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Report on annual workshop of the European Network of Paediatric Research at the EMA (Enpr-EMA), 22 & 23 March 2012

On 22 & 23 March 2012 the European Medicines Agency (EMA) convened the annual two-day workshop of the European network of paediatric research at the EMA (Enpr-EMA). Enpr-EMA is a network of research networks, investigators and centres with recognised expertise in performing clinical studies in children, with the aim to foster high-quality ethical research on quality, safety and efficacy of medicines to be used in children. (Enpr-EMA)

Day one of the workshop, organised with the assistance of "The Organisation for Professionals in Regulatory Affairs" (TOPRA), was dedicated to strengthen the links and communication between all stakeholders: patient/parent organisations, network representatives, pharmaceutical industry staff responsible for paediatric studies and regulators.

The morning of Day two was dedicated to discussions between members of the Enpr-EMA network; in the afternoon the Enpr-EMA coordinating group had their quarterly meeting to analyse the outcome of day one, and to discuss and define priority tasks for the year 2012-2013.

Day 1

The morning session started with a report by the chair of Enpr-EMA coordinating group (CG) on the activities in the past year and challenges encountered. From an administrative point Enpr-EMA has been formally implemented, the mission statement, the mandate of the CG, as well as the policy for transparency have been adopted and published on the Enpr-EMA webpage. (Mandate, Mission Statement, Policy for Transparency)

First queries from industries were received; a transparent, flexible process has now to be developed within CG and Enpr-EMA secretariat to allow quick and efficient responses to incoming queries within the available staff and time resources.

One major activity of the previous year was to initiate the development of new European networks in those therapeutic areas where no Europe wide paediatric networks currently exist: gastroenterology, cardiology and diabetes/endocrinology. A first meeting, convening key players in those 3 paediatric specialties was held in late 2011 in order to scope the possibilities for networks in each specialty and to make concrete plans to develop new clinical trial networks. A support letter from EMA/Enpr-EMA was sent to the presidents of the above mentioned learned societies emphasizing the need for the

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development of clinical trial networks; the presidents or an official representative of the three learned societies were invited to attend day 1 of this workshop to allow face-to-face discussion with representatives of these three core groups, who presented the planned steps and action points to initiate the creation of European-wide clinical trial networks in the three therapeutic areas.

Representatives from two successfully established and operating clinical trial networks (CTNs), the European Cystic Fibrosis Society CTN (ECFS-CTN) and The Paediatric Rheumatology International Trials Organisation (PRINTO) reported on the organisational structure and shared the experience with running their CTN. (Tim Lee Presentation, Nicola Ruperto Presentation)

Two presentations outlined the interface between industry and CROs as networks facilitating a study, i.e. being responsible for project set up, investigator selection, facilitation, fast recruitment and CROs managing the study, i.e. being responsible for study initiation and management, assurance of regulatory compliance, data analysis, and finalisation of study report. Due to these different but complementary roles, close communication and collaboration between CRO and networks is important in order to achieve benefit for industry: efficient and rapid study completion (Martine Dehlinger-Kremer Presentation, Andrew Rose Presentation)

To set the scene for break-out discussions in small groups, the afternoon session started with presentations, outlining the perspective from various stakeholders i.e. patients, networks, and industry on how to use Enpr-EMA. (Presentations: Jose Drabwell, Jenny Newman, Ali Harrison, Helen Shaw, Dave Coghill, Kalle Hoppu, Valls-i-Soler)

Break-out Group 1 discussed proposals on the development and fostering of new networks. The need for both was acknowledged as specialty networks have the expertise to deal with strategic issues and trial design, and national networks provide the infrastructure to support the conduct of the trials. It was acknowledged that it is difficult to start without any core infrastructure and experience has shown that efforts to develop networks are more successful when patient registries are available and/or when a condition targeted by the CTN is life threatening. A good starting point to foster a new network could be on conclusion of a successful multi-centre trial. Learning from successful networks (i.e. information about logistics, funding, etc.) would also be helpful.

As far as obtaining the required resources is concerned, it was also pointed out that in addition to support required at national level learned societies have a big responsibility in supporting European wide specialty networks. Equally important as funding would be the bringing together of a core group of appropriate enthusiastic individuals and Enpr-EMA should be the platform to encouraging the founding of new networks. (Presentation break-out group 1)

Group 2 presented proposals on how to encourage clinicians to participate in clinical trials.

