EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The Paediatric Regulation as an instrument for European paediatric research

ENPREMA, London 10/11 March 2011

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Head of Paediatric Medicines, European Medicines Agency

Why is there a EU Paediatric Regulation?

for

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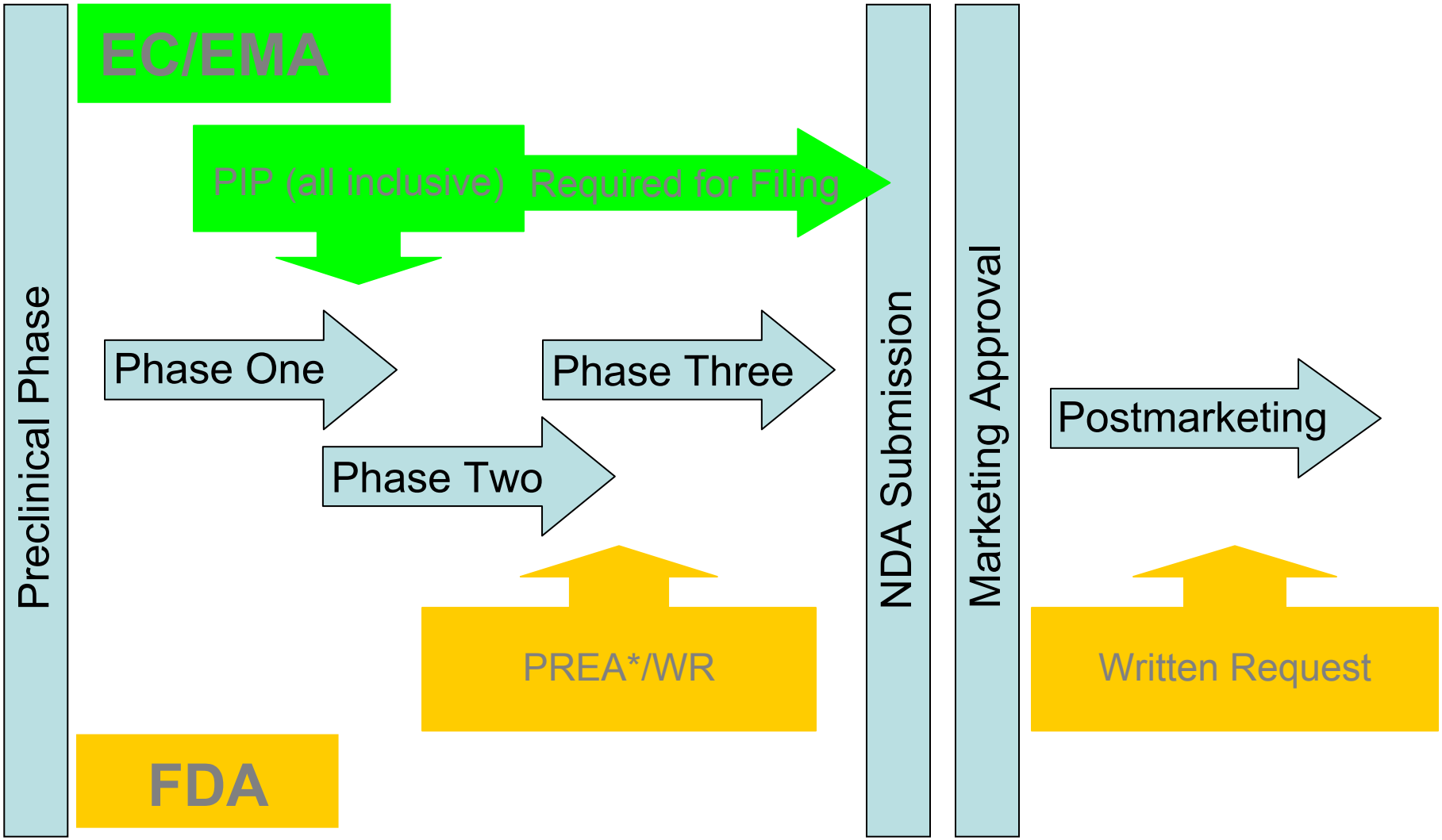
Objectives of the EU Paediatric Regulation

- Improve the health of children:
  - Increase high quality, ethical **research** into medicines for children
  - Increase **availability** of authorised medicines for children
  - Increase **information** on medicines
- Achieve the above:
  - Without unnecessary studies in children
  - Without delaying authorization for adults

