The TEDDY Working Group on Health data

Why this Working Group?

THE IMPORTANCE OF HEALTH DATA
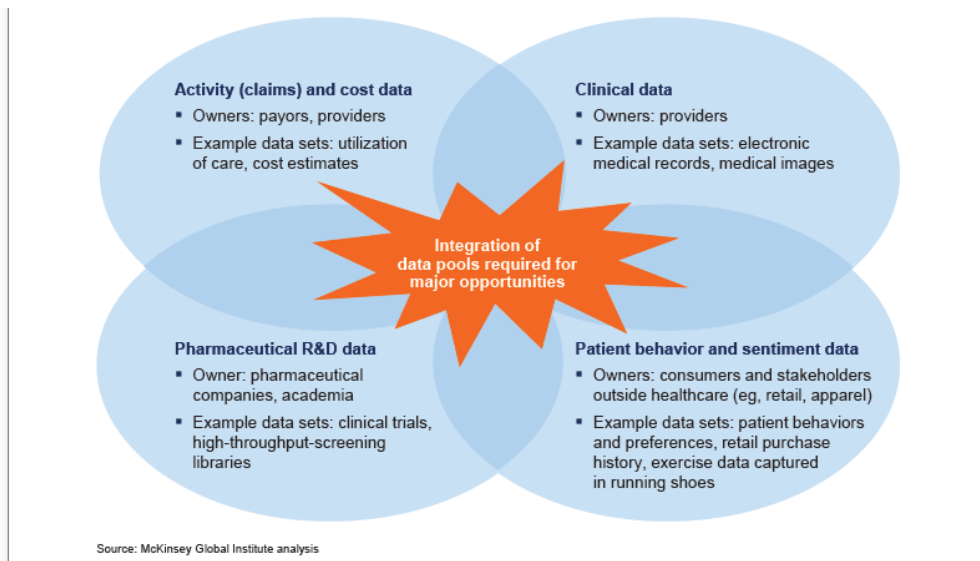
Health data – and electronic health records (EHRs) - are widely viewed as a potential treasure trove for medical research

Why this Working Group?

Paediatric patients represent a 'small population'

- ✓ Recruitment challenges
- ✓ Geographical dispersion
- ✓ No active control available
- ✓ Adequate statistical power needed
- ✓ Surrogate and validated endpoints needed
- ✓ Sample size to be minimised

