INCiPiT Italian Network for Paediatric Clinical Trials

# LIMITI E PROSPETTIVE DELLA RICERCA CLINICA INTERNAZIONALE

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# Il punto di partenza

## ADULTI

•Farmaci adeguatamente studiati

Requisiti di:

- Sicurezza
- Efficacia
- Alta qualità

•Scoperta di farmaci innovativi

## BAMBINI

•50-90% medicinali utilizzati in pediatria NON è appositamente studiato

Rischi:

•ADRs (sovradosaggio)

•inefficacia (sottodosaggio)

•formulazioni inadeguate

•ritardi nell'accesso a farmaci innovativi

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# Le sperimentazioni cliniche in pediatria

- Gli studi clinici in pediatria sono più difficili da condurre, necessitano di più tempo e costano di più:
  - Motivi di tipo medologico ed etico
  - Ridotto numero di pazienti
  - Diversità dagli adulti (anatomia, fisiologia, sviluppo dei vari organi)
  - Eterogeneità delle popolazioni pediatriche (neonati/adolescenti)
  - Estrapolazione dati da adulto non sempre possibile
  - Patologie solo pediatriche

- L'uso pediatrico rappresenta un mercato minore per l'industria farmaceutica

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# Trial (di efficacia) negli adulti e in pediatria per lo stesso farmaco antiipertensivo

## ADULTI

- N = 220 pazienti
- Paesi = 1
- N. Siti = 8
- Tempo impiegato per lo studio = 5 mesi
- 24 pazienti per sito

## IN PEDIATRIA (6-16 aa)

- N = 253 pazienti
- Paesi = 4
- N. Siti = 70
- Tempo impiegato per lo studio = 1 anno e 2 mesi
- 3-5 pazienti per sito

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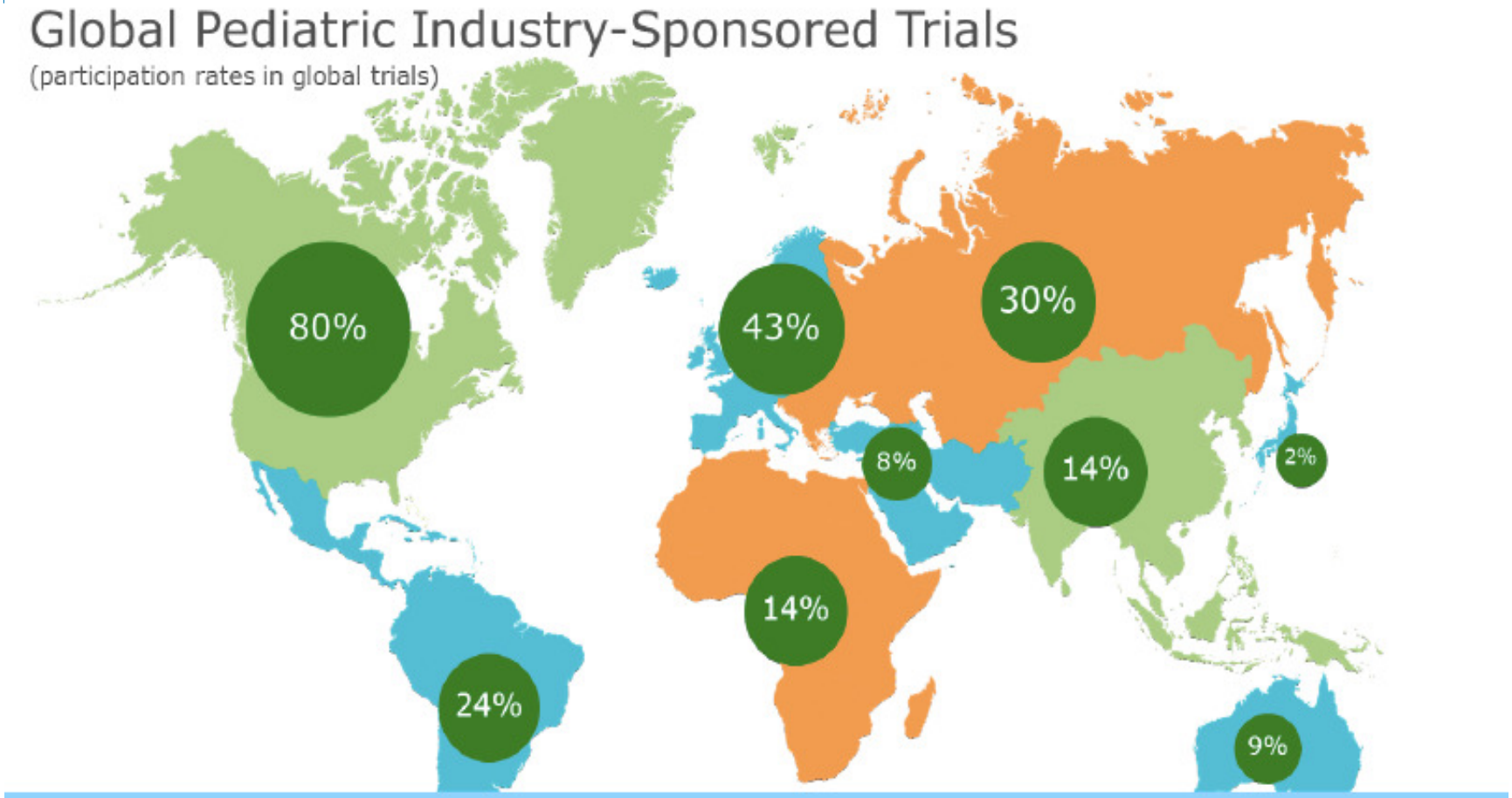
# Global Reach, Low Per Site Participation




