

RICERCA, INNOVAZIONE E COMPETITIVITÀ:

QUALI VANTAGGI PER IL PAESE E PER I PAZIENTI?

IL FARMACO: UN SETTORE TRAINANTE PER LA RICERCA E LO SVILUPPO?

DA INDUSTRIA 2015 A HORIZON 2020

Lunedì 3 dicembre 2012 ore 8.30 – 14.00

I network di ricerca in pediatria TEDDY e GRIP

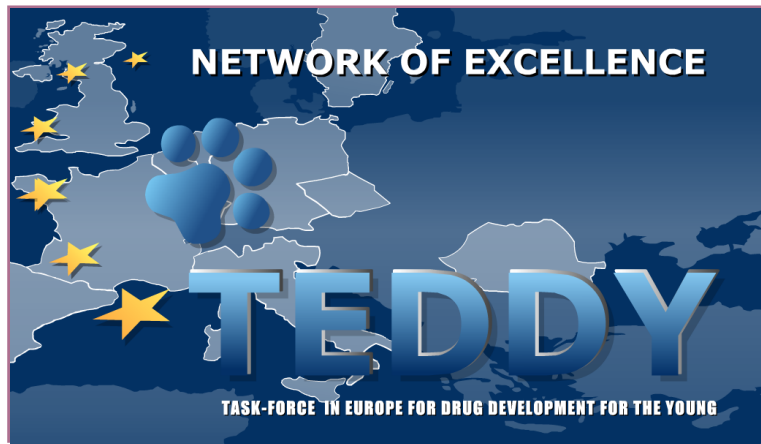
Paola Baiardi

TEDDY e GRIP oggi

TEDDY

Task-force in Europe for Drug Development for the Young

European multispecialty Network aiming at promoting paediatric drug development through good clinical research



GRiP

Global Research in Paediatrics

E' un progetto mondiale finanziato nell'ambito del 7° Programma Quadro (2011- 2015)

AIM: to implement an infrastructure matrix to stimulate and facilitate the development and safe use of medicine in children. This implementation entails the development of a comprehensive training programme and integrated use of existing research capacity, whilst reducing the fragmentation and duplication of activities.



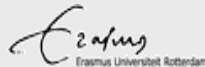
Teddy Network of Excellence

Funded under the Community's Sixth Framework Programme



TEDDY was established as a **Network of Excellence** funded under the 6 Framework Program (2005-2010), encompassing 19 Research Centers and 10 European Countries and Israel. The project involved with more than 200 researchers and experts

Aimed at increasing availability of paediatric safe and efficacious drugs



...how TEDDY was born...

2003 FP6 LSH-2003-1.2.1.1

Medicines for children

aimed at structuring efforts on:

- Clinical and biological research
 - ❖ Hoping and reality
 - ❖ Ethics and methodology
- Drug use in children
- Dissemination of knowledge



...how TEDDY has grown...

TEDDY has grown in the context of the Paediatric Regulation entered into force since 2007

to share and support EU Authorities for:

- Therapeutic Needs and Research Priorities
- Methodology for Paediatric Trials
- Ethics
- Paediatric drug authorisation
- Database of paediatric drugs, prescriptions and AEs