Trials are more difficult, take longer and cost more
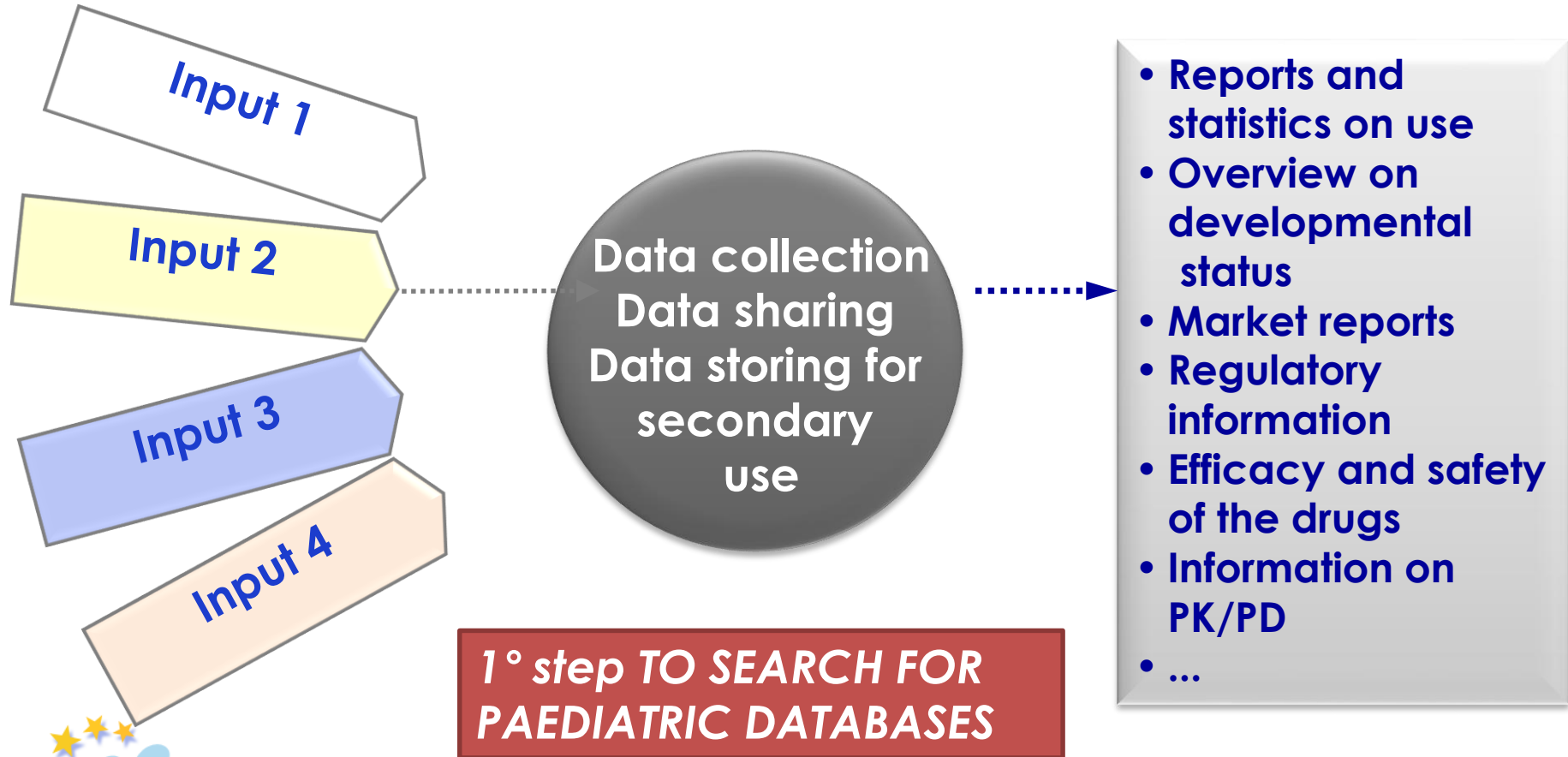
PAEDIATRICS

Large population for CTs and other studies are needed

Studies involving "small populations" are typically multi-centre and multi-national

TEDDY
NETWORK
European Network of Excellence
for Paediatric Clinical Research

Why this Working Group?

AND WHEN A LARGE POPULATION IS NOT AVAILABLE ?

Input 1

Input 2

Input 3

Input 4

Data collection Data sharing Data storing for secondary use

1° step TO SEARCH FOR PAEDIATRIC DATABASES

- Reports and statistics on use
- Overview on developmental status
- Market reports
- Regulatory information
- Efficacy and safety of the drugs
- Information on PK/PD
- ...