**30% of sites do not enroll (NA and EU)***

**< 1.1 patients per site per year****

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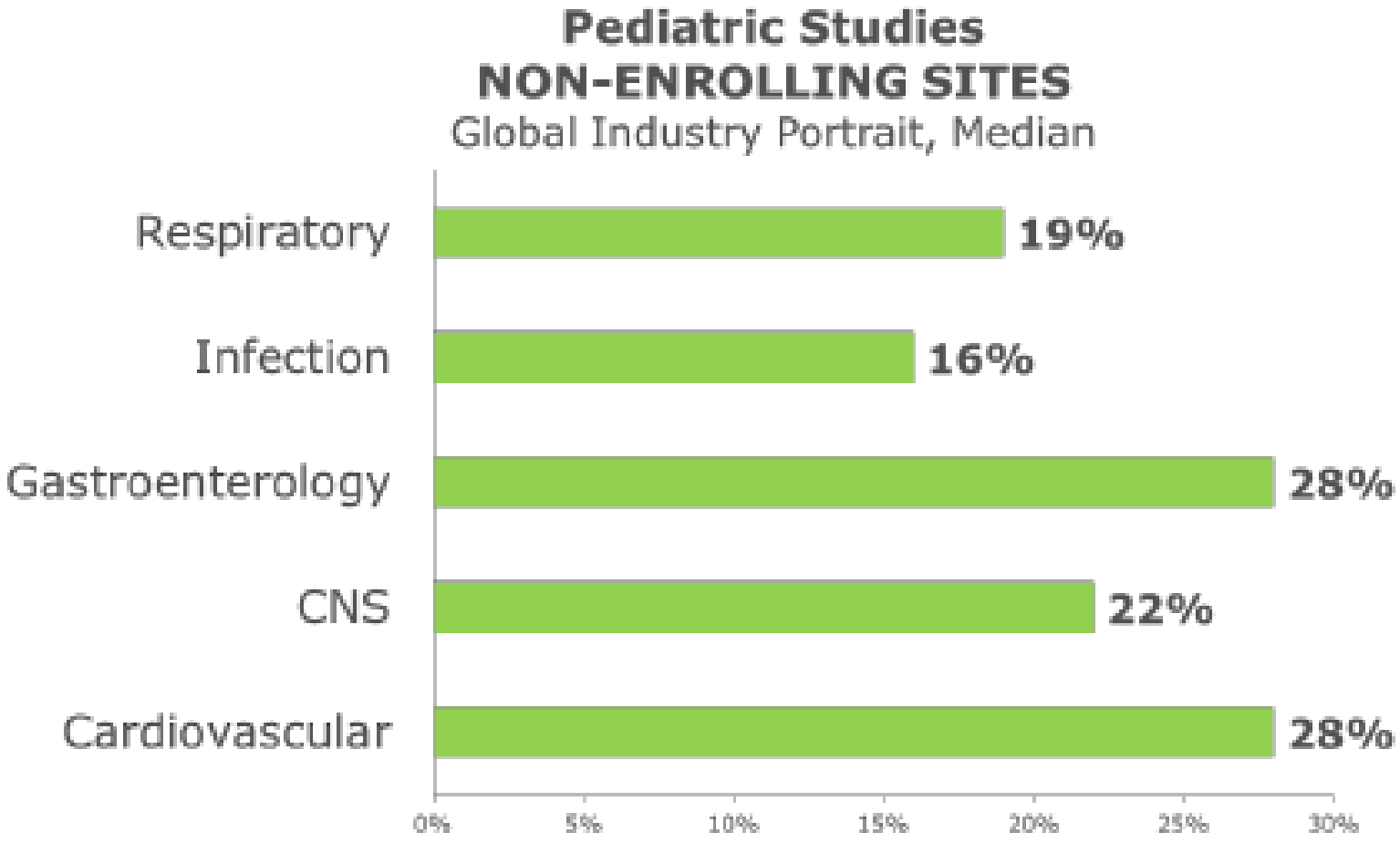
# Number of Non-Enrolling Sites is very High