New Drug Development Process: US vs EU



From Dianne Murphy, FDA

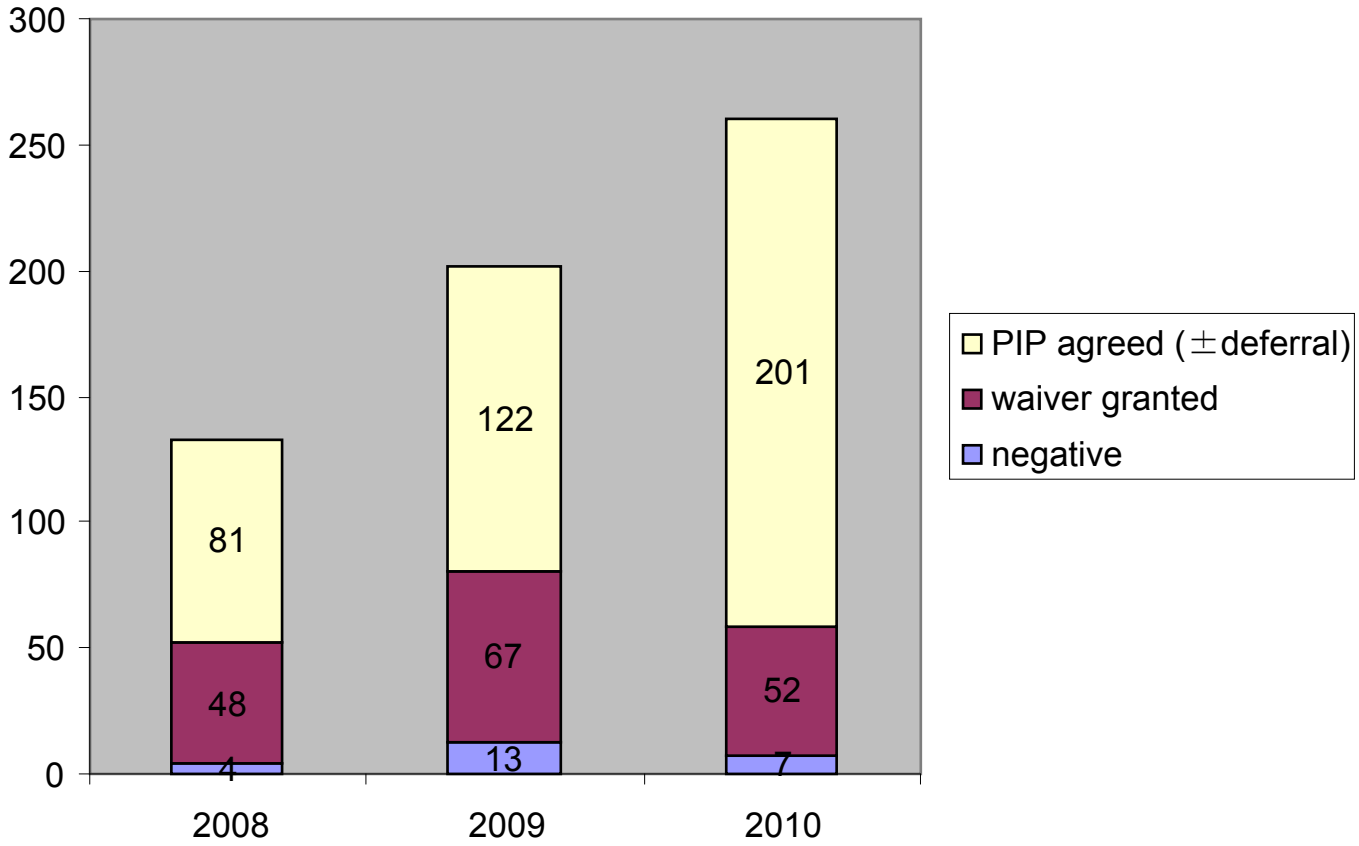
Paediatric Investigation Plan

- Basis for development and authorisation of a medicinal product for all paediatric population subsets
- Includes details of the timing and the measures proposed, to demonstrate:
  - Quality
  - Safety
  - Efficacy

