

Pediatric Academic Societies: 2013

How do we optimize global trial development and why networks are so critical?

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May 2013

Disclaimer

- Any statements or opinions provided by the speaker are mine only and do not reflect an official statement or opinion of the FDA
- I have no conflicts of interest

Alternative Question

- Children now have a Permanent Seat at the Research Table for product development, but do we have the utensils to implement participation in pediatric trials ?

FACT: After 2 decades of work we have PERMANENT legislation to ensure pediatric product development

BUT:

Do we have the **Networks** and programs in place to accomplish what is effectively an **International effort**?

Overview

- Brief Background on history and relationship of US and European pediatric programs
- Differences that can be barriers
- FDA's International Pediatric Program
- Pediatric Networks
- Conclusions

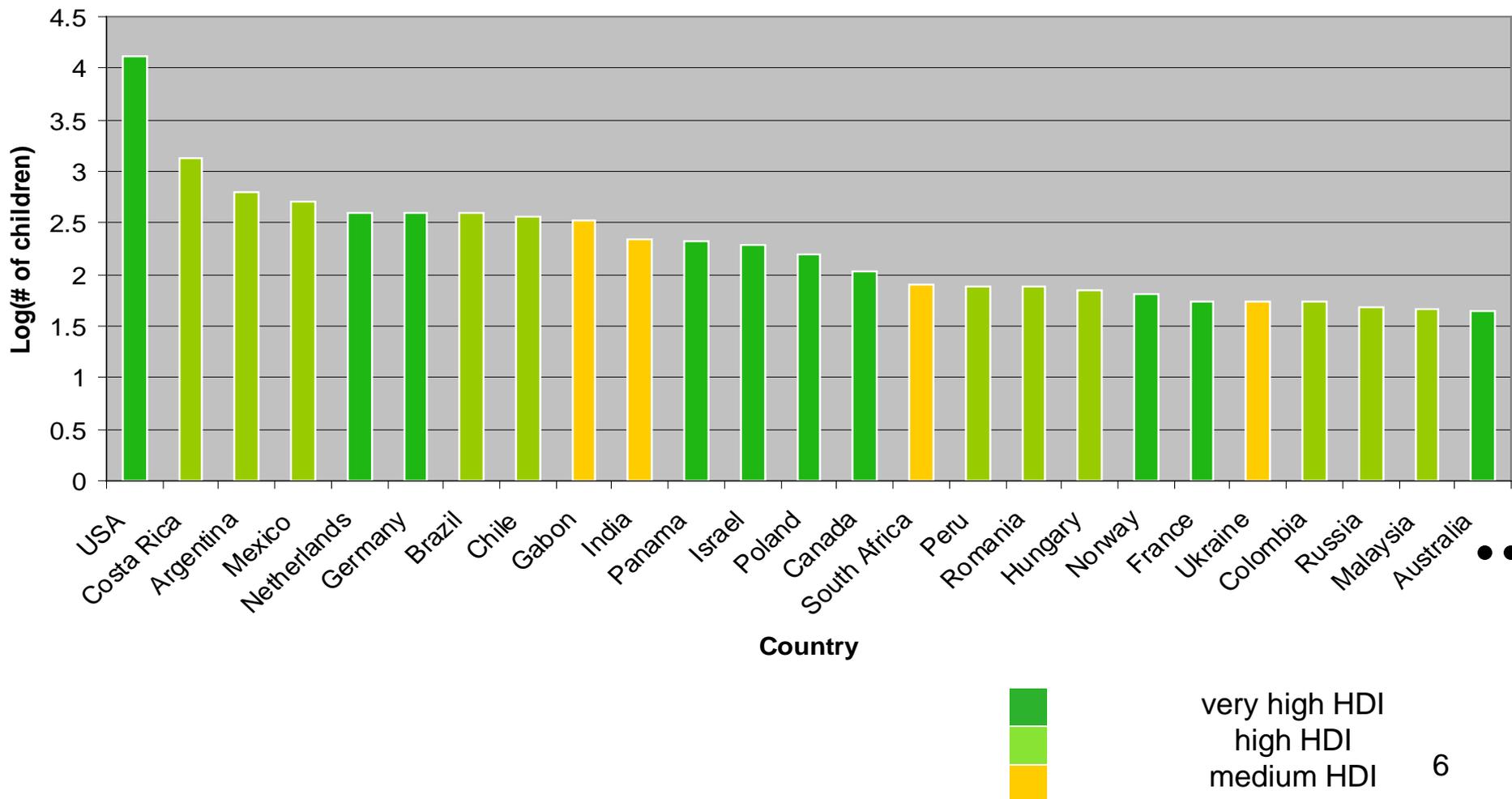
Pediatric Legislation: U.S. and EU

**Pediatric Product Development on a Global Scale:
Small populations require the world for clinical trials**



Pediatric Product Development: Global Logarithmic Scale

Number of pediatric patients from Written Requests: 2002-2007



Pediatric Legislation: U.S. and EU

- **The U.S., since 1997, and the EU, since 2007, have incentive and requirement programs for the development of therapeutics in the pediatric population.**
 - **There are similarities and differences between the U.S. and EU pediatric legislations.**
 - **U.S. has 2 separate processes: the incentive (BPCA) and requirement (PREA) that are only partially unified**
 - **EU's pediatric process is unified under their legislation.**
 - **Timing: European process is asking for information earlier in development.**
- Legislation passed in 2012 will facilitate moving the US and Europe closer together in the requirements for timing of discussion of pediatric plans**

Progress: Coordination of US pediatric programs

- **The US Exclusivity program, where appropriate, is being integrated with the Requirement program.**
 - **Since 2007 a Pediatric Review Committee (PeRC) at FDA has been working to increase coordination between the exclusivity and requirement programs.**
- **The US and European regulators have been working since 1998 to ensure some coordination of pediatric efforts.**