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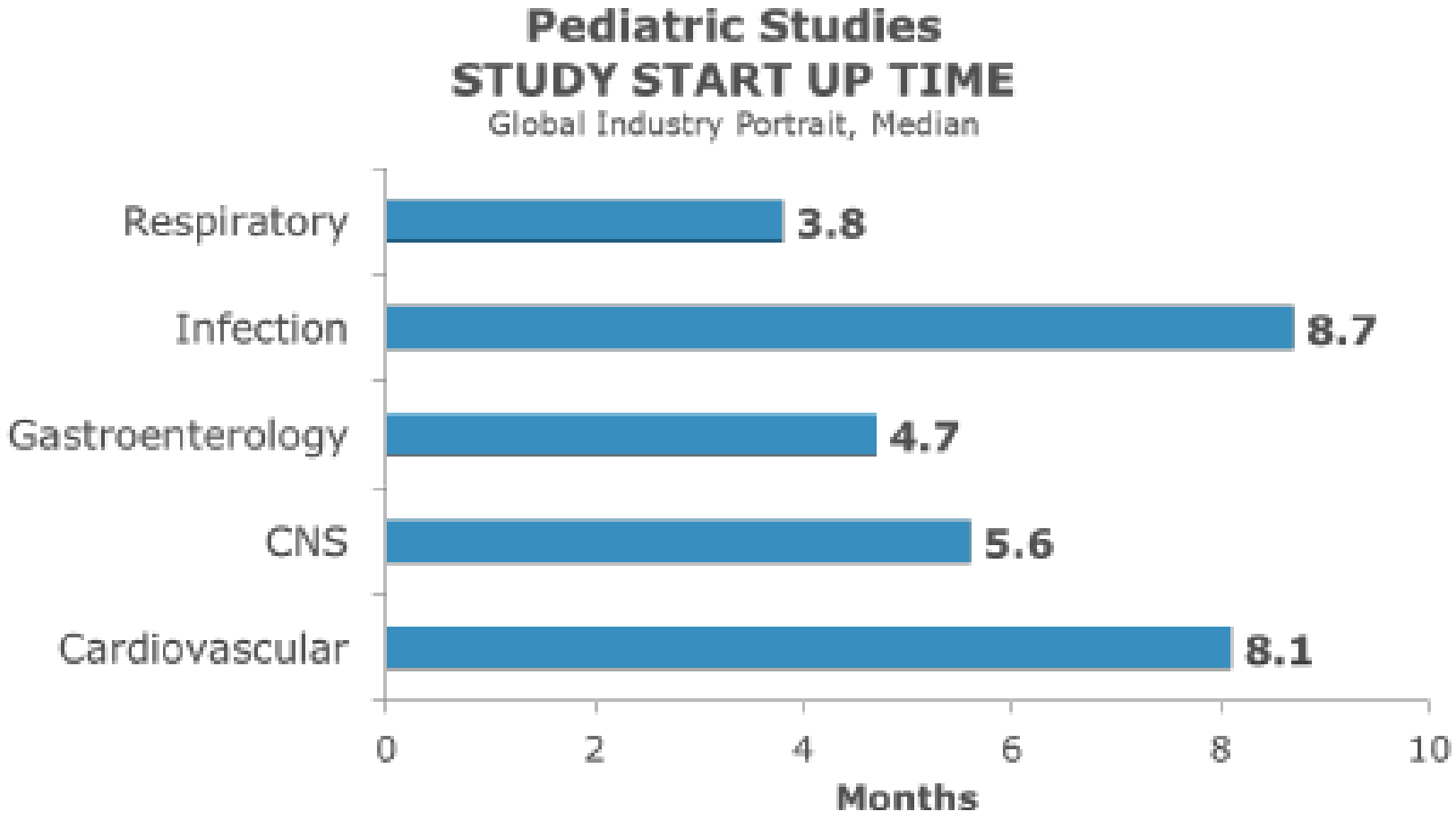
# Start up is very long

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# Dopo 10 anni di Regolamento

| | Compliance Checks | Waiver | Initial PIP | Modifications |
|---|---|---|---|---|
| 2007 | 0 | 18 | 71 | 0 |
| 2008 | 9 | 75 | 198 | 9 |
| 2009 | 29 | 76 | 195 | 77 |
| 2010 | 48 | 65 | 267 | 107 |
| 2011 | 59 | 61 | 126 | 155 |
| 2012 | 45 | 70 | 108 | 181 |
| 2013 | 58 | 60 | 138 | 202 |
| 2014 | 85 | 57 | 104 | 214 |
| 2015 | 62 | 60 | 112 | 211 |
| Total | 395 | 542 | 1319 | 1156 |

| | |
|---|---|
| Endocrinology-Gynaecology | 435 |
| Infectious Diseases | 431 |
| Oncology | 416 |
| Cardiovascular | 376 |
| **Pneumology - Allergology** | **359** |
| Immunology-Rheumatology | 344 |
| Neurology | 249 |
| Haematology-Hemostaseology | 247 |
| Vaccines | 196 |
| Other | 183 |
| Dermatology | 175 |
| Gastroenterology-Hepatology | 170 |
| Pain | 122 |
| Uro-nephrology | 104 |
| Psychiatry | 103 |
| Ophthalmology | 88 |
| Diagnostic | 44 |
| Oto-rhino-laryngology | 43 |
| Neonatology | 32 |
| Anaesthesiology | 17 |
| Nutrition | 5 |