TEDDY is not a Scientific Society



TEDDY is not a Clinical Trials Center

TEDDY is not a Consultative Body



TEDDY IS A NEW RESEARCH INSTRUMENT

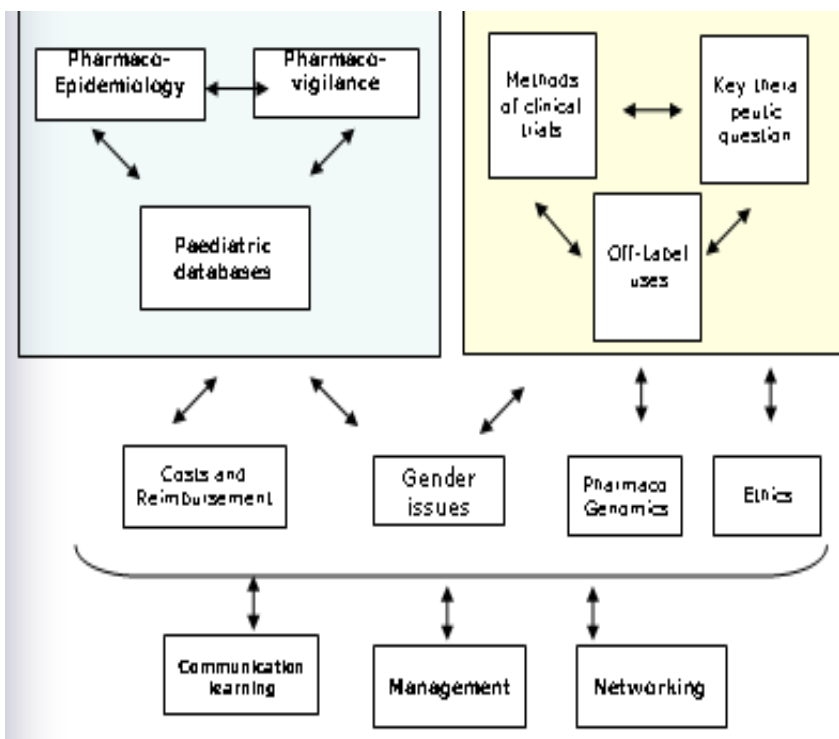
to straightening paediatric research and supporting both TEDDY Research groups and the existing external Networks, Societies and Experts to perform common and innovative initiatives

including those that would be more difficult to execute in lack **of a supportive action.**

Networking is the core of the mission of TEDDY



TEDDY NoE STRUCTURE 7 objectives/12 WPs



WP1
Pharmacoepidemiology

WP2
Genomics and pharmacogenomics

WP3
Clinical Trial Methodology

WP4
Key Therapeutic questions

WP5
Rare Diseases

WP6
Post-marketing studies

WP7
Ethics

WP8
Paediatric Drug Database





WP9
Communication, Information

WP10
Project Management

WP11
Joint Initiatives

WP12
Gender Issues

Networking Methodology

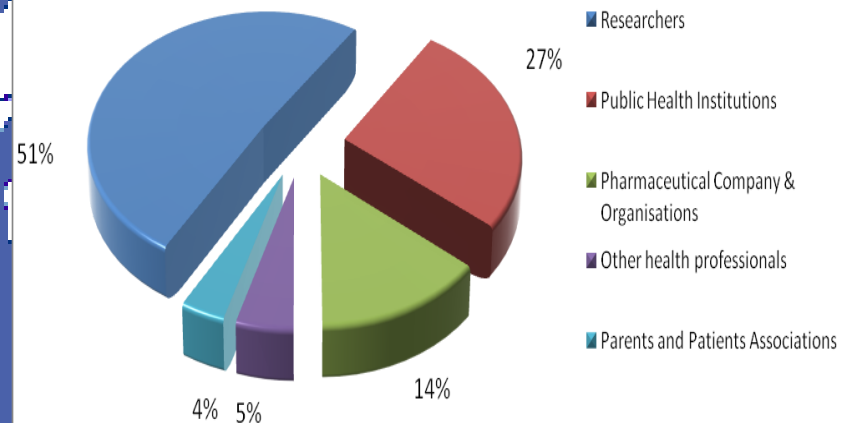
- Contact and interconnect 'noncompeting' people having similar interest or concerns
 Search for sector of interest and knowledge
- Create consensus on content and instruments to be used for common research
 Surveys, focus groups, questionnaires
- To circulate knowledge and skills along the 'points' and the 'nodes' of the Network
 Personnel exchange, e-learning courses
- Favour relationship among interested parties
 Open conferences, working groups

TEDDY networking

**Internal (145 TEDDY Experts)
and external (970 global
Contacts) expertise**

TEDDY collaboration with Paediatric Scientific Groups

SIOP Europe, EU Paediatric Cardiology Association (**AEPC**), EU Society for Paediatric Endocrinology (**ESPE**), EU Society for Paediatric Infectious Diseases (**ESPID**), EU Respiratory Society (**ERS**), Società Italiana per le Malattie Respiratorie Infantili (**SIMRI**), EU Society for Paediatric Gastroenterology, Hepatology and Nutrition (**ESPGHAN**), Società Italiana di Pediatria (**SIP**), Société Française de Pédiatrie, Paediatric Spanish Society, **EUCROF**-Paediatric Initiative