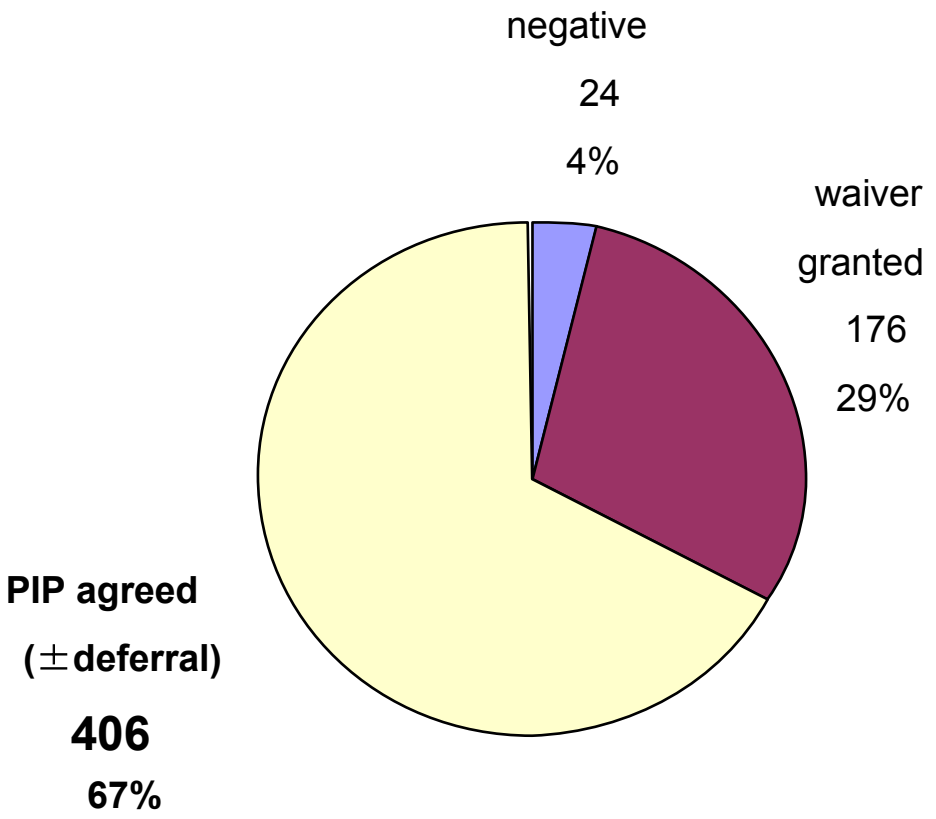
  } Marketing Authorisation Criteria
- To be agreed upon and/or amended by the PDCO
- Binding on company → compliance check
  (but modifications possible, at the company's request)

PDCO Opinions on Paediatric Investigation Plans and Clinical Trials

PDCO opinions on applications 2008-2010



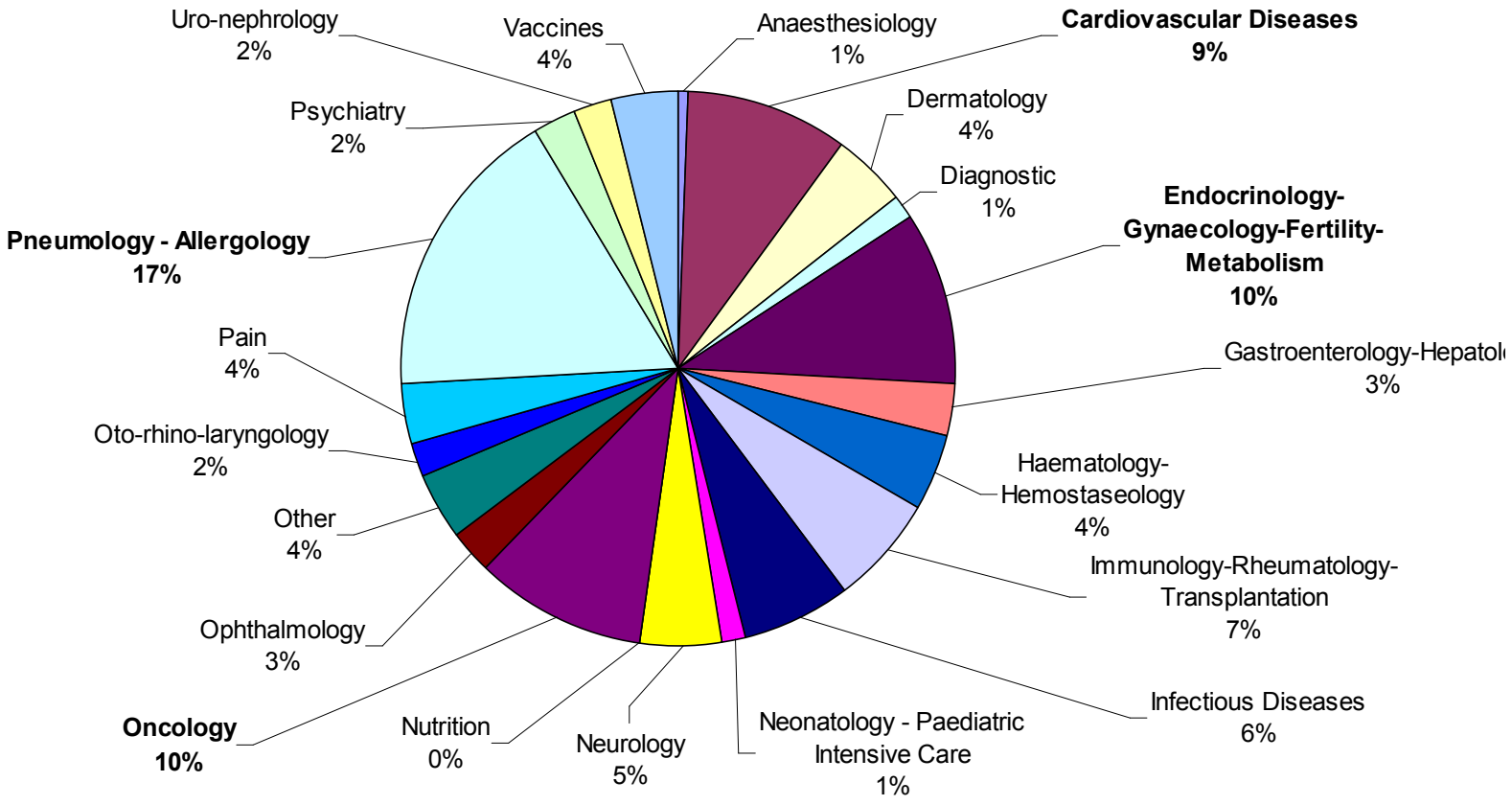
PDCO opinions on applications 2007-2010, total



