Enpr-EMA Working group on clinical trial preparedness

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Disclaimer : the views expressed are personal and might not reflect those of PDCO and/or MHRA

Why We Need Pediatric Clinical Trials ?

- Children get sick - they need medications !!!
- Children should have access to medicines that have been properly evaluated for use in the intended population.

Enpr-EMA : overview

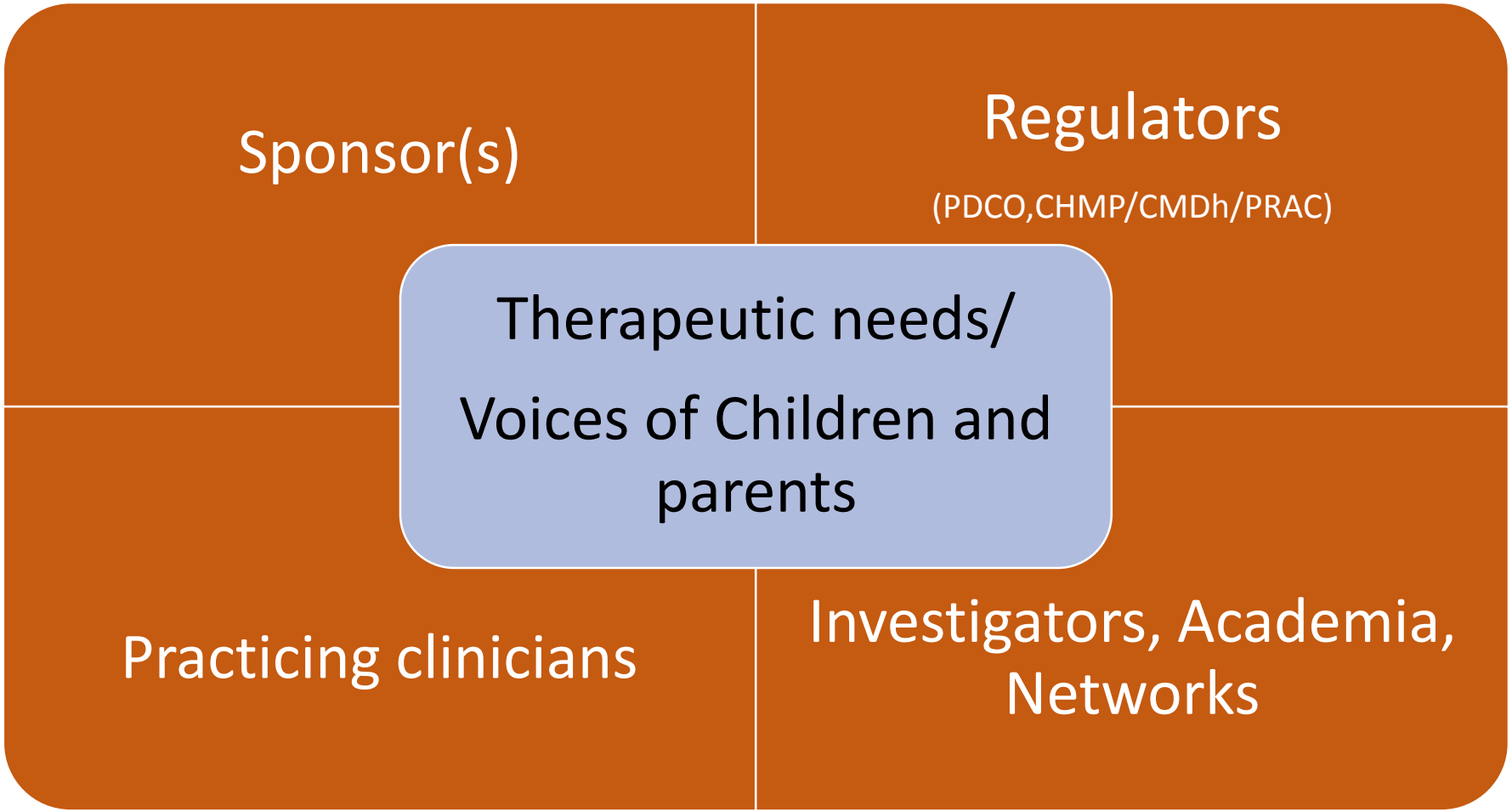
Legal basis -> European Paediatric Regulation:

"The EMA shall, with the scientific support of the Paediatric Committee, develop 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 is a network of research networks, investigators and centres with recognised expertise in performing clinical trials in the paediatric population

Members perform research with children (newborns to adolescents), in multiple therapeutic areas, and ranging from pharmacokinetics to pharmacovigilance