**European Countries: 25
Non EU Countries: 8**

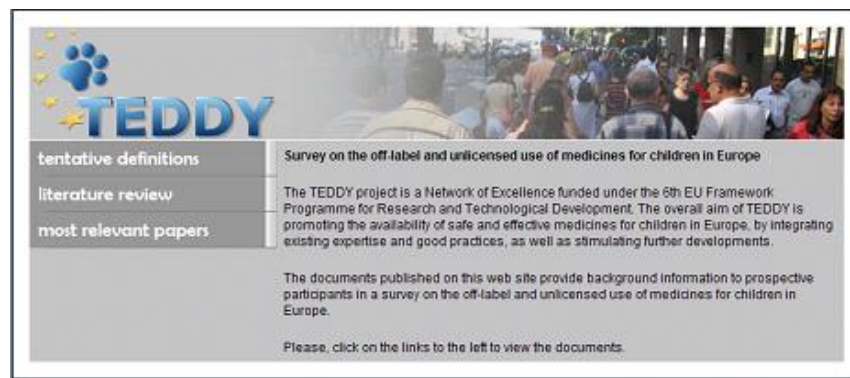
Defining off-label and unlicensed use of medicines for children: results of a Delphi survey

The aim of this Delphi survey is to develop common definitions for unlicensed and off-label drug use in children to be used for research and regulatory purposes. After a literature review on the current status of unlicensed/off-label definitions, a two-stage, web-based Delphi survey was conducted among experts in Europe. Results were then consulted with the European Medicines Agency (EMA)

The lowest level of consensus reached was for questions related to a different formulation or if a drug was given although contraindicated. At the final step, **85% of the responding experts agreed on the proposed definition for off-label** (use of a drug already covered by a Marketing Authorisation, in an unapproved way) **and 80% on the definition for unlicensed.**

Table 1: Composition of the Expert Panel

	Invited % (n)	participants % (n)
Health Professionals	14.29 (12)	20.59 (7)
Industry	8.33 (7)	8.82 (3)
Regulatory	20.24 (17)	14.71 (5)
Scientists	52.38 (44)	55.88 (19)
Other	4	0
Total	84	34



E-learning courses

www.teddylearning.com



NETWORK OF EXCELLENCE

TASK-FORCE IN EUROPE FOR DRUG DEVELOPMENT FOR THE YOUNG

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The Courses in the **TEDDY e-learning Platform** summarize the recent advancement in the sector of paediatric medicines and are based on the results of the Network as well as the contribution of well recognise high level experts collaborating with TEDDY.

The following Courses are available or are on-going:

- » CHILDREN ARE NOT LITTLE ADULTS
- » THE EUROPEAN PAEDIATRIC REGULATION
- » PAEDIATRIC STATUS AND OFF-LABEL USE OF DRUGS IN CHILDREN
- » CLINICAL TRIALS INVOLVING CHILDREN - Methodological aspects
- » CLINICAL TRIALS INVOLVING CHILDREN - Ethical aspects
- » PHARMACOEPIDEMOLOGY AND DRUG UTILISATION IN CHILDHOOD
- » PHARMACOVIGILANCE AND DRUG ADVERSE REACTIONS IN PAEDIATRICS
- » INNOVATIVE MEDICINES AND ORPHAN DRUGS FOR CHILDREN
- » THERAPEUTIC NEEDS IN THE PAEDIATRIC POPULATION
- » TEDDY RESULTS

Multidisciplinarietà Pubblicazioni

Recommendation for drug development for children

M. Catapano^a, C. Manfredi^a, P. Paolucci^b, H. Cross^c, K. Verhamme^d,
M.J. Mellado Peña^e, I. Grosch-Wörner^f, C. Knibbe^g and A. Ceci^{h,*}

^aConsorzio per Valutazioni Biologiche e Farmacologiche, Pavia, Italy

^bDepartment of Mother and Child, University of Modena and Reggio Emilia, Modena, Italy

^cUniversity College London, London, UK

^dPharmacoeconomics Unit, Department of Pharmacology and Biostatistics, Erasmus University Medical Center, Rotterdam, The Netherlands

^eDepartment of Paediatrics, Hospital General de Valencia, Valencia, Spain

^fCharité Universitätsmedizin Berlin, Berlin, Germany

^gDepartment of Clinical Pharmacy, University of Groningen, Groningen, The Netherlands

^hDepartment of Clinical Pharmacy, University of Groningen, Groningen, The Netherlands

One of the main challenges for the development and use of medicinal products for children is the new provisions established by the Paediatric Directive (2003/54/EC) and the needs in some therapeutic areas.