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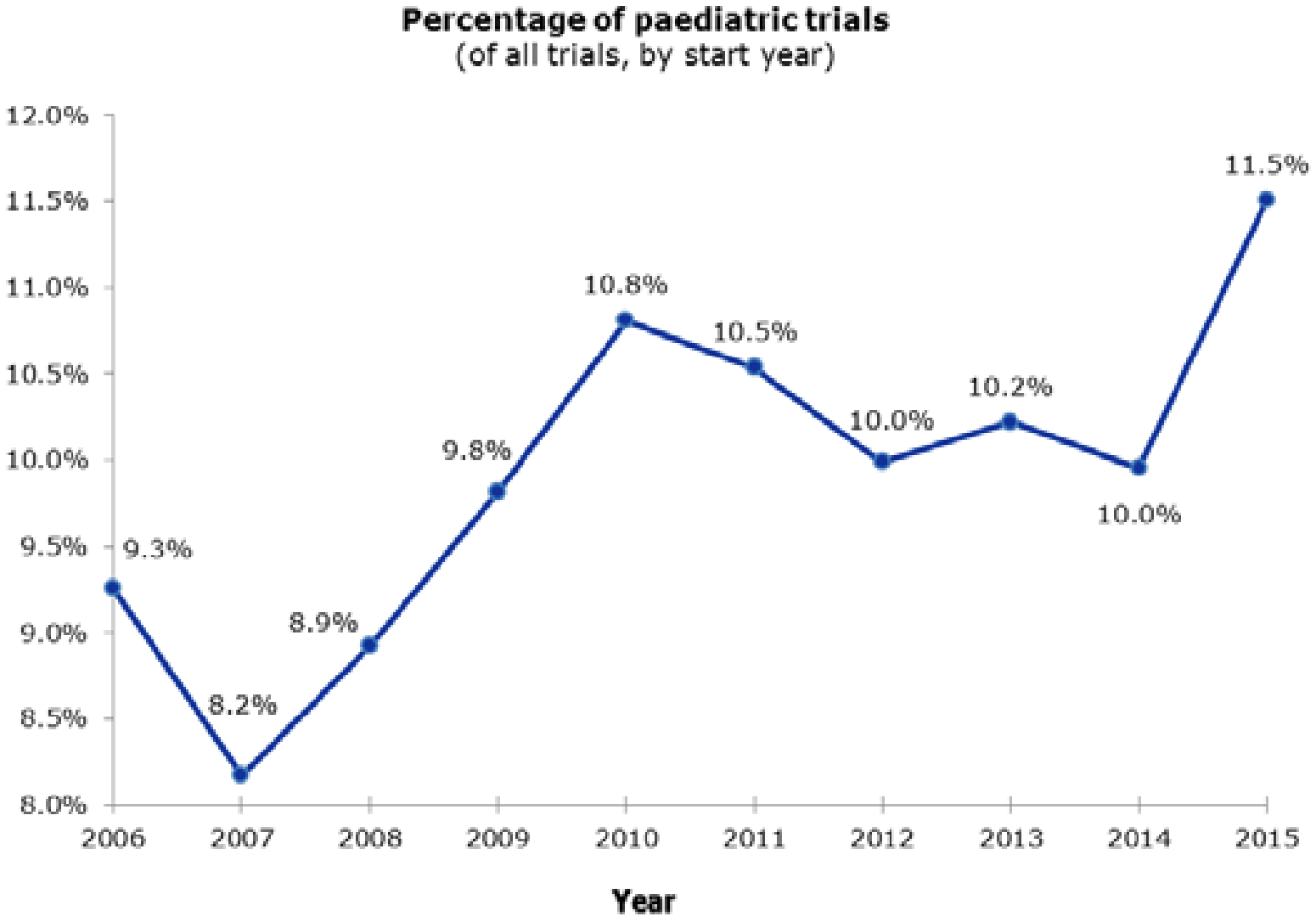
# Aumento degli studi clinici in pediatria



# I numeri del regolamento pediatrico oggi

- 770 PIPs ad oggi (2016) sono in corso
- 750 clinical trials da completare
- 260.000 pazienti da arruolare per il completamento degli studi!