Overlapping interests



Experience so far with paediatric drug development

- COMMON AIMS:

  - ✓Improve the methodology, design and feasibility of paediatric clinical studies
  - ✓Develop standardized (innovative?) methods and tools for monitoring and evaluating the efficiency, effectiveness, and safety of therapeutic interventions for children
  - ✓Increase availability of high quality licensed paediatric medicines

Experience so far with paediatric drug development

- BRIDGES TO BUILD :

  - ✓Research questions vs. licensing demands
  - ✓Trial design expertise vs. trial conduct experience
  - ✓Meeting regulatory requirements vs. technical support to industry
  - ✓Business sustainability vs. prediction of scientific and regulatory future landscape
  - ✓Adult-driven drug development pipelines vs. true paediatric therapeutic needs
  - ✓Local treatment protocols vs. global trials
  - ✓Meaningful early interactions vs. successful Marketing authorization applications

Enpr-EMA working group on clinical trial preparedness

Enpr-EMA mission statement : Enpr-EMA will facilitate studies in order to increase availability of medicinal products authorised for use in the paediatric population.

OBJECTIVE

To create a guidance document on trial preparedness.

Trial preparedness = the set of contributing factors which could increase the ability to complete high quality clinical trials in a timely manner.

MANDATE

Facilitation of the conduct of pediatric clinical trials related to drug development by focusing on identification and resolution of feasibility barriers at the planning stage

- Promote dialogue among different parties to consolidate proposals for the conduct of pediatric clinical trials.
- Agree on factors and practicalities recognized by all parties to have critical impact on successful completion of high-quality pediatric clinical trials.
- Gather relevant examples of good as well as suboptimal practice for the development and conduct of pediatric clinical trials in order to feed in to the preparedness-orientated strategic guidance.
- Develop preparedness-orientated strategic guidance to facilitate development, implementation and successful completion of paediatric clinical trials.

Working Group Members

Co-Chairs	Angeliki Siapkara (PDCO), Ruth Ladenstein (Enpr-EMA)
EMA	Irmgard Eichler, Roberto De Lisa, Gunter Egger, Ingrid Vilimelis
PDCO	Dimitrios Athanasiou, Siri Wang, Marek Migdal, Sabine Scherer
EnprEMA	Donato Bonifazi, Segolene Galliard, Jackie O'Leary (Geraldine Boylan) Carmelo Rizzari, Samantha Scarlett, Christina Seren Trasorras, Mark Turner, Ivan Foeldvari, Nicola Ruperto, Joana Claverol .
Pharma	James Barnes, Niyati Prasad (EUCOPE – Vertex), Claudio Fracasso (EuropaBIO – Pfizer), Solange Rohou, Ensio Norjavaara (SEBE - AstraZeneca), Tillmann Taube (EFPIA – Boehringer-Ingelheim), Loïc Notelet (Vaccines Europe – Sanofi).

ACTION POINTS

Action Point #1
Review the current regulatory guidance and academic publications in relation to the conduct of trials in the paediatric population to identify discussion on preparedness
Deliverable: Short summary and links to guidance documents
Angeliki Siapkara (lead),
Cristina Seren, Tillmann Taube, Donato Bonifazi, Mark Turner

Action Point #2
Summarise previous initiatives on paediatric clinical trials (e.g. DIA/EFGCP, ACCELERATE, IMI2, ERN, Enpr-EMA and EPAC community) to identify existing valuable guidance on overcoming challenges.
Deliverable: List of initiatives on trial conduct
Ruth Ladenstein (lead),
Dimitrios Athanasiou, Solange Rohou

ACTION POINTS

Action Point #3
Utilise deliverables from other Enpr-EMA WGs which have an impact on paediatric clinical trial conduct.
Deliverable: Summarise output from previous Enpr-EMA working groups
Mark Turner (lead),
Pirkko Lepola, Gunter Egger

Action Point #4
Elaborate, perform, and analyze structured interviews and surveys to identify factors and practicalities from groups of stakeholders involved in the pediatric clinical research and its outputs.
Deliverable: Collect critical points and suggestions from various players in pediatric medical/regulatory/patients/operational environment.
Claudio Fracasso (lead),
Siri Wang, Niyati Prasad, Segolene Galliard, Donato Bonifazi, Carmelo Rizzari, Solange Rohou, Angeliki Siapkara, Cristina Seren Trasorras, Loic Notelet, James Barnes, Ruth Ladenstein.