The European Medicines Agency (EMA) has developed for children by EMEA-PDCO, a new regulatory framework for medicinal products. Moreover, the study

considers the impact of the new provisions established by the Paediatric Directive (2003/54/EC) and the needs in some therapeutic areas.

Keywords:

1. Introduction

The Paediatric Directive (2003/54/EC) has imposed several obligations on the pharmaceutical industry devoted for children.

One of the main purposes of the Directive is to create an inventory of the medicinal products marketed by the Paediatric Committee.

*Corresponding author: Prof. A. Ceci
Via Palestro 26, 27100 Pavia, Italy.
cec@unipv.it

Health-care Development

Challenges in prescribing drugs for children with cancer

Paolo Peduzzi, Kathy Pritchard Jones, Maria del Carmen Cano Garduño, Marina Caviglioli

Paediatric oncology has achieved high cure rates despite the limited and studied for use in children with cancer. Efficacy of these drugs has no permanent side-effects in growing children need to be considered. A stable studies, schedules defined by age, and appropriate formulations can lead groups, resulting in a potential lack of benefit, development of resistance. These major clinical concerns have prompted initiatives in Europe and Regulation aimed at improving the risk-benefit ratio of such drugs in children. However, to undertake the appropriate support is essential. Europe is now showing its commitment to prescribing for children with cancer by introducing measures that will. All those involved, including researchers, paediatric oncologists, health agencies, and pharmaceutical companies, need to become more familiar with new regulation, which is aimed at providing an increased cooperation between the benefit of children.

Introduction

Success in the treatment of children with cancer is a complex task. It requires a multidisciplinary approach involving paediatric oncologists, paediatric nurses, paediatric pharmacologists, and paediatric radiologists. The aim of this paper is to review the challenges in prescribing drugs for children with cancer.

BMJ

Downloaded from bmj.com on 27 January 2009

THE LANCET Oncology

RESEARCH

Drug use in children: cohort study in three European countries

Miriam C J M Sturkenboom, professor in analysis of observational data,^{1,2} Katrien M C Verhamme, assistant professor in pharmacoepidemiology,³ Alfredo Nicolosi, director, senior associate research scientist,^{4,5} Macey L Murray, teaching and research fellow,⁶ Angel Neubert, postdoctoral research fellow,⁷ Daan Caudri, researcher,⁸ Gino Piccoli, analyst,⁹ Elif Fatma Sen, PhD student,¹⁰ Carlo Giugliano, head of clinical research unit,¹¹ Luigi Cantarutti, director,¹² Paola Balardi, director,¹³ Maria-Grazia Felici, researcher,¹⁴ Adriana Ceci, scientific coordinator,¹⁵ Ian C K Wong, professor of paediatric medicines research,¹⁶ on behalf of the TEDDY European Network of Excellence

ABSTRACT

Objective To provide an overview of drug use in children in three European countries.

Design Retrospective cohort study, 2000-5.

Setting Primary care research databases in the Netherlands (PCP), United Kingdom (IMS-DL), and Italy (pediaweb).

Participants 675 868 children aged up to 14 (Italy) or 18 (UK and Netherlands).

Main outcome measure Prevalence of use per year calculated by drug class (anatomical and therapeutic).

Prevalence of 'recurrent' (chronic) use (three or more prescriptions a year) and 'non-recurrent' or 'acute' use (less than three prescriptions a year) within each therapeutic class. Descriptions of the top five most commonly used drugs evaluated for off-label status within each anatomical class.

