EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Enpr-EMA

European Network of Paediatric Research at the European Medicines Agency

Collaboration with PDCO

An agency of the European Union

Irmgard Eichler, MD

Collaboration with PDCO
Proposals made at last year's workshop

- Networks should be engaged in elaboration with model PIPs

- Networks should be engaged to support PDCO when discussing several PIPs for similar products in the same therapeutic area

Networks should be engaged in elaboration with model PIPs

Standard Paediatric Investigation Plans: Rhabdomyosarcoma - Acute myeloid leukaemia

- Developed in interactions between academic networks, the EMA Paediatric oncology task force and EMA / PDCO
- Public consultation
- Comments received currently compiled
- PDCO to re-discuss together with EMA oncology working party and EMA scientific advice working party
- Final version will be published

http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2013/02/WC500139183.pdf

Networks should be engaged to support PDCO when discussing several PIPs for similar products in the same therapeutic area

Workshop on PIPs for medicines to treat Type 2 Diabetes Mellitus

- Participants: regulators, experts, industry
- To discuss feasibility and better alignment with clinical practice and medical needs:

  - Few available paediatric T2DM patients

  - Many simultaneous, competing paediatric drug developments in T2DM

  - Few consortia/networks of specialised centres to facilitate recruitment of patients

Workshop Type 2 Diabetes Mellitus
Potential solutions discussed

- Staggered development of products from the same class, by means of different lengths of deferrals
- Multi-company, multi-agent study for products being developed concurrently: need for only one control group
- Single-company, multiple-agent study: need for only one control group.
- Simplified PK studies (peak and trough levels, dried blood spots)
- Potential broadened role for extrapolation (efficacy)
- Establishment of an Enpr-EMA diabetes/endocrinology network

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/05/WC500143022.pdf

CF Workshop on outcome measures at EMA

- In collaboration with ECFS and ECFS-CTN
- Participants: experts, patients, industry, regulators, HTA
- Focus on outcome measures for CF lung disease and gastrointestinal manifestations
- Patient population limited - drug development pipeline ↑
- Novel treatments targeting basic defect - need for new outcome measures

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/05/WC500143022.pdf

CF Workshop on outcome measures at EMA Conclusions:

- List of core outcome measures proposed
- Endpoints for added clinical benefit in view of HTA and to maintain orphan status
- CF registries should be used more widely

  - to compare disease course in differing patient groups to identify optimal patient cohorts for interventional studies
  - to describe variability of outcome parameters without interventions in different age groups and perform power calculations
  - for feasibility assessment

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2013/05/WC500143022.pdf

Human medicines
Pre-authorisation
Post-opinion
Post-authorisation
Product information
Scientific advice and protocol assistance
Scientific guidelines
Innovation Task Force
Regulatory and procedural guidance
SME office
Paediatric medicine

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Supporting information

In this section you will find information on:

- Paediatric needs
- Clinical trials
- Off-patent medicines
- Formulations
- Workshops
- Publications
- Deadlines for placing a product on the market

In the Partners and Networks section of the website you can find further information on the EU Paediatric Network.

Paediatric workshops

The European Medicines Agency regularly organises **workshops** on topics related to paediatrics:

- Workshop on Paediatric Investigation Plans in Type 2 Diabetes Mellitus (25/02/2013)
- Joint EMA/FDA workshop for paediatric Gaucher disease type I: exploring the way forward (17-18/10/2012)
- Workshop on endpoints for cystic fibrosis clinical trials (27-28/09/2012)
- Workshop on Paediatric Formulations for Assessors in National Regulatory Agencies (8/11/2011)
- Ethical considerations for paediatric trials - how can ethics committees in the European Member States and the Paediatric Committee at the European Medicines Agency work together? (29-30/11/2011)
- Workshop on clinical development and scientific advice in ophthalmology (27-28/10/2011)
- Expert meeting on clinical investigation of new drugs for the treatment of chronic hepatitis C in the paediatric population (04/04/2011)
- High grade glioma expert group (03/12/2010)
- Expert group meeting on paediatric heart failure (29/11/2010)
- Paediatric rheumatology expert group meeting (17/11/2010)
- Expert meeting on paediatric asthma (20/10/2010)
- Expert meeting on gastroenterology and rheumatology (28/06/2010)
- Expert meeting on neonatal and paediatric sepsis (08/06/2010)
- Expert meeting on specific immunotherapy (18/01/2010)
- Workshop on paediatric formulations for assessors in national regulatory agencies (31/05/2010)
- Second workshop on European Paediatric Network (16/03/2010)
- Paediatric rheumatology expert group meeting (04/12/2009)
- Paediatric epilepsy expert group meeting (01/09/2009)