Deferral: 82% of trials (until after adult development)

Therapeutic areas of applications

(all applications, 2007 – today)



Deferrals

(Study in the first 96 PDCO procedures)

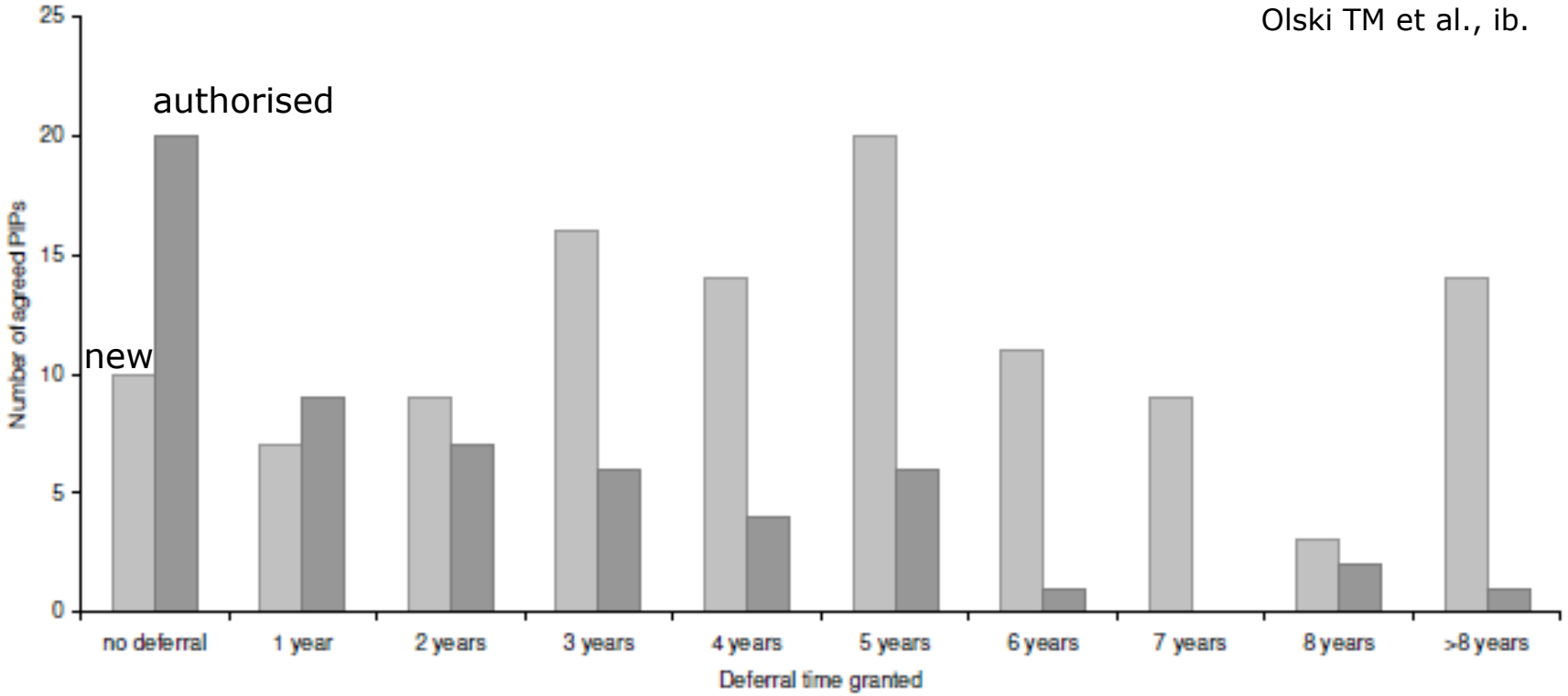
- At least one deferral granted in:
  - 91% of applications for new products
  - 64% of applications for already authorised products
- Usual deferral duration: 3-5 years from MAA in adults
- Deferral is the instrument to avoid delaying marketing authorisation in adults