Results Three levels of drug use could be distinguished in the study population: high (10/100 children per year), moderate (1-10/100 children per year), and low (1/100 children per year). For all age categories, antiepileptic, dermatological, and respiratory drugs were in the high use group, whereas cardiovascular and antineoplastic drugs were always in the low use group. Essential, topical steroids, and asthma drugs had the highest prevalence of recurrent use, but relative use of low prevalence drugs was more often recurrent than acute. In the top five highest prevalence drugs topical inhaled and systemic steroids, oral contraceptives, and topical or systemic antifungal drugs were most commonly used off-label.

Conclusion This overview of outpatient paediatric prescription patterns in a large European population could provide information to prioritise paediatric therapeutic research needs.

Introduction

Recent years have seen growing concerns about the incompleteness of the evidence relating to the efficacy and safety of drugs used in children. Almost all of the

drugs prescribed to children are the same as those originally developed for adults. They are often prescribed on an unlicensed or 'off-label' basis (percentages ranging from 11-80%) simply by extrapolating data for adults, without conducting any paediatric clinical, kinetic, dose finding, or formulation studies in children. Diseases in children, however, might be different from their adult equivalents, and the processes underlying growth and development might lead to a different effect or an adverse drug reaction unseen in adults (Reye's syndrome is an outstanding example).

To provide legitimate and appropriate treatment for children's diseases, new legislation was approved in the United States in 2003 and the European Union in 2007. Both the Food and Drug Administration (FDA) and the European Medicines Agency for the Evaluation of Medicinal Products (EMA) now offer extensions of drug licenses to companies who provide evidence concerning the efficacy and safety in children of new drugs or off-label drugs.^{1,2} The World Health Organization underlines the need for these actions and in December 2007 launched a global campaign to 'make medicines child size' to address the need for improved availability and access to safe child specific medicines for all children.³

We investigated the current use of paediatric drugs in children in three European countries, using population based data on primary care prescriptions.

METHODS

Setting

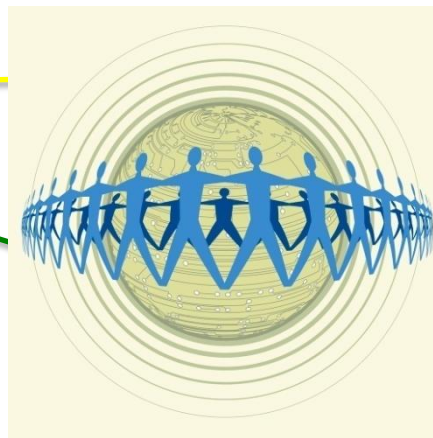
The primary care of children is entrusted to general practitioners in the UK and the Netherlands and to paediatricians in Italy.^{4,5} Access to health care is free in Italy and the UK and fully covered by healthcare insurance in the Netherlands. In these countries, primary care physicians are responsible for children's health care, which means that all clinical information



124 Deliverables



NETWORK



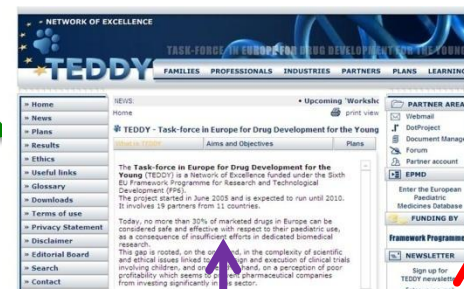
Scientific Publication
 certifying the
 multidisciplinary
 /multinational
 efforts in the
 paediatric
 research domain

FP6-EU -
LSHB-CT-2005-
005216



NEW PROJECTS
 generated in the
 European Paediatric
 Research context

Based on the multidisciplinary of the Network
Dermatology, Gastroenterology, Haematology, Infectious
disease, Intensive care, Neonatology, Nephrology, Neurology,
Oncology, Pain, Rare diseases, Respiratory



E-learning
Platform

Website

Database

Products
 demonstrating the
 practical interest
 around the
 paediatric issue



NeoMero

European multicenter network to evaluate pharmacokinetics,
safety and efficacy of Meropenem in neonatal sepsis and meningitis.

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To evaluate PK, safety and efficacy of meropenem in comparison to standard care in late-onset sepsis and describe PK and safety in bacterial meningitis in neonates and infants aged less than 3 months.