The need for early participation and training in clinical research was identified, starting already in medical schools and continuing during clinical training.

Networks should encourage more colleagues to become involved in and to participate in clinical research. (Presentation break-out group 2)

Group 3 discussed proposals as to how patients can be involved in networks and in clinical trials: There was agreement:

- that early involvement of patients is critical;
- on the added value of involving children in addition to parents/carers, as children's views complement those obtained from parents (e.g. burden and acceptability of intervention) and should therefore be sought, keeping in mind that children's contributions may vary depending on the disease, cultural differences, age, etc.;

- Patients/carers should be involved in:
  - Quality control for a network to improve outcome.
  - Assent/consent forms.
  - Ethics committees (not only lay people and professionals).
- Training of parents/carers/children is needed to prepare them for active contributions.

(Presentation break-out group 3)

During the following plenary discussion it became clear that although all stakeholders involved seem to have a high interest in Enpr-EMA, there is still little interaction between the annual face to face meetings and consequently the discussion focused on how to improve interaction between the various stakeholders, particularly between networks, industry and PDCO.

Network representatives clearly expressed their interest and their perceived need to be involved as early as possible in the PIP development and encouraged industry to use their expertise not only for facilitating the conduct of clinical trials requested in PIPs, but much earlier in designing the paediatric development.

With regard to interaction between networks and PDCO the following proposals were made:

- Academic investigators frequently consider industry sponsored clinical trials less valuable than investigator initiated trials. Enpr-EMA should be used as instrument to better communicate and to inform academia about the scientific evaluations and discussions of the PDCO in order to raise their interest and awareness of the trials requested.
- Networks should be engaged in elaboration of model PIPs.
- Networks could be engaged to support the PDCO when discussing several PIPs for similar or "me-too" products in the same therapeutic area with a limited paediatric population available.

Enpr-EMA should focus on establishing links between the various stakeholders and on becoming the central point to link networks (national and specialty networks), industry and PDCO.

Day 2

The morning was reserved to representatives of more than 30 networks, including the Mother Infant Child Youth Research Network in Canada and the National Centre for Child Health and Development in Japan, together with representatives of several learned societies.

The following conclusions / recommendations were made:

- Enpr-EMA should
  1. strive to build confidence/trust between industry – networks – PDCO by guidelines/policies for interaction, ensuring confidentiality and encouraging high quality of networks to becoming members of Enpr-EMA
  2. make available evidence of continued activities of individual networks
  3. continue fostering new/emerging networks by enabling contact/liaison with existing networks, interaction with learned societies
  4. increase involvement of young people in networks and develop codes of conduct for involving young people

5. establish link with paediatric networks in the US as trials are increasingly being conducted globally

6. improve the current website, as information is not readily found and does not have search functions; it should include a secure platform for members for exchange of information and an open platform to post calls for collaboration.

7. advocate at national government/European level for the funding of (national) networks and the required infrastructure to perform clinical trials. Experience from existing national networks shows that without such funding networks are not able to sustain themselves solely through industry sponsored studies. (Negative example: PaedNet Germany, positive example NIHR MCRN-UK)

- PDCO to have access through Enpr-EMA to expertise and data available within networks (eg disease registries)

The afternoon session was reserved to the coordinating group.

The following activities were agreed:

- Closer collaboration between Enpr-EMA and the SME office at EMA.
- To increase involvement of young people within the individual networks. As a first step to develop and distribute a questionnaire on the current level of involvement of young people.
- To set up additional T-conferences with emerging networks to maintain momentum.
- To develop a work plan for the next 1-2 years.
- Regarding companies' request on feasibility of studies: should Enpr-EMA develop in collaboration with CROs, pharmaceutical companies, PDCO and networks a generic template for top level feasibility of proposed trials?
- To include in the self-assessment report contributions such as responses to consultations to PDCO and industry enquiries and assistance to emerging networks. Networks to forward information on completed clinical trials so that Enpr-EMA can map to previously agreed Paediatric Investigation Plans (PIPs)

The following suggestions for performance indicators were made:

- involvement of eastern European countries in conduct of CT/s;
- possibility of networks to have a say into protocol development;
- %age of trials when Enpr-EMA was consulted / involved.

All presentations will be publicly available on the EMA webpage as well as the TOPRA webpage