TEDDY
NETWORK
European Network of Excellence
for Paediatric Clinical Research

TEDDY EXPERIENCE

Assessment of 16 databases from 10 EU Countries including 8 million children

Category	Item	Cohort Case-Control Studies	Drug utilisation studies	IMS DA UK	Pedianet	IPCI	GPRD	THIN Data	GRESEA RCH	SPICE	IMS DA FRANCE	IMS DA AUSTRIA	IMS DA GERMANY	PHARMO	IADB	The Danish Prescription Database (NPD)	Finland prescription register	PEM	Swedish Medical Birth Register
	Unique Identifier	yes	no																
	Age	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
	Gender	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
	Death	yes	no	yes	yes	yes	yes	yes	yes	yes	no	no	no	yes	yes	no	no	yes	limited
Prescriptions (Drug exposure)	Prescriptions	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
Prescriptions (Drug exposure)	Unique product code	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
Prescriptions (Drug exposure)	ATC Code	yes	yes	yes	yes	yes	no	no	yes	yes	yes	yes	yes	yes	yes	?	yes	yes	yes
Prescriptions (Drug exposure)	Date of prescription	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	yes	no
Prescriptions (Drug exposure)	Dosage of prescription	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	yes	yes	yes
Prescriptions (Drug exposure)	Duration of prescription	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	yes	yes
Outcomes	Laboratory values	yes	no	yes	yes	yes	yes	yes	yes	no	yes	yes	yes	yes	no	no	no	yes	no
Outcomes	Diagnostic data (e.g. x-ray, MRT, etc.)	yes	no	yes	yes	yes	yes	yes	limited	no	no	yes	yes	yes	no	no	no	yes	no
Outcomes	Treatment outcome	yes	no	yes	yes	yes	yes	yes	yes	no	no	no	no	yes	no	no	no	yes	no
Outcomes	Hospital admission	yes	no	yes	yes	yes	yes	yes	limited	no	no	yes	yes	yes	no	no	no	yes	no
Outcomes	Hospital discharge diagnosis	yes	no	no	yes	yes	yes	yes	limited	no	no	no	no	yes	no	no	no	yes	no
Outcomes	Referral to specialist	yes	no	yes	yes	yes	yes	yes	limited	no	no	yes	yes	yes	no	no	no	yes	no
Outcomes	Results of referral visits	yes	no	yes	yes	yes	yes	no	limited	no	no	no	no	yes	no	no	no	yes	no
Confounders	Diagnosis	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	no	no	no	yes	yes
Confounders	Medical history (anamnesis)	yes	no	yes	yes	yes	yes	yes	yes	yes	no	no	no	yes	no	no	no	no	no
Confounders	Vaccination	yes	no	yes	yes	yes	yes	yes	yes	yes	no	no	no	yes	no	yes	no		no
Confounders	Allergies	yes	no	yes	no	yes	yes	yes	yes	yes	no	no	no	yes	no	no	no	limited	no
Confounders	Indication for prescription	yes	no	yes	no	yes	yes	limited	limited	no	yes	yes	yes	no	no	no	limited	yes	no
Confounders	Height	yes	no	yes	yes	yes	yes	yes	yes	no	no	no	no	yes	no	no	no	no	yes
Confounders	Weight	yes	no	yes	yes	yes	yes	yes	yes	no	no	no	no	yes	no	no	no	no	yes
Confounders	Environmental and life-style characteristics	yes	no	yes	yes	yes	yes	no	no	no	no	yes	yes	yes	no	no	no	no	no
Data access	Access to raw data	yes	no	yes	no	yes	yes	yes	yes	no	yes	yes	yes	yes	no	no	yes	no	yes
Data access	Access to original medical charts	yes	no	no	yes	yes	yes	no	no	no	no	no	no	yes	no	yes	no	no	no