Welcome in NeoMero

NeoMero project aims at adapting an off-patent medicine to the specific need of paediatric populations: in specific to evaluate PK, safety and efficacy of meropenem in comparison to standard care in late-onset sepsis and describe PK and safety in bacterial meningitis in neonates and infants aged less than 3 months in order to be able to register it for use in this age group with a PUMA.

This project has been funded with support by the European Commission under the FP7 programme

Latest News

3 September 2012

Randomisation 1st Patient

We are very happy to announce you that the first patient has been randomized this morning in...

[Read more](#)

13 March 2012

**NeroMero Tials registration on
Clinicaltrials.gov**

**NeoMero Trials were registered on
Clinicaltrials.gov**

Progetto in Ematologia



**DEFERIPRONE
EVALUATION IN
PAEDIATRICS**



Home

Background

DEEP Project

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Project Structure

News and Events

Reserved Area

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place at the Grand Nile Tower Hotel in Cairo, Egypt.

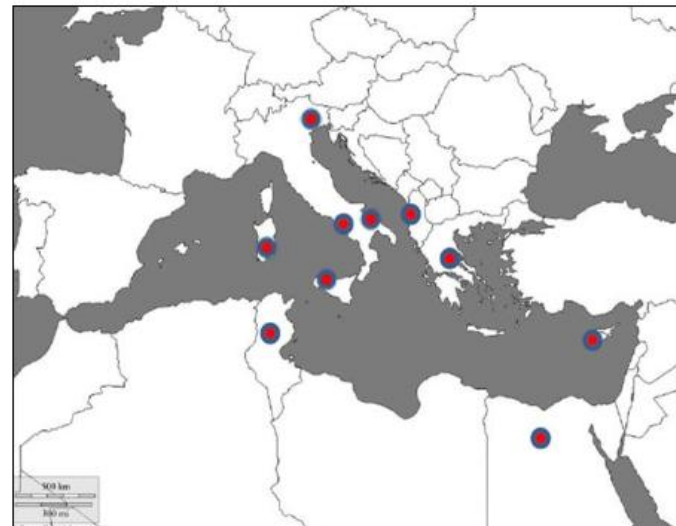
DEEP Partners will discuss the state-of-the-art of the project after the submission to the European Commission of the first official report and the relevant issues linked to the start of the clinical trials.

Nicosia (Cyprus), May 16th - 18th, 2012

**Cleopatra Hotel - Workshop on
GCP & Investigator Meeting
DEEP1/DEEP3**

DEEP Project: what it is?

- DEEP is a 4 years multinational Project
- The DEEP Consortium is composed of 12 recruiting European Centres (from Italy, Greece, Cyprus) and 3 recruiting non-European Centres (from Egypt, Albania, China) with scientific partners from EU
- A pharmaceutical group (ApoPharma and APOTEX) based in Canada and in Europe, is part of the DEEP Consortium



Informative Package for children

Age < 6 years

Quale medicina funziona meglio? Scopriamolo insieme!

Quest'anno Gianni e Sara
vogliono scoprire qual è la medicina migliore per loro.



Una volta alla settimana vanno in ospedale.
L'infermiera Vera preleva una provetta di sangue.

Una volta al mese fanno una visita con il dottor Cacciaferro.



A casa, Gianni prende uno sciroppo tre volte al giorno.
Sara invece prende una compressa
che si scioglie nell'acqua e fa le bollicine.



Alla fine dell'anno, il dottore controllerà se le due medicine
funzionano bene e se può darle anche agli altri bambini.

Vuoi fare anche tu come Gianni e Sara?

Informative Package for children

Age from 6 to 12 years



Progetto GRiP

[Http://www.grip-network.org/](http://www.grip-network.org/)



The screenshot shows the homepage of the GRiP (Global Research in Paediatrics) network. The header features the GRiP logo on the left, the title "Global Research in Paediatrics Network of excellence" in the center, and a small cartoon character on the right. Below the header is a search bar with the text "Search...." and an "OK >>" button. The main content area is divided into three columns. The left column contains a "Main Menu" with links to "Homepage", "The GRiP project", "The GRiP Blog", "News", and "Events". Below this is a "Partners Menu" with a link to "Management area". The middle column is titled "Homepage" and contains a paragraph about the GRiP project, which is an EU-funded project started on 1 January 2011 and expected to last until 31 December 2015. It aims to improve the health of children globally by stimulating and facilitating the development and safe use of paediatric medicines. The right column is titled "GRiP Newsletter" and contains a form for signing up, with fields for "Name", "Surname", and "E-mail". It also has a "Receive" section with radio buttons for "Text" and "HTML", a "Terms and Conditions" checkbox, and a "Subscribe" button with a checkmark icon.