- **A chart of FDA vs EMA (European Medicines Agency) studies is provided by FDA's Office of Pediatric Therapeutics (OPT) for all products scheduled for discussion at the weekly PeRC meeting**
- **FDA/OPT coordinates a monthly Pediatric Cluster meeting with the EMA. Japan and Canada are recent full participants.**



Legislative Comparison: post FDASIA

	U.S. BPCA	U.S. PREA	EU
Development	Optional	Mandatory	Mandatory (optional for off-patent)
Instrument	Written Request	Adult submission	Paediatric Investigation Plan
Waiver	--	criteria for full and partial waivers	criteria for full and partial waivers
Timing	anytime adequate information available	End of Phase 2	End of Phase 1
Reward	6 months patent extension	--	6 months patent extension
Drugs & Biologics	Yes	Yes	Yes
Orphan	Included	Excluded	Included
Decision	FDA	FDA	EMA- PDCO

The Pediatric Cluster

- Now 5 years old
- Coordinated by OPT's International Team
- Originally focused on PIP's coming into EMA
- Japan (PMDA) and Canada (HC) were Observers for 2 years but now are full participants and suggest topics also.

Monthly FDA, EMA, PMDA and HC: Process of Information Exchange

- **EMA sends monthly list of Ped Invest Plan (PIP)s**
- **FDA & EMA usually identify products and scientific issues for discussion.**
- **EMA sends the Summary Reports**
- **FDA develops a spreadsheet with data we have on pediatric trials for products to be discussed.**
- **FDA prepares Agenda after OPT's international team identifies experts from FDA who will participate in the discussion and receives list of EMA experts who will be participating.**
- **At Japan's or Canada's request, a topic they have suggested would mean coordination with their experts.**

FDA, EMA, PMDA and HC: Triggers for Discussion

- **Ethical or data integrity issues**
- **Trial design issues**
- **Choice of endpoint**
- **Safety concerns**
- **Different pediatric indications for development**
- **Pediatric study feasibility issues**
- **Pediatric studies completed (to avoid duplication)**
- **Outcome of pediatric studies, including negative studies.**
- **Marketing approval differences**

FDA, EMA, PMDA and HC Collaboration

- **Scope of Information Exchanged (August 2007-March 2013):**
 - **Product specific discussions**
 - 298 products were discussed
 - 212 of 298 product discussions included participation by FDA review divisions
 - **General topics discussed (not product specific): n= 54**