Olski TM et al., Three Years of Paediatric Regulation in the European Union. Eur J Clin Pharmacol 2011 (in press)

Deferral granted in 91% of new medicinal products and 64% of authorised (2007-2009)

Figure 3. Deferral time granted for PIPs

Olski TM et al., ib.



Clinical trials design

(Study in first 96 PDCO procedures)

- PDCO increased studies in neonates from 15% to 26%
  (subsequent data showed an increase in proposed neonatal studies)
- Staggered approach proposed, encouraged and occasionally imposed
- N. of patients required: PDCO requested an
  - ✓ Increase in 5/54 (9.3%)
  - ✓ Decrease in 8/54 (14.8%)

Olski TM et al., ib.

Clinical trials design

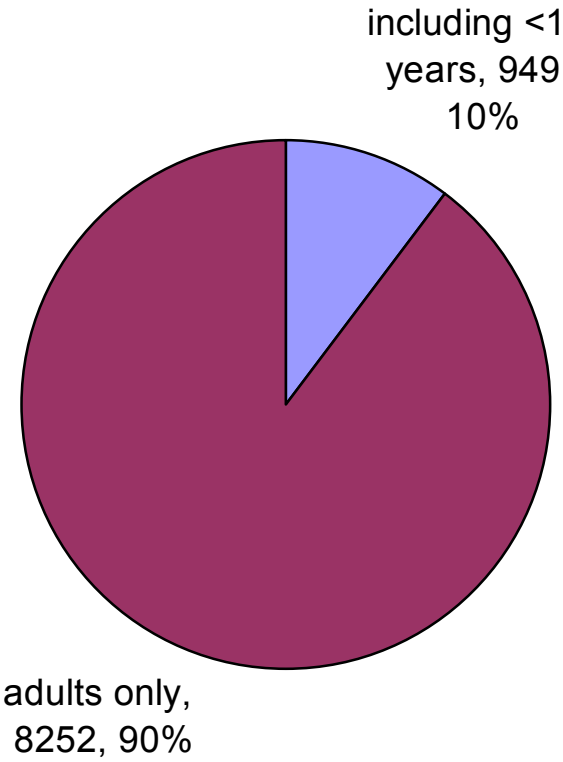
(study in the first 96 PDCO procedures)

- Primary endpoint accepted in 90% of cases
- General design endorsed in almost all cases (97%):
  - ✓ 2/96: double-blinding imposed
  - ✓ 23 additional trials imposed (20 comparative, 6 active-controlled, 12 placebo-controlled, 2 dose-comparison)

Olski TM et al., ib.

Clinical trials in Europe (data from EudraCT)

