European network for pediatric research of the European Medicines Agency (Enpr-EMA)

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Outline

• The EU situation: Enpr-EMA
• Trials in Canada
• MICYRN
Legislated January 2007

Improve the health of children:
• increase high quality ethical research into medicines for children
• increase availability of authorized medicines for children
• increase information on medicines

Achieve the above:
• without unnecessary studies in children
• without delaying authorization for adults

Requirement to:
• develop a European network to coordinate studies
Enpr-EMA: Key Operational Goals

- To link together 64 existing networks
- To liaise with Industry and other stakeholders
- To define consistent and transparent quality standards
- To harmonize clinical trial procedures
- To define strategies for resolving major challenges
- To facilitate recruitment because this is a problem
- To strengthen research in Europe on European children
Enpr-EMA: Coordinating Group

- To be as diverse as possible (therapeutic areas; ages; activities; trials/network organizations)
- Self-assessment process to qualify (# trials; ethics; GCP...)
- Wanted to include a total of 20 networks; only 16/32 met minimum criteria
- National networks: UK, Scottish, Finnish, Netherlands, Itl, MICYRN
- Specialty networks: CA-BMBT (4), PRINTO, ECFS, GNN, UKPVG, PENTA, but no Cardio, Critical Care/Pain,
Secretariat of Enpr-EMA – provided by EMA

- To provide secretarial support
- To organize and host meetings of the network
- To coordinate exchange of information between network partners
- To coordinate exchange of and provide information to external partners and stakeholders
Enpr-EMA Coordinating Group: First Steps/next year

• Launch meeting held March, 2011 (London, UK)
• Nomination of Chair of CG: Peter Helms (Scottish National Network)
• Main Goal established: Communication between Industry, Regulators, Patient Organizations
• 1st Action point: webpage, resource database
• Agreement to determine 3 main topics to develop model Paediatric Investigation Plans (PIPs)
Paediatric Committee (PDCO) Opinions on PIP Applications 2008-2010

High number of biologics
Outcome after PDCO Review: 82% Deferrals to avoid delay in marketing authorization for adults

- 91% for new products
- 64% for existing products
- deferral of 4-5 years, up to 8y from MAA in adults

Olski TM et al Three years of the Pediatric Regulation in Europe Eur J Clin Pharmacol 2011 (in press)
Effectiveness of the Regulation: Trials in Children?

Remains 9-10% relative to adult trials

# Pediatric Trials

EU (pop 500M)

Canada (pop 34M)
Effectiveness of the Regulation: Are Trials Moving?

# Investigator Sites*

* sites involved in pivotal clinical trials submitted for marketing authorization approval to the EMA per region per year
Canada

- World leader in pediatric pharmacology and development of trials methodology with contribution to international regulatory framework
- Biotech industry #2 in world (14.7B) and 80% of R&D directed to health products
- A Canadian child receives 4 prescriptions a year from a range of more than 1200 different drugs
- 75% of these drugs do not have dosing or safety data for use in children (90% for prematures)
- No legislation or incentives for Pediatric trials
Canada:EU
Population comparisons

Population 0-14 years: 16%
Pediatric Trials in Canada
2005-2009

114,495 registered clinical trials (August 16th, 2010)

18,511 (16 %) trials in children

13,420 pediatric trials registered 01/01/2005 – 31/12/2009

1,036 listed Canada as a country of recruitment

Excluded Observational studies (n=85):
- establishing biobank or registry
- chart, outcome review
- survey of patient experience

Excluded Interventional studies (n=86) with:
- no projected subject number listed
- no lower age limit given and “adult” disease like Parkinson’s or radical prostatectomy
- recruitment outside Canada
- not yet recruiting
- expanded drug access program
- study on medical student education

865 Interventional clinical trials meeting criteria

http://www.who.int/ictrp/en/
Health Conditions studied by more than 15 Pediatric Trials