GRiP

Global Research in Paediatrics
Network of excellence

Search.... OK >>

Main Menu

- Homepage
- The GRiP project
- The GRiP Blog
- News
- Events

Partners Menu

- Management area

Homepage

The "Global Research in Paediatrics – Network of Excellence (GRiP)" is an EU-funded project [Seventh Framework Programme: FP7/2007-2013, Grant Agreement n° 261060], started on 1 January 2011 and expected to last until 31 December 2015.

GRiP aims to improve the health of children globally, by stimulating and facilitating the development and safe use of paediatric medicines.

To achieve this, GRiP will implement a comprehensive educational programme in paediatric pharmacology and will build an infrastructure which allows the integrated use of existing research

GRiP Newsletter

Name

Surname

E-mail

Receive ☐ Text ☒ HTML

☐ Terms and Conditions

Subscribe

GRiP Partnership

Id.	Participant organisation name	Acronym	Country	Lead Scientist
1	Azienda Ospedaliera di Padova	AOPD	Italy	Carlo Giaquinto
2	National Institutes of Health	NICHD-NIH	USA	Steven Hirschfeld
3	European Medicines Agency	EMA	UK	Agnes Saint-Raymond
4	Erasmus Universitair Medisch Centrum Rotterdam	EMC	The Netherlands	M Sturkenboom
5	University of Liverpool, MCRN	ULIV-MCRN	UK	Mark Turner
6	Ospedale Pediatrico Bambino Gesù	OPBG	Italy	Paolo Rossi
7	Institut national de la santé et de la recherche médicale	INSERM	France	Evelyne Jacqz Aigrain
8	National Center for Child Health and Development	NCCHD	Japan	Hidefumi Nakamura
9	St George's Hospital	SGUL	UK	Mike Sharland
10	Consorzio per le Valutazioni Biologiche e Farmacologiche, TEDDY	CVBF-TEDDY	Italy	Adriana Ceci
11	Rijksuniversiteit Leiden	UL	The Netherlands	Oscar Della Pasqua
12	Academic Medical Center	AMC	The Netherlands	Martin Offringa
13	Fundación Vasca de Innovación e Investigación Sanitarias	BIOEF	Spain	Adolfo Valls-i-Soler
14	Instytut Pomnik Centrum Zdrowia Dziecka	PCZD	Poland	Marek Migdal
16	World Health Organization	WHO	Switzerland	Sue Hill
17	School of Pharmacy	SoP	UK	Ian Wong
18	Helsingin Ja Uudenmaan Sairaanhoidopiirin Kuntayhtymä	HUS	Finland	Kalle Hoppu
19	Brighton Foundation	BF	Switzerland	Jan Bonhoeffer
20	PENTA Foundation	PENTA	Italy	Silvia Faggion
21	Vereniging Samenwerkende Ouder - En Patientenorganisaties (NL)-EGAN	VSOP-EGAN	The Netherlands	Cor Oosterwijk
22	The Hospital for Sick Children	SICKKIDS	Canada	Shinja Ito

Struttura in WPs



Global Research in Paediatrics

Global Research in Paediatrics (GRiP) is a Network of Excellence which aims to improve the health of children globally, by stimulating and facilitating the development and safe use of paediatric medicines