Clinical trials involving children (<18)
2010, EEA

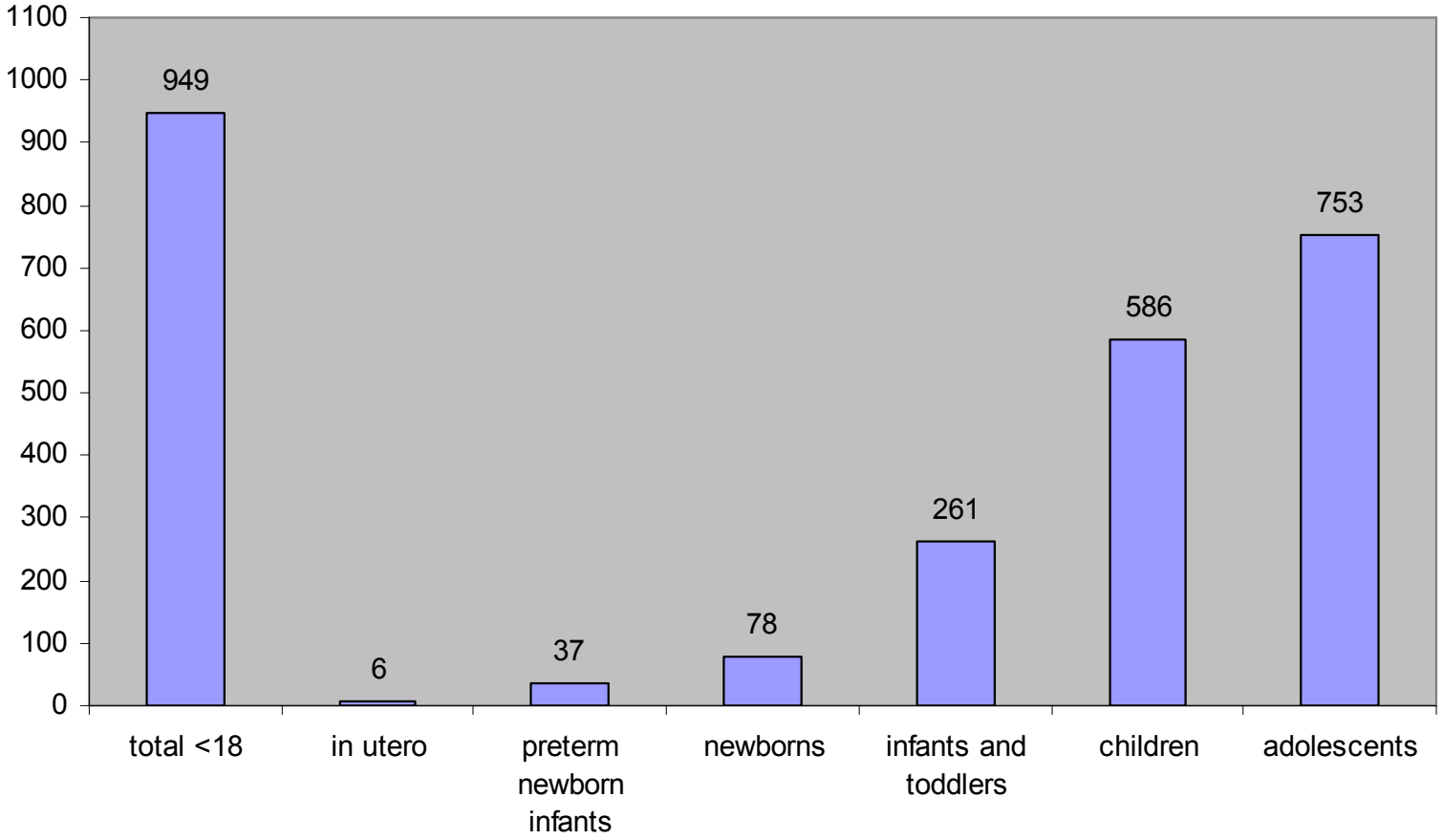


Clinical trials in children (2010, EEA)

paediatric only vs. paed. + adult

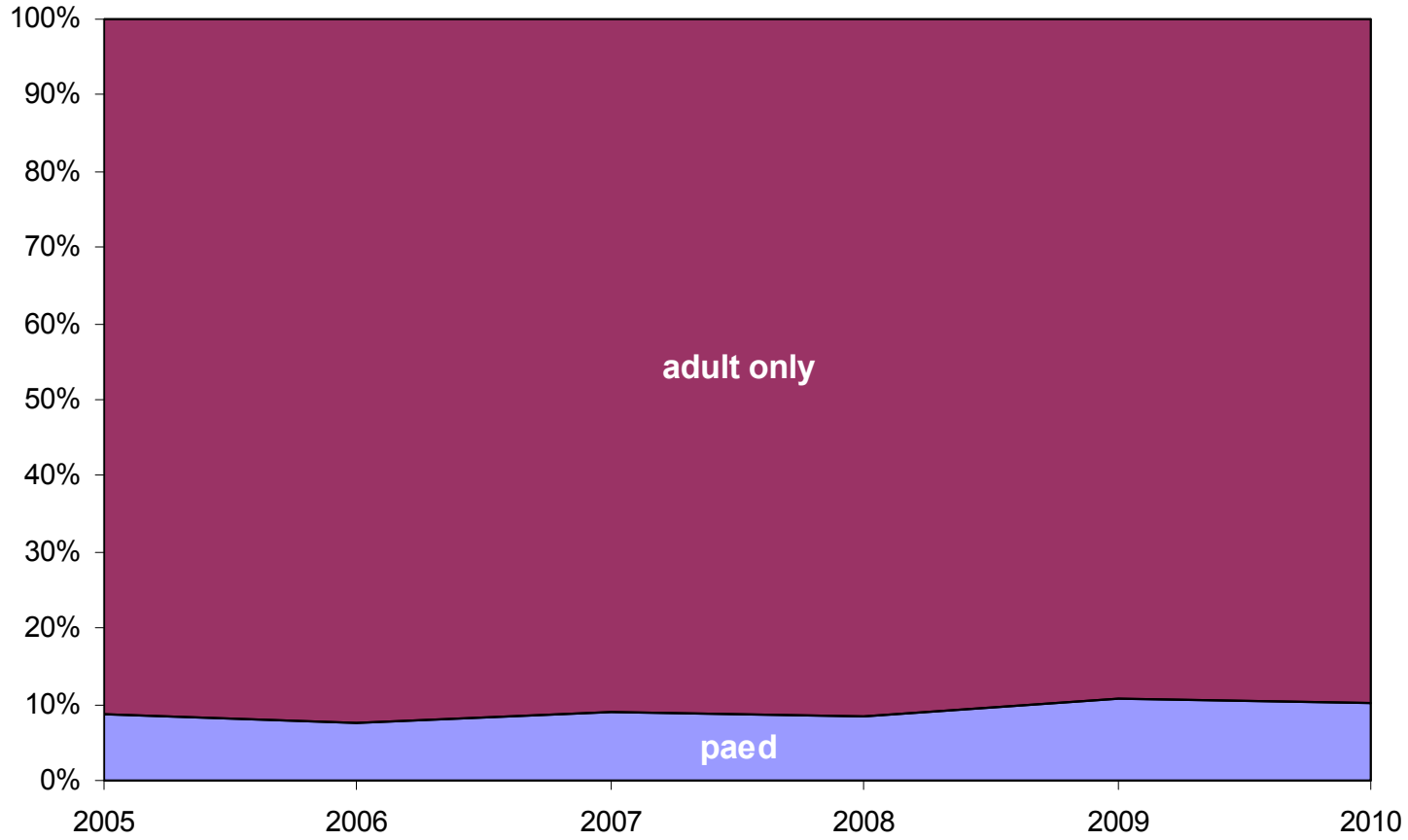
Paediatric clinical trials by age groups (2010, EEA)