# ….and subjects*

| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---|---|---|---|---|---|---|---|---|---|
| Preterm neonates | 0 | 0 | 0 | 327 | 82 | 2,527 | 1,552 | 3,634 | 4,997 | 1,979 |
| Term neonates | 0 | 98 | 5 | 184 | 169 | 1,353 | 2,283 | 1,488 | 2,168 | 1,749 |
| Infants and toddlers | 530 | 119 | 20 | 54,715 | 2,224 | 13,318 | 62,226 | 17,772 | 39,095 | 122,295 |
| Children | 2,683 | 706 | 270 | 5783 | 2,771 | 21,665 | 30,831 | 27,994 | 65,824 | 48,358 |
| Adolesecents | 435 | 36,458 | 285 | 5801 | 4,869 | 20,206 | 22,680 | 17,628 | 45,717 | 36,921 |
| Total | 3,648 | 37,381 | 580 | 66,810 | 10,115 | 59,069 | 119,516 | 68,516 | 157,261 | 211,302 |

*planned to be enrolled in clinical trials, by age by year of authorisation of the trial (or, if not available, by year of protocol upload into EudraCT).

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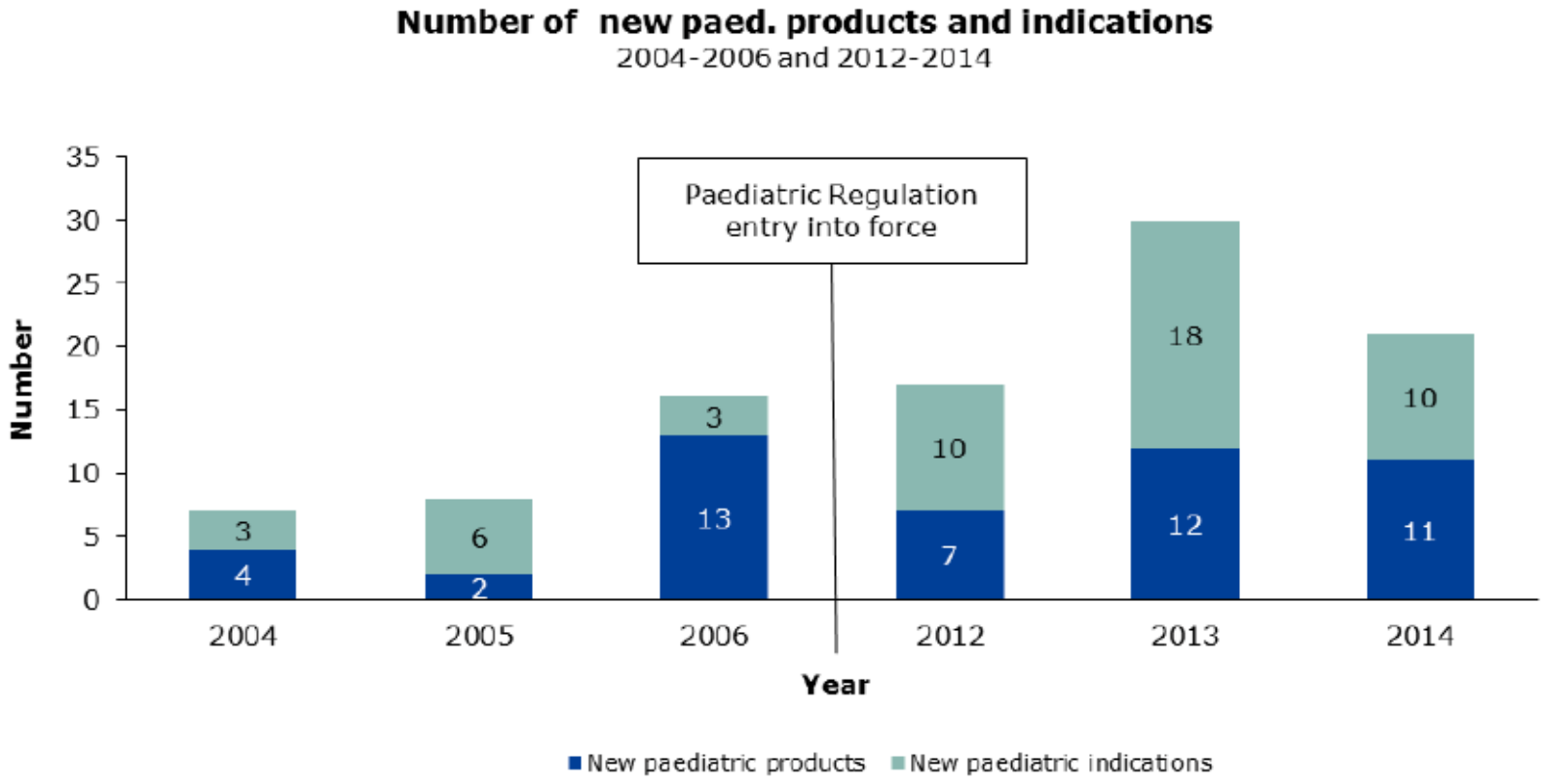
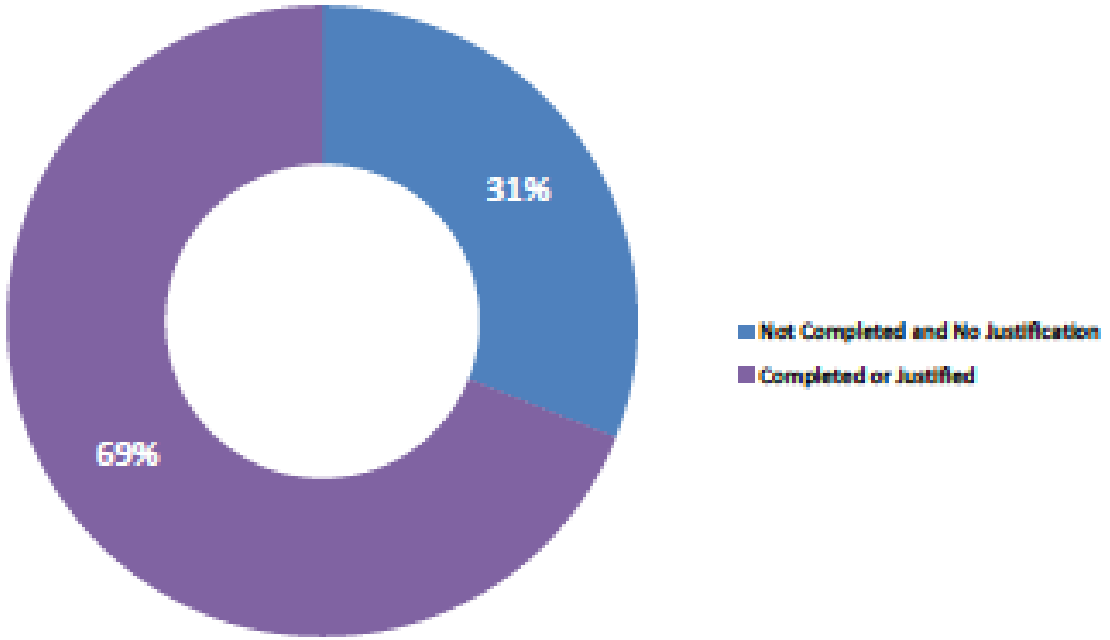
# Più farmaci disponibili