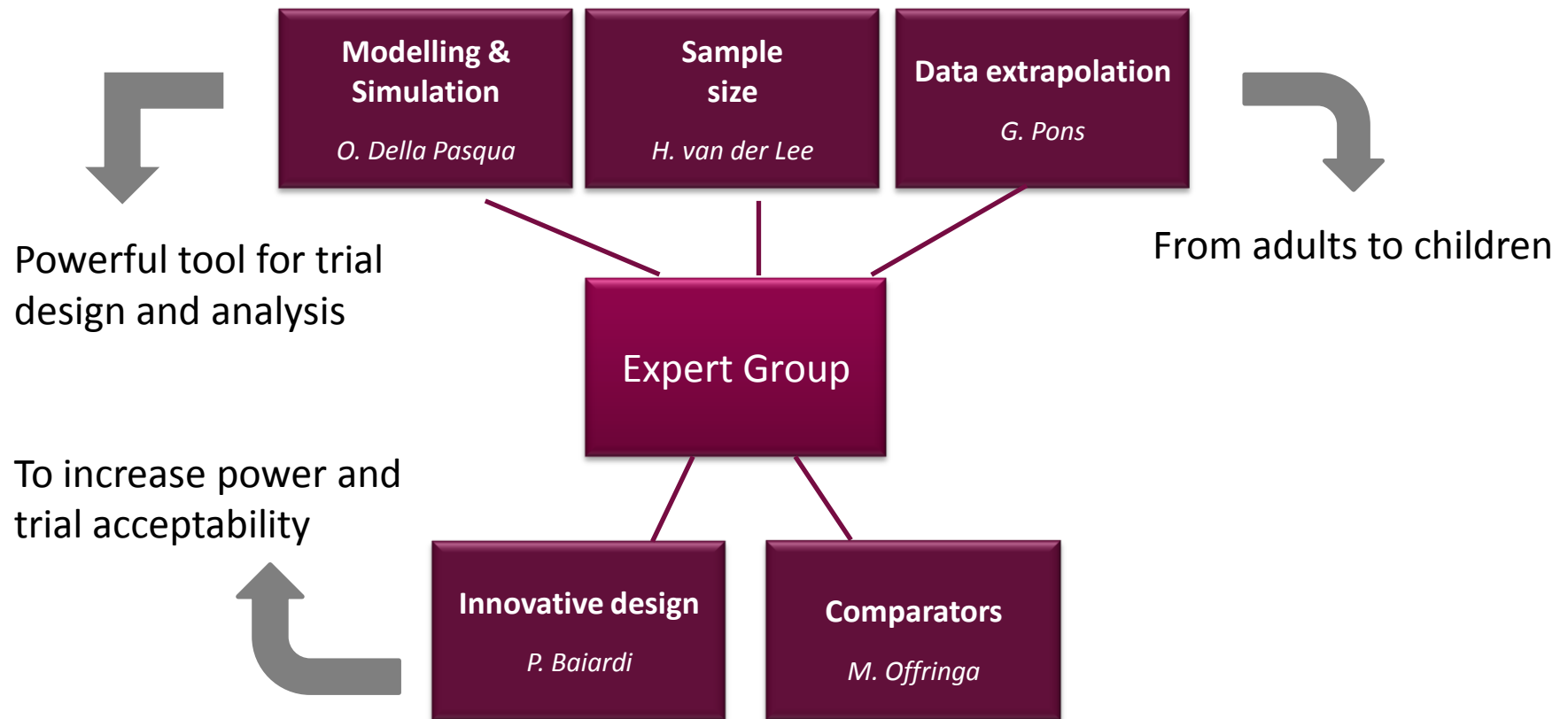
WP 4

NEW METHODS FOR CLINICAL STUDIES IN PAEDIATRICS

A structured approach to clinical drug development has been established for adults, but this is not automatically applicable to children. Drug development programs in children need to be considered on a case-by-case basis depending on the drug, the condition and the target population, and a specific approach

paediatric clinical research methods used in studies that have already been performed. WP4 will begin from the identification of innovative approaches that are likely to be accepted by the Regulatory Authorities and the scientific community. It will then focus on achieving a scientific consensus on:

WP4 - New methods for clinical study in paediatrics



From “test of hypothesis” to “evidence synthesis”
To create «new» protocols

Conclusioni

- Networking in the Paediatric Research sector is well accepted and represent an useful tool
- Collaboration with Existing Networks, Regulatory Bodies, Professional Associations, Pharmaceutical Industry, Patients/parents Associations is possible
- Multidisciplinarity and Multisectoriality of participants lead to building up critical mass of capacities and knowledge