle Hoppu, Tim Lee, Stephen Greene, Carlo Giaquinto, Nicola Ruperto, Saul Faust, Saskia de Wildt, David Coghill, Evelyne Jacqz-Aigrain, Ralph Bax, Adriana Ceci, Stephanie Laeer, Heike Rabe, Gilles Vassal; Will Treem (Janssen); Geraldine Boylan

2014 activities:

The WG published the article Successful private-public funding of paediatric medicines research: lessons from the EU programme to fund research into off-patent medicines in the European Journal of Pediatrics.

The WG was closed because its objective has been fulfilled.

4.2.6. WG on organisation of multi-stakeholder meetings

WG topic	A framework for networks to interact with industry and regulators when implementation/conduct of clinical trials agreed in PIPs is no longer possible
Objectives	What can networks offer to industry when they submit modifications of agreed PIPs because the conduct of agreed studies is no longer feasible? What information are regulators looking for when considering requests for modification to PIPs?
Chair(s) Members	Saul Faust (MCRN-UK), Ron Portman, Angeliki Siapkara (PDCO, MHRA), Ivan Foeldvari (JSWG of PRES), Tim Lee (ECFS-CTN), Christina Peters (EBMT PDWP), Carmelo Rizzari (I-BFM-SG), Stefanie Breitenstein (Bayer), Ensio Norjavaara (AstraZeneca); Lynley Marshall (The Royal Marsden Hospital NHS Foundation Trust & The Institute of Cancer Research), William Treem (Janssen)

Agreed actions:

- To implement the guideline to address generic issues during the study preparation at early stage, by identifying therapeutic-specific needs and develop a strategy on how to address them.
- To look at lessons learned from the meeting on type 2 diabetes mellitus.
- To find inputs from the interactive framework guideline currently under development by EMA.
- To run a pilot preparedness-oriented meeting.

2015-2018 activities:

- The WG drafted a standard operating procedure on how to organise and manage multi-stakeholder meetings.

In the context of the 2018 EMA-EC action plan on paediatrics c4c started organising multi-stakeholder meetings, also building on the experience of the ACCELERATE platform.

The WG was closed because its objective has been fulfilled.

4.2.7. WG on neonatology

WG topic	Neonatology issues
Objectives	To discuss neonatology issues and propose solutions
Chair(s) Members	Mark Turner (Enpr-EMA, NIHR CRN) Ralph Bax (EMA), Wolfgang Goepel (GNN), Hector Rojas, Heike Rabe (Neo-Circulation), Irja Lutsar (PDCO), Stefanie Breitenstein (Bayer)

This WG was formed and initially operated under Enpr-EMA. The members then started participating in and actively contributing to the International Neonatal Consortium (http://c-path.org/programs/inc/).

The WG was closed because its objective has been fulfilled.

4.2.8. WG on paediatric pharmacovigilance

WG topic	Paediatric pharmacovigilance (joint Enpr-EMA/ENCePP WG)
Objectives	To discuss and contribute to the revision of the paediatric pharmacovigilance guideline. Important aspects to be addressed are: • Specific methods of pharmacovigilance activities (e.g. risk management plans, signal management, post-authorisation safety studies) which need to be considered when applied to the paediatric field. Experience from networks/investigators that have already performed paediatric PV studies should be incorporated. • Operation of the EU regulatory network capturing the lifecycle transition of PDCO concerns into PIP opinions and subsequently into PRAC/CHMP requests for PASS and PAES. The revision of the paediatric pharmacovigilance guideline should aim to be suitable for a paediatric module of the good pharmacovigilance practices (GVP). To discuss the planned specific paediatric chapter in the ENCePP Guide on Methodological Standards in Pharmacoepidemiology. This would involve the group collecting relevant paediatric literature articles and guidance documents on methodological standards in paediatric pharmacovigilance studies. These would be submitted, each with an accompanying brief review/justification for inclusion, for consideration by the ENCePP WG on Research Standards and Guidance for incorporation in the paediatric chapter.
Chair(s) Members	Dirk Mentzer (PDCO), Andrea Margulis Elaine Gunn, Antonio Clavenna, Xavier Kurz (EMA), Peter Helms, Nicola Ruperto (PRINTO), Roberto De Lisa (EMA), Ana Marta Anes, Rachael Williams, Genevieve Durrieu, Giovanni Fiori, Xavier Fournie, Susan Jordan, Sandra Kruchov Thygesen

Agreed actions:

- To contribute to the drafting of the revised paediatric pharmacovigilance guideline.
- To provide comments on the new GVP module on paediatric pharmacovigilance.

2013-2015 activities:

- The WG provided input to the paediatric pharmacovigilance guideline and the GVP module on paediatric pharmacovigilance.

The WG was closed because its objective has been fulfilled.

4.2.9. WG on paediatric clinical trials with antibiotics

WG Topic	Harmonisation of the design and conduct of paediatric trials for the investigation of antibiotics
Objectives	The overarching principle of this WG is to harmonise paediatric and adult core components of CT design wherever possible. To that end, the WG will: 1. Review the current international regulatory guidance for the conduct of

	antimicrobial trials in neonates, children and adolescents. 2. Review the literature of conducted and planned (as registered on Clinicaltrials.gov) paediatric antibiotic CTs from 2000 to 2016 and PIPs with an EMA Decision. 3. Summarise the key similarities and differences between children and adults in the evaluated CIS that may influence CT design and conduct. At which extent extrapolation of efficacy[3] could be applied will be addressed from a qualitative point of view based on the identified similarities and differences between adults and children in the CIS mentioned above. 4. Summarise the key barriers by that have been identified internationally in the design and conduct of paediatric AB CT conduct. 5. Produce a summary document, based on the available evidence and expert opinion of the key components of CT design for paediatric AB studies. This document would include guidance on the key components of a) inclusion and exclusion criteria b) primary and secondary outcomes c) timing of endpoints d) length of therapy (including the switch from IV to oral therapy) e) study duration and f) key factors where study design differs from adult CTs. Reference: Addendum to the guideline on the evaluation of medicinal products indicated for treatment of bacterial infections to address paediatric-specific clinical data requirements
Chair(s) Members	Mike Sharland Academia Professor Paolo Rossi* Professor Irja Lutsar* Professor Emmanuel Roilides Professor John van den Anker Dr Joe Standing* Professor Sarah Walker Pharma John Rex AZ Hasan Jafri Medimmune Other recommendations from EFPIA members of Enpr-EMA Regulatory Dr Maria Fernandez Cortizo Francesca Rocchi Irmgard Eichler Radu Botgros

2017-2018 activities:

- A systematic review on trial design in urinary tract infection antibiotic trials was published in Pediatrics. 2017;140(6):e20172209.
- A systematic review on safety reporting in paediatric antibiotic trials was published (Drugs. 2018 Feb;78(2):231-244.)

- An article on standardising paediatric antibiotic clinical trial design and conduct was published (BMJ Open 2019;9:e032592. doi:10.1136/bmjopen-2019-032592)

The WG was closed because its objective has been fulfilled.