# Cionostante…

## Still Struggling




**Ninety Pediatric Investigation Plans (PIPs) were scheduled to be finished in June 2013:**

- **31% were not completed and no justification provided**
- **69% were completed or provided justification and were granted more time**

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# Some Reasons For Existing Challenges

- Misalignment between the goals from Regulatory Authorities, Academia and Pharmaceutical Companies
  - Government: Public Health Aim
  - Industry: Regulatory Compliance and/or Market Incentive
  - Academia: Authorship, Academic Promotion, Patient Care
- Desire for Retaining Independence and Autonomy
  - Industry traditionally is competitive, much less in Paediatrics
  - Academic Centers also compete with each other and have different standards of care
  - Lack of Harmonization between regulatory authorities

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# Criticità

- Paediatric research infrastructure needed to conduct such studies is not developing at the same pace to meet this growing need.
- Paucity of patients available for study in many paediatric indications and need for multiple capable sites to satisfy enrolment in trials: clinical trial infrastructure across the EU is not sufficiently organised
- Lacks adequate funds and scale to consistently and efficiently deliver both industry-sponsored and academic non-industry sponsored clinical trials

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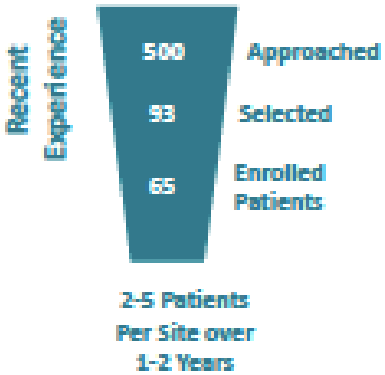
# Opportunity for Efficiency

## Efficiency lowers R&D investment and increases likelihood of success

1

**Site Selection & Throughput**




2-5 Patients Per Site over 1-2 Years

2

**Aligning CDA, Contracts and have a single ICF**

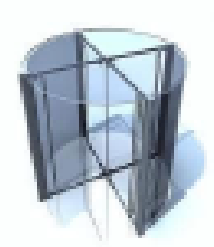
3

**Minimize Protocol Amendments**

9 amendments slowed enrollment

4

**Staffing Consistency**



# IMI2 Call

- IMI2: Partnership tra CE e EPFIA per finanziamento progetti
- Call10-T4: Creation of a Pan-European paediatric clinical trials network