ACTION POINTS

Action Point #5
Development of preparedness-orientated guidance document including (a) narrative, (b) Q&A, (c) decision tree, (d) risk management strategy
Deliverable: First draft of preparedness guidance document
Mark Turner (lead),
Loic Notelet, Jackie O'Leary, Niyati Prasad, Carmelo Rizzari, Sabine Scherer, Margaret Patton

TIMELINES


2017
2018
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Kick-off Meeting: London, October 18th
Final Actions Definition
Summary of regulations and academic publications (#1)
List of initiatives on trial conduct (#2)
Summary of other EnprEMA WGs (#3)
Early draft of the Guidance Document (#5)
Interviews/Survey outcomes (#4)
Draft for Public Consultation
Final Guidance Release

ACTION #1 : Literature/Regulatory Guidance review

Terms used were: drug development, paediatrics/pediatrics, children and relative terms, AND regulat*
Dates 2007 (date of the EU Paeds R) to today
Exclusions: disease-specific , drug-specific
Results ~ 120 articles
Manual individual review of abstracts : **In total 31 articles selected**

Additions proposed by group members :

- **Survey of current guidance for child Health clinical trials** Fracking et al
- **Standards for Research in Child Health: The StaR Child Health Project** (2012)
- **StaR Child Health: developing evidence-based guidance for the design, conduct and reporting of paediatric trials.** Van't Hoff et al
- **Evidence-based guidelines for pediatric clinical trials: focus on StaR Child Health** Sampson et al
- **ICH E11:** CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS IN THE PEDIATRIC POPULATION including **Addendum to ICH E11**
- **Various EMA/FDA guidelines on paediatric topics.**

Scope : To create a short overview with the findings from the papers assessed and create an list of factors identified – leading a comprehensive definition of preparedness.

ACTION #3 : Deliverables from other Enpr-EMA WGs

With many thanks to Pirkko Lepola for the update below for the ***Enpr-EMA Working group on public-private partnership*** :

The WG conducted two surveys and collected data on pharma's and the Enpr-EMA networks´ experiences, examples of good practice, challenges, and ideas for communication and visibility -> a recommendation document and diagram to guide companies in taking advantage of scientific and logistic expertise available from networks -> prepare a pilot period with a survey to selected networks to specify services available.

Next steps; Task 3: logistics & timing (I-VI = Jan-Mar/Apr, VII-VIII = Mar/Apr):

I. Group members – re-organization to primary members and co-members
II. Design Invitation Letter for a) Companies (previous suggestion; IMI2 Call 10 sponsors ?) and b) Networks
III. Done / sending via Enpr-EMA mailing lists
IV. Send Invitation to both and
V. For networks also the simple "tick-box" Survey (template from Task 2. -> ready)
VI. Selection of interested partners for pilot; max. 5 for both a) Industry and b) networks
Pilot period - time? –TBD
VII. **After pilot phase; survey to these companies; evaluation and analysis of these services – did they bring any value?-> PoC**
VIII. **Publication of the survey results; collected experience**
IX. Results to the next Enpr-EMA annual conference 7.-8.June 2018
X. **Decision of the continuation**

ACTION #4 : Interviews & Surveys

- Interviews will be conducted to few representatives of selected stakeholder groups according to an established questionnaire and the answers collected through a form to facilitate later elaborations. Questions will dive in details relevant to the phases of drug developments: Project preparations (eg. trials design, feasibility), conduction (eg. enrollment), and completion (till drug MAA).

- Interviews will be anticipated by an explanatory document (ie. scope of the project; list of questions; expected outcome/s).

- The questionnaire for completion (eg. through Survey Monkey) will be use to reach larger stakeholder groups (eg. those not selected for interviews), and, eventually, followed by structured interviews on identified cases based on the results of the survey.

- **Timelines** : material is under preparation , contact stakeholders late February/early March

ACTION #4 : Potential stakeholders list

Proposed list of interviewees:

- CRO representatives (EUCROF)
- Patient associations (eYPAGNet)
- HTA experts (EUnetHTA)
- Study Coordinators (through Country Networks, eg. RECLIP, INCIPIT)
- Pharma Associations (EBE, EuropaBIO, EFPIA, Vaccine Group)
- Representatives from Eastern Countries (eg. Polish Country Network)
- ERNs (eg. Pediatric Cancer Network, Metabolic Network)
- EURORDIS (EPAG)
- EPF
- EFGCP (especially Children's Medicines Working Party)
- CTN (Cystic Fibrosis)
- UPPMD (Global Organization for Duchenne)
- Regulators Representatives (EMA, PDCO, CHMP, CTFG - Clinical Trial Facilitation Group)
- General Pediatricians
- ENPREMA networks (to be decided)

Any further stakeholder that will be identified in the course of the actions will be added to this list.