Examples from Specific Discussions

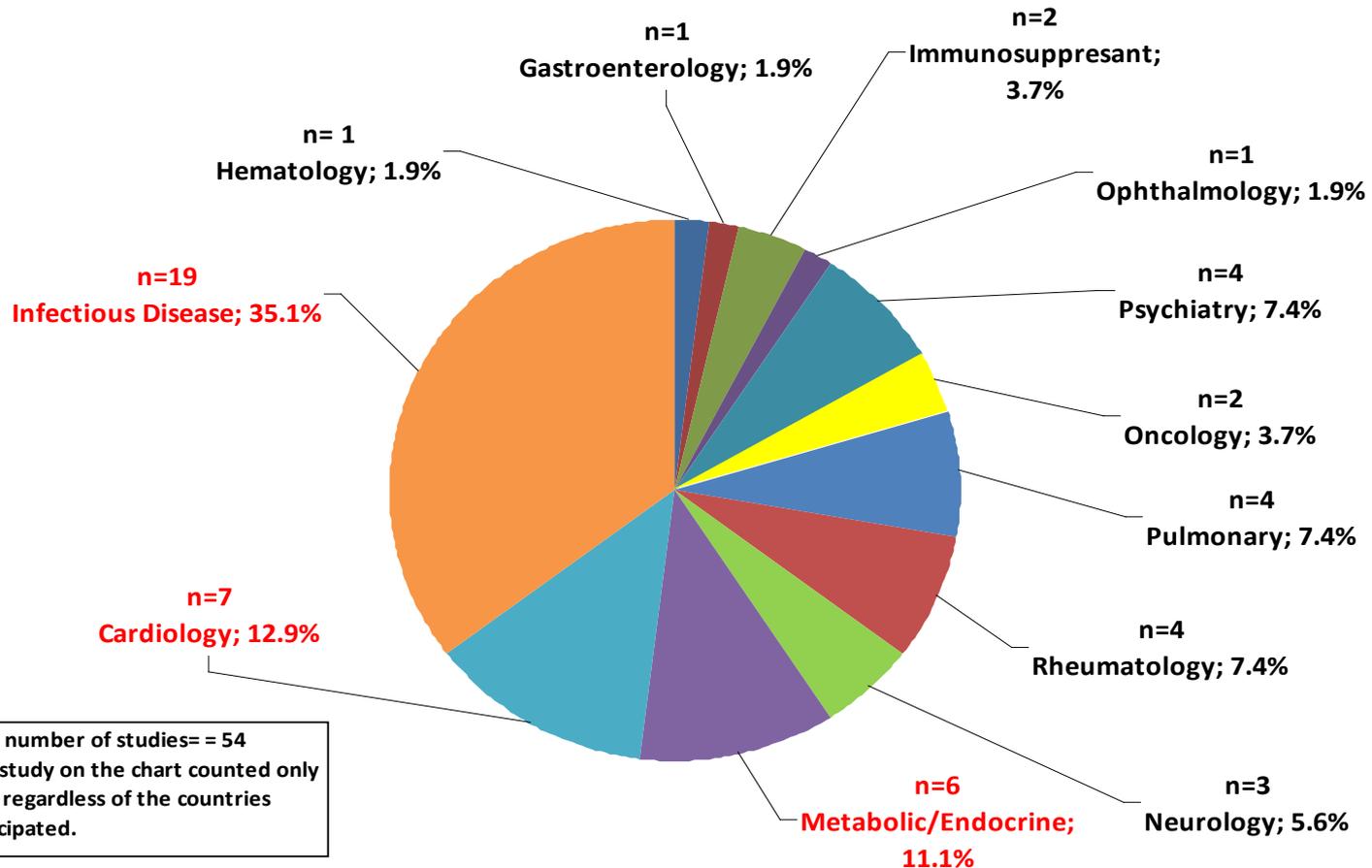
- **Information not shared by sponsor with the other agency**
- **Safety concerns**
- **Endpoint differences**
- **Indication differences**
- **Age differences**
- **Timing of initiation of pediatric studies**
- **Juvenile animal studies**

Recent and Future Activities

- The collaboration with EMA, Japan and Canada is well established and busy.
- Analysis of where pediatric studies were being conducted indicated around 20% are from Latin America.
- There has been no Central group (aka EMA Pediatric Committee) organizing the regulators in LA but much development of their pediatric research infrastructure

FDA and Latin America Initiative

Latin America Pediatric Trials by Therapeutic Class in FDA's Database
(2002-2007)



FDA and Latin America Collaboration Background

- **Confidentiality commitments to exchange pediatric trial information in place with regulators in Mexico (COFEPRIS), Brazil (ANVISA) and Chile (ISP).**

FDA and Latin America Collaboration Activities to Date

- **Teleconferences with Latin America investigators**
 - Description of regulatory process for pediatric clinical trials
 - Roles of local, regional and (where applicable) national ethics committees
 - Successes and challenges
 - Timeline for product approvals
 - Influences of national governments
 - Perspectives on developing or collaborating with regional partnerships
 - Regulatory flow chart
- **Teleconferences with regulators**
 - ANVISA in Brazil (regularly)
 - COFEPRIS in Mexico

The Need Is Obvious

- Pediatric Trials bear special responsibilities and it is our job to ensure a coordinated trial program
- Because of the limited number of children with certain diseases and the difficulty in conducting pediatric trials, experienced PEDIATRIC researchers are needed.
- These researchers need to be linked with common protocols, data entry, analysis and reporting if they are to maximize data obtained while minimizing risk and ensuring quality
- They also need to be able to talk with each other

The Future: Needs & Populations

- Needs

- Almost 50% of the therapies used in pediatrics remain without appropriate studies: particularly difficult to study are the neonatal population and rare diseases.
- Long term studies
- Researchers with an understanding of the differences in performing product development trials where the data is going to be submitted to FDA or other regulatory body.