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS 4 CHILDREN

- Creazione del Consorzio C4C: Tutti (o quasi) i Network Nazionali organizzati + Network Disease Specifici + grandi Ospedali/centri di ricerca pediatrici
- C4C risponde alla call (2 stages: 1 step 28/03/2017; 2 step settembre 17; partenza progetto 2018)

ITALIA partecipa come INCiPiT – Italian Nework for Paediatric Clinical Trials

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# Building on successful initiatives

- Trial delivery
- Innovative methodologies
- Interactions with Industry and Regulators
- Involvement with young people and children
- Diverse funding opportunities
- Education

# Network Vision

Europe will use a coordinated approach to deliver high quality “regulatory grade” and independent clinical trials in:

- Multiple countries
- Multiple sites
- All paediatric age groups
- All paediatric disease groups

# Network Mission

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COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS 4 CHILDREN

- Improve availability of information about medicines used by children
- Promote the delivery of high quality trials of medicines for children by supporting:
  - Trial implementation using resources shared between studies
  - Trial design through a combination of information about natural history, feasibility and expert opinion

Public- and industry-funded studies

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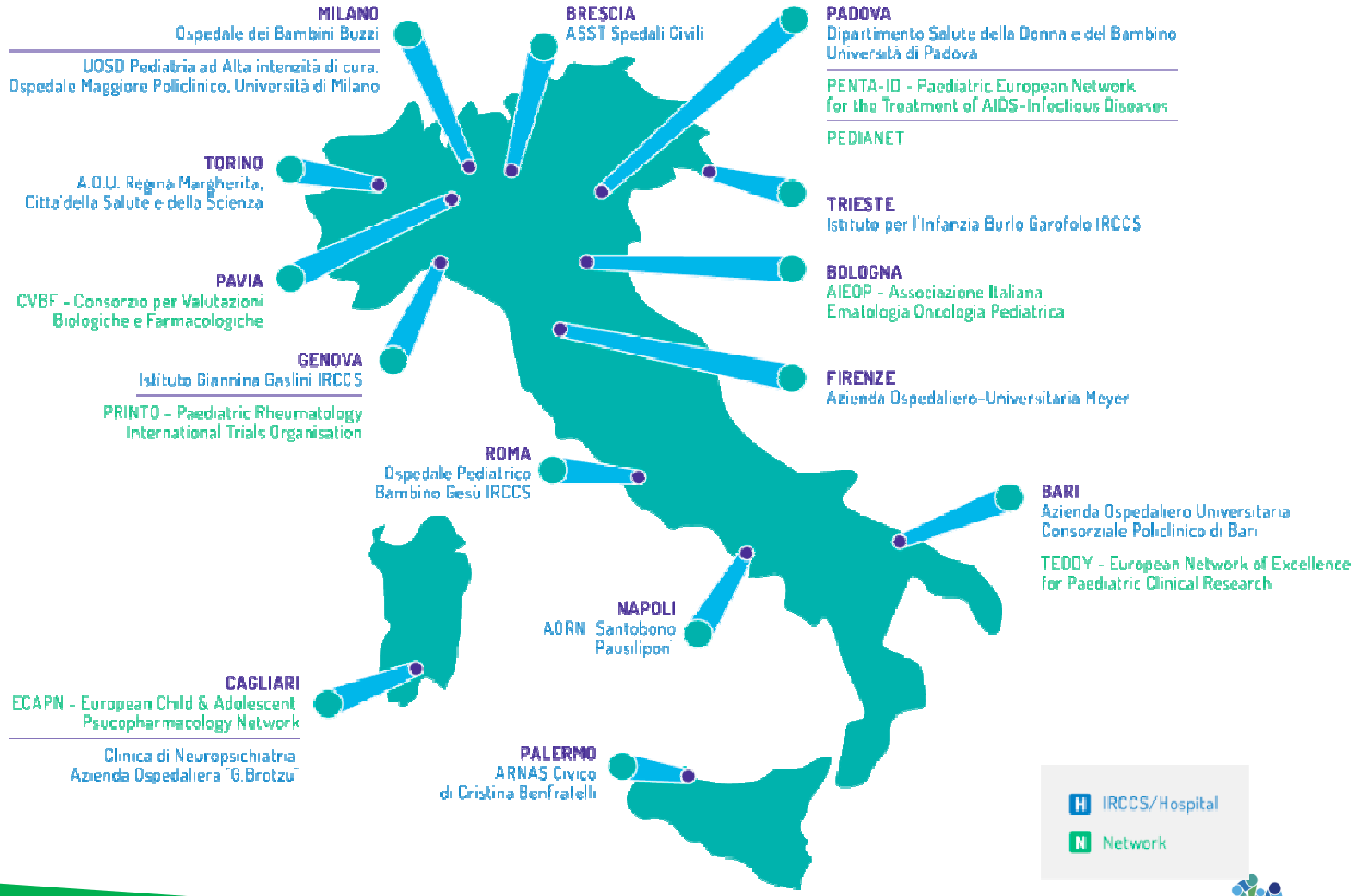
# Network Values