Note:
Multinational trials are counted in each country



Is the number of paediatric trials increasing in the EEA?

The % of paediatric trials is substantially stable (appr. 9-10%, EEA)



Are clinical trials moving outside the "first world"?

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PERSPECTIVE

A New Colonialism? — Conducting Clinical Trials in India

Samiran Nundy, M.Chir., and Chandra M. Gulhati, M.D., D.T.M.&H.
N Engl J Med 2005; 352:1633-1636 | April 21, 2005

This article has no abstract; the first 100 words appear below.

In January 2005, the government of India enacted a new rule that allows foreign pharmaceutical companies and other interested parties to conduct trials of new drugs in India at the same time that trials of the same phase are being conducted in other countries. This new rule supersedes a directive of India's Drugs and Cosmetics Rules that required a "phase lag" between India and the rest of the world. According to the old rule, if a phase 3 study had been completed elsewhere, only a phase 2 study was permitted in India. Even under the new rule, phase 1 trials . . .

MEDIA IN THIS ARTICLE

A Private, "One-Man" Clinic in New Delhi Where Letrozole Was Tested.

ARTICLE ACTIVITY

15 articles have cited this article

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

5 November 2010
EMA/INS/GCP/154352/2010
Compliance and Inspection

Clinical trials submitted in marketing authorisation applications to the EMA

Overview of patient recruitment and the geographical location of investigator sites

- updated with data from marketing authorisation applications submitted in 2009

A substantial proportion of patients in adult CTs is from outside the EU

- 61% of the patients in pivotal trials submitted in MAA to the EMA during the observation period from January 2005 to December 2009 were from third countries, comprising 25.9% from the ROW region (Africa, Middle East/Asia/Pacific, Australia/New Zealand, Central/South America, CIS, Eastern Europe-non EU), and 35.2% from North America.
- 7.8% of patients in pivotal trials submitted in MAA to the EMA during the observational period from January 2005 to December 2009 were included in trials in Middle East/Asia/Pacific.
- 9.2% of patients in pivotal trials submitted in MAA to the EMA during the observational period from January 2005 to December 2009 were included in trials in Central/South America.

Clinical trials submitted in marketing authorisation applications to the EMA
EMA/INS/GCP/154352/2010

Are clinical trials moving outside the "first world"?