- Populations

- Emerging countries have huge pediatric populations: India & China's annual birth rate are **each** more than Brazil, Egypt, Mexico, Poland, Russia, Ukraine and Turkey added together

Networks

- Required in European law to be established
- Just because you do adult trials well, does NOT mean you can do pediatric trials well
- The next areas of focus for study is neonates and long term studies
- Other countries and continents are developing well organized and scientifically solid pediatric networks
- Data from all over the world is accepted in trials submitted to the FDA and can be the basis of a product's approval.

Pediatric Networks-Examples

- US

COG: Children's Oncology Group

NRN: NICHD's Neonatal Research Network

PTN: NICHD's Pediatric Trials Network

CARRA: The Childhood Arthritis and Rheumatology Research Alliance =350 US pediatric rheumatologists and researchers

CF-RDP: Cystic Fibrosis Research Development Program is a Network of Research Centers involved in Drug Development

PECARN: Pediatric Emergency Care Applied Research

Pediatric Networks: Examples

- EU

UK's MCRN: Medicines for Children Research
(18 different networks)

PRINTO: Pediatric Rheumatology International Trials
Network

PENTA: Pediatric European Network for TX for AIDS

ENPR: European Network of Paediatric Research
(Enterprise-EMA) Network of Networks

Conclusions

- **Pediatric trials: unique and often global**
- **Pediatric legislation: driving global development**
- **Global collaboration and information sharing: critical to assure enrollment of children in scientifically and ethically sound trials that answer a needed question.**
- **Pediatric therapeutic knowledge gap: closing, but challenges and gaps remain.**
- **To address these challenges and gaps, we must work together.**
- **Better/More Pediatric Networks need to be established.**

How to find information on pediatric trials on FDA's website

- FDA's Main page has a "Science and Research" box which includes pediatrics-is on the right side = click there
- On the Science page, on the right you will see "Pediatrics" = click there
- On the Office of Pediatric Therapeutics page is a link to Medical, Pharmacology and Statistical reviews for products studied in pediatrics.
- Drugs@FDA will list a product and you can search through the list of products and try to find the pediatric reviews, but you need to realize that most are reviews of "supplements"



www.fda.gov/pediatrics

Office of Pediatric Therapeutics

Pediatrics - Windows Internet Explorer

C:\Documents and Settings\mmurphy\Local Settings\Temporary Internet Files\OLK40A\Pediatrics (2).htm

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Pediatrics

Home Science & Research Science and Research Special Topics Pediatrics

Science and Research Special Topics

- Pediatrics**
- Pediatric Safety
- Pediatric Ethics
- Pediatric Science and Research Activities
- International Collaborations
- Humanitarian Use Devices and Humanitarian Device Exemption
- Publications
- Presentations

Resources for You

- Pediatric Product Development
- MedWatch: The FDA Safety Information and Adverse Event Reporting Program
- Pediatric Medical Devices
- MedSun: Medical Product Safety Network
- Vaccines, Blood & Biologics
- Vaccine Adverse Events

Pediatrics

- New Pediatric Labeling Information Database
- Safety Reporting Updates
- Pediatric Study Characteristics Database
- List of Exclusivity Determinations (PDF - 179KB)
- Medical, Statistical, and Pharmacology Reviews 7/9/2012- present
- Medical, Statistical and Pharmacology Reviews 9/2007-7/2012
- Medical, Statistical and Pharmacology Review Summaries 1/2002-9/2007

Persons with disabilities having problems accessing the above PDF files may call 301-796-8653 for assistance.

Safety
Resource for pediatric safety information related to drugs, biologics and devices

Pediatric Ethics

Spotlight

- 2013 Meeting Materials, Pediatric Advisory Committee to the FDA
- Giving Medicine to Children
- Teaching Kids About Using Medicine Safely
- AAP News FDA Updated
- FDA Pediatric Safety Communications

Related Links

- Pediatric Formulations Platform
- HHS for Kids
- Medicines for Children (WHO)
- Children's Oncology Group
- American Academy of Pediatrics
- Glaser Pediatric Research Network

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