- Collaborate on information and processes through learning together
- Share resources between studies / specialties
- Consistently follow procedures based on common standards that are adapted to local circumstances
- Children and young people are at the heart of our work
- Efficient communication between Sponsors and sites
- Trusted relationships based on predictability and reliability

# INCiPiT Italian Network for Paediatric Clinical Trials

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# INCiPiT www.incipit-ped.net

## CHI SIAMO:

INCiPiT è un Network composto da i principali IRCCS e Ospedali Pediatrici Italiani, i grandi dipartimenti di Pediatria e Networks Nazionali e Internazionali che si occupano di sperimentazione in pediatria

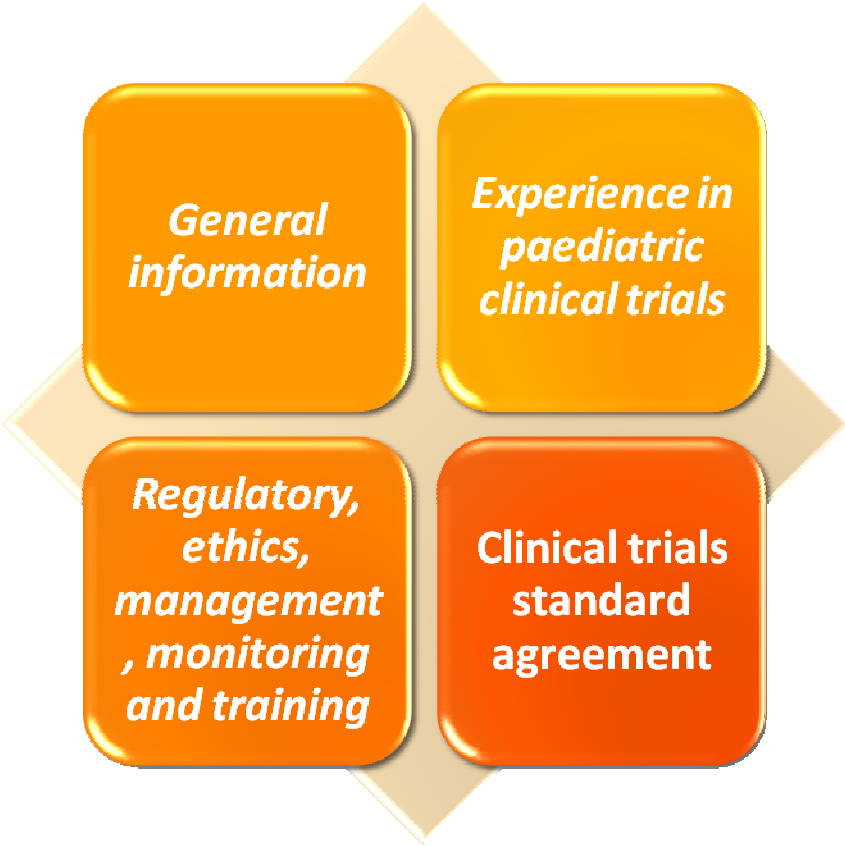
## MISSION

La mission di INCiPiT è incrementare e supportare l'ideazione, la realizzazione e il completamento di tutti i tipi di studi clinici profit e no-profit (fase I-IV) condotti in Italia in pediatria

# SURVEY

60 domande raggruppate in sezioni, concordate e finalizzate con diversi interlocutori a livello europeo

Inviata a tutti Parners INCiPiT per identificare l'esperienza dei centri nella sperimentazione in pediatria

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# Cosa è emerso

- Fotografia complessiva dei centri INCiPiT
- Valutazione complessiva dell'esperienza della ricerca clinica pediatrica in Italia – grande potenzialità ma margine di miglioramento!
- Ogni ente: ricognizione ed autovalutazione del proprio pregresso ed expertise nell'ambito degli studi clinici pediatrici
- Indagine non appropriata per i Networks partners  INCiPiT – step successivi
- Tempi di compilazione lunghi e Sistema self-report
- Pronti con la II survey per mappare meglio potenzialità/gap (per aree terapeutiche, feasibility)

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# Conclusions

- The Pediatric regulation has paved the way for developing Medicines tailored for children
- The gap between PIPs and new available Medicines reveals a poor efficiency of the “System”
- The problem of the “old Medicines” has not been solved.
- There is a need for more organized, “well trained”, multidisciplinary Pediatric Trial Sites
- C4C Network (INCIPIT) may contribute to efficiency and opportunities

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