- Connective tissue disorder
- Cancer
- Infectious Diseases incl vaccine
- Respiratory diseases incl asthma, CF
- Metabolic incl Diabetes Obesity, Nutrition
- Surgery & Surgical specialties
- Neonate
- Mental Health incl ADHD
- Anesthesia & Pain
- Critical Care, ER, Trauma
- Neurology
- Dermatology
- Hematology incl immune deficiency
- Cardiac
- GI

Health Conditions studied by more than 15 Pediatric Trials.
Non-Industry organizations are Primary Sponsor for 64% of Registered Pediatric Trials
Academic Institutions are sponsors for 94% of non-Industry Registered Pediatric Trials

- **Canadian sponsor n=401**
  - Institutions n=377 includes province-based research institutes, hospitals and universities
  - Provincial organizations n=15 includes health authorities and provincial foundations
  - National organizations n=9 includes Canadian foundations and research consortiums

- **USA sponsor n=63**
  - Institutions n=30 includes USA state-based research institutes, universities and hospitals
  - USA national organizations n=33

- **Non-USA International sponsors n=87**
  - Institutions based in Europe, Australia, New Zealand n=6
  - Global, international organizations n=81
Research Activity in Canada: Registered Paediatric Trials

- Only 12% of non-industry trials included sites outside Canada
- Only 14% of industry trials limited to Canada
- 96 different companies conducted 314 trials (2005-2009)
- 54% of trials by 12 companies
- 51 companies did only 1 study
### Multi-national nature of Pediatric Clinical Trials

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Company</th>
<th>Enrollment Target</th>
<th>Number of Countries listed for recruitment</th>
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</thead>
<tbody>
<tr>
<td>Hemophilia</td>
<td>Bayer</td>
<td>139</td>
<td>25</td>
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<tr>
<td>Arthritis</td>
<td>Novartis</td>
<td>122</td>
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<tr>
<td>Influenza treatment</td>
<td>Hoffman LaRoche</td>
<td>250</td>
<td>19</td>
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<tr>
<td>Kidney disease</td>
<td>Sanofi Aventis</td>
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<td>11</td>
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<tr>
<td>Asthma</td>
<td>Glaxo Smith Kline</td>
<td>300</td>
<td>11</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>UCB Inc</td>
<td>357</td>
<td>11</td>
</tr>
</tbody>
</table>

- 25% of Industry trials listed an average of 12 countries to enroll ≤500 study subjects.
Maternal Trials in Canada
2005-2009

60 studies: 77% interventional, 23% observational

- Canadian sponsor n=55
  - Institutions n=50
    - Includes Province-based research institutes, universities, hospitals and health authorities
  - Provincial organizations n=1
    - Includes research consortiums
  - National organizations n=4
    - Includes Canadian Foundations and research consortiums

- USA sponsor n=4
  - Institutions n=2
    - Includes USA State-based research institutes, universities and hospitals
  - USA National organizations n=2

- Non-USA International sponsors n=1
  - Institution based in Australia n=1
Maternal Trials in Canada 2005-2009
Maternal or Paediatric Trials in Canada

- 2nd to USA in total number of trials
- 3rd after Australia and Netherlands in number of trials/M births (maternal) or children (paediatric)
- Province-based academic organizations responsible for 94% of Canadian-sponsored trials
• Now incorporated as federal nonprofit society
• Joins the 17 child – maternal research organizations in Canada
• Principal agenda to support multi-center collaborations
• Member interest in developing a national framework for multi-centre studies
Agenda for the Eastern Townships Workshop

- What works and what doesn’t in doing Trials in Canada?
  - Methodologies, Ethics, New Frontiers
- How should we be engaging with patients, families and patient organizations?
- How should we be engaging with Industry?
- What do academic organizations require (reduce vulnerability) to support investigator-initiated studies? (DM, monitoring..)
- What can the academic organizations do to support networks?
- Determine how to qualify for CIHR-SPOR support as a (virtual) Support Unit or as a network of Support Units