Clinical trials submitted in marketing authorisation applications to the EMA
EMA/INS/GCP/154352/2010

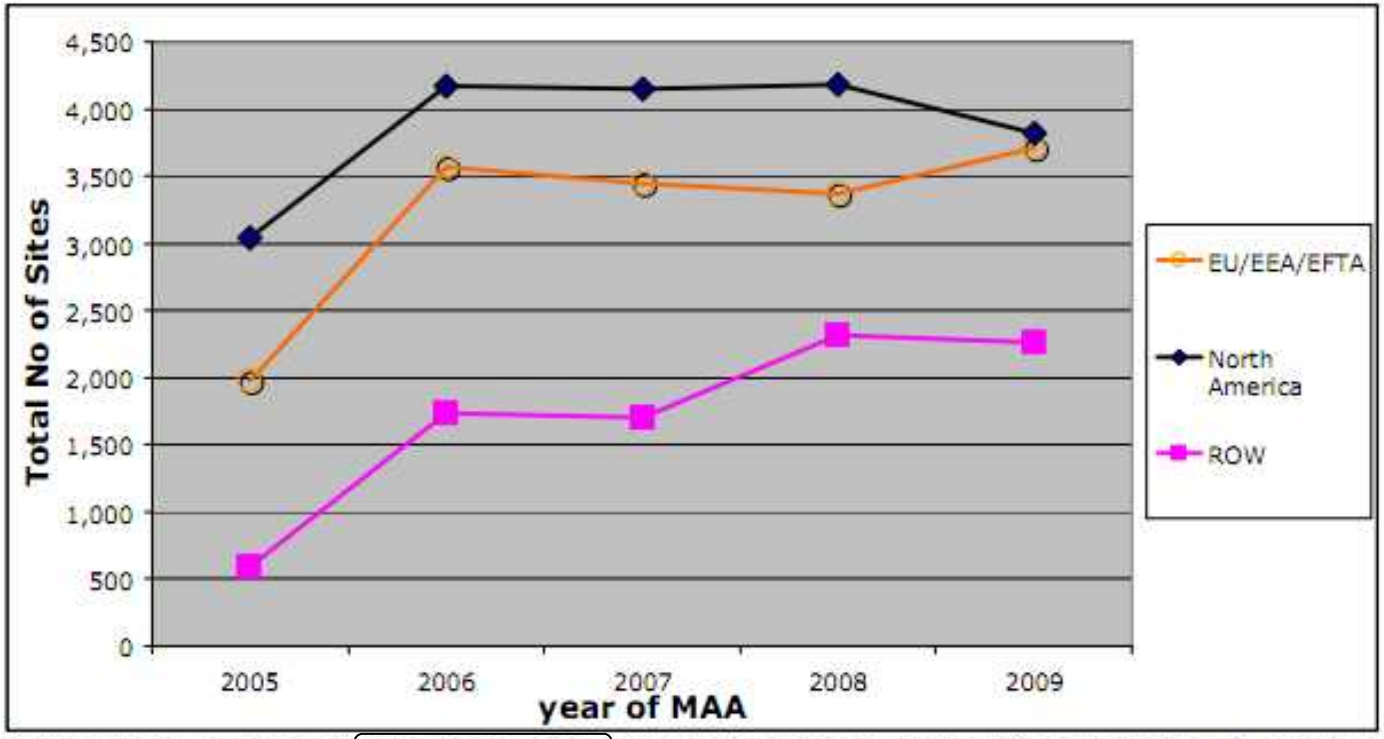
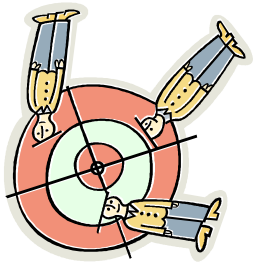


Figure 7: The number of investigator sites involved in pivotal clinical trials submitted in MAAs to the EMA per region and year. The data are shown as three "global regions" – EU/EEA/EFTA, North America and ROW (Rest of the World).

The role of ENPREMA



Key operational goals

- **Collaboration and communication**
  (between existing networks and stakeholders)
- **Facilitation of recruitment in clinical trials**
  (providing expertise and access to infrastructure for industry to conduct studies in children)

- **Building competences**
  (defining strategies for resolving major challenges)
- **Avoiding unnecessary studies**
- **Stimulating high quality research**
  (consistent and transparent quality standards; harmonising clinical trial procedures)
- **Strengthening the foundations of the European Research Area**

What ENPREMA is **NOT** supposed to do

- To **fund** studies
- To **conduct** studies
- to **decide** on areas of paediatric research, which is under the responsibility of:
  - the Member States
  - the Commission through the Community programmes
  - each individual network

Paediatric Regulation and Clinical Trials in Children - Conclusion

- Paediatric development has gone from very very optional to compulsory in principle (unless a waiver is granted)
- Paediatric Investigation Plans, agreed between EMA and pharmaceutical companies, require a substantial increase in n. of clinical trials in paediatric age groups
- Unless capacity is sufficient in Europe, companies will need to find alternatives

Thanks for listening

PDCO meeting at EMA