Report from the Commission to the European Parliament and the Council
Better Medicines for Children

Enpr-EMA provides the added value of a holistic approach by bringing together national and European networks, investigators and centres with specific expertise in designing and conducting high-quality studies in children.

http://ec.europa.eu/health/human-use/paediatric-medicines

Number of children enrolled in clinical trials

Number of subjects	2006	2007	2008	2009	2010	2011	2012
Preterm newborns	0	0	0	207	82	2281	1712
Newborns	0	0	5	64	169	1105	1172
Infants / toddlers	330	21	20	59	351	2788	3141
Children	2142	181	200	2230	2055	10325	20677
Adolescents	368	111	205	1577	2861	9054	13193
Sum of above	**2840**	**313**	**430**	**4137**	**5517**	**25553**	**39895**
Reference: paediatric trials - N	316	355	342	404	379	334	332

EudraCT Data, EC report 2013

http://ec.europa.eu/health/human-use/paediatric-medicines

Back-up slides

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Better Medicines for Children

- The European Network for Paediatric Research at the EMA (Enpr-EMA) was established in 2009. While a closely-knit network of experts existed prior to the introduction of the Regulation in disease areas such as paediatric oncology, Enpr-EMA provides the added value of a holistic approach by bringing together national and European networks, investigators and centres with specific expertise in designing and conducting high-quality studies in children.

http://ec.europa.eu/health/human-use/paediatric-medicines

Report from the Commission to the European Parliament and the Council Better Medicines for Children

- However, question still remain as to whether this expertise translates into sufficient capacity within the EU to conduct trials in specialised investigation settings
- Well-developed research networks capable of facilitating the necessary research to fulfil the commitments included in paediatric investigation plans do exist in some but not all Member States

http://ec.europa.eu/health/human-use/paediatric-medicines

5 years Paediatric Regulation – What has been achieved ?

More medicines for children:

- 34 new medicines with paediatric indication
- 72 medicines with an extension of indication to children
- 26 medicines with new age appropriate formulation

More information on medicines:

- 87 changes to product information
- 89 additions of dosing information, 77 of new study data and 134 of safety information

Report from the Commission to the European Parliament and the Council
Better Medicines for Children

- 31 out of 152 new medicines authorised for paediatric use
- 72 new paediatric indications approved for medicines already authorised, including 30 indications
- 26 new pharmaceutical forms were authorised for paediatric use, including 18 adapted forms for centrally authorised medicines

Report from the Commission to the European Parliament and the Council Better Medicines for Children

If the Regulation is to be a success, it is not only necessary that data on the use of a specific product in the paediatric population are collected, but that these data are then also appropriately communicated to, and used by, paediatricians in their day-to-day work for the benefit of their patients.

Report from the Commission to the European Parliament and the Council Better Medicines for Children

- *Some studies published suggest a failure on the part of practitioners to recognise the actual amount of off-label prescribing to children. It is claimed that the prescribing habits of practitioners are often strongly influenced by personal experience rather than by evidence-based information for paediatric medicine.*
- *These studies, in making generalisations, may not have taken into account the heterogeneity of healthcare professionals, whose receptiveness varies greatly according to their work setting and specific area of specialisation. At the same time, such observations may point to a substantial hurdle in achieving the goal of the Paediatric Regulation.*

Standard rhabdomyosarcoma paediatric investigation plan

Study	1	2	3	4
Objective(s): To evaluate	Single-agent dose-finding (maximum tolerable dose and / or biologically optimal dose) and tolerability	Safety and dose-refinement in combination	Activity, efficacy and safety (benefit/risk)	Activity, efficacy and safety (benefit/risk)
Design	Single arm, successive cohorts, e.g., rolling six design or continual reassessment method	•In combination with standard of care, or • In combination with novel medicine	Randomised add-on to multi-agent chemotherapy, futility interim analysis	Randomised, in combination with a front-line treatment regimen

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