TEDDY
NETWORK
European Network of Excellence
for Paediatric Clinical Research

TEDDY EXPERIENCE

- Verhamme K, Sturkenboom M. Study designs in paediatric pharmacoepidemiology. Eur J Clin Pharmacol. 2011 May;67 Suppl 1:67-74.
- Neubert A, Verhamme K, Murray ML, Picelli G, Hsia Y, Sen FE, Giaquinto C, Ceci A, Sturkenboom M, Wong IC; On behalf of the TEDDY Network of Excellence.
- The prescribing of analgesics and non-steroidal anti-inflammatory drugs in paediatric primary care in the UK, Italy and the Netherlands. Pharmacol Res. 2010 Sep;62(3):243-8.
- Hsia Y, Neubert A, Sturkenboom MC, Murray ML, Verhamme KM, Sen F, Giaquinto C, Ceci A, Wong IC; on behalf of the TEDDY Network of Excellence. Comparison of antiepileptic drug prescribing in children in three European countries. Epilepsia. 2010 May;51(5):789-96.
- McCarthy S, Cranswick N, Potts L, Taylor E, Wong IC. Mortality associated with attention-deficit hyperactivity disorder (ADHD) drug treatment: a retrospective cohort study of children, adolescents and young adults using the general practice research database. Drug Saf. 2009;32(11):1089-96.
- Neubert A, Sturkenboom MC, Murray ML, Verhamme KM, Nicolosi A, Giaquinto C, Ceci A, Wong IC; TEDDY Network of Excellence. Databases for pediatric medicine research in Europe--assessment and critical appraisal. Pharmacoepidemiol Drug Saf. 2008 Dec;17(12):1155-67.
- Sturkenboom MC, Verhamme KM, Nicolosi A, Murray ML, Neubert A, Caudri D, Picelli G, Sen EF, Giaquinto C, Cantarutti L, Baiardi P, Felisi MG, Ceci A, Wong IC; TEDDY European Network of Excellence. Drug use in children: cohort study in three European countries. BMJ. 2008 Nov 24;337:a2245. doi: 10.1136/bmj.a2245.
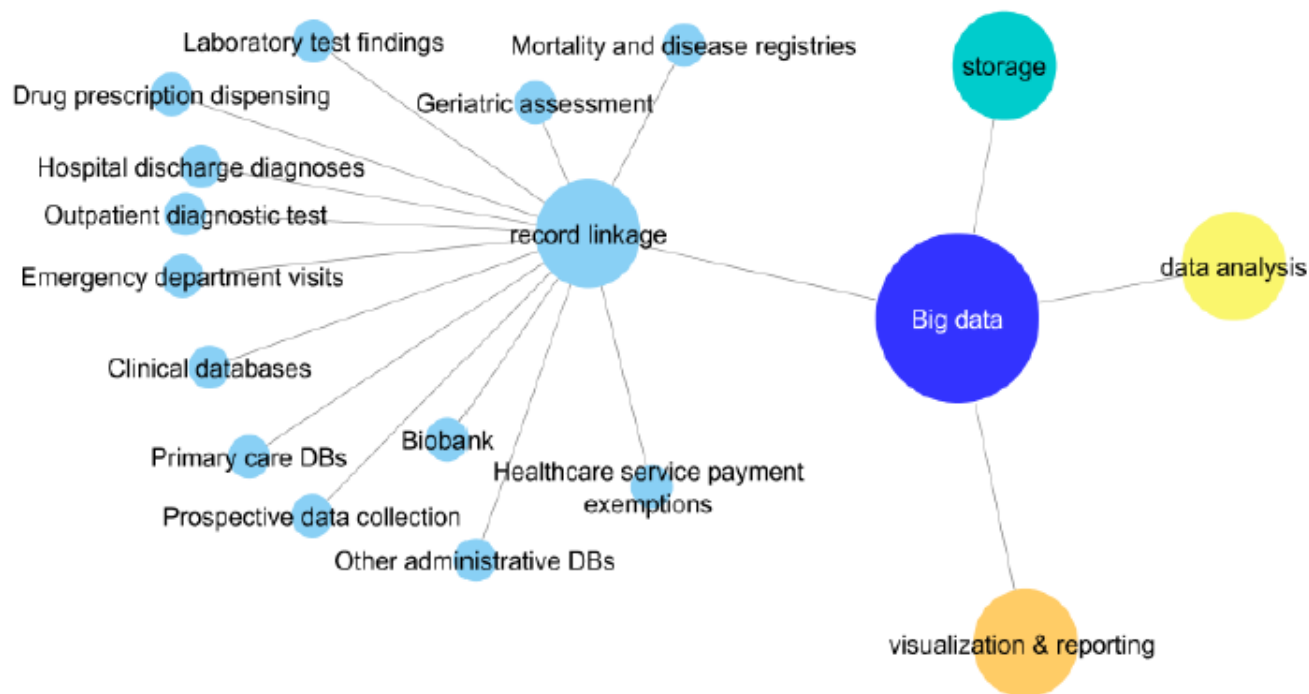
Participation in EPTRI WP4

Participation in c4c WP5

Participation in GRiP WP2

TEDDY NETWORK

European Network of Excellence for Paediatric Clinical Research

TEDDY participation to the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance – WG3 on Inventory of EU data sources and methodological approaches for multi-source studies

ENCePP® is a network coordinated by the European Medicines Agency

The landscape of healthcare databases

Laboratory test findings
Mortality and disease registries
Drug prescription dispensing
Geriatric assessment
storage
Hospital discharge diagnoses
Outpatient diagnostic test
record linkage
data analysis
Emergency department visits
Big data
Clinical databases
Primary care DBs
Biobank
Healthcare service payment exemptions
Prospective data collection
Other administrative DBs
visualization & reporting

Trifirò G, Sultana S, Bate A. From big data to smart data for pharmacovigilance: the role of healthcare databases and other emerging sources. Drug Saf. 2017 Aug 24. [Epub ahead of print]

WHAT COULD WE DO?

Considering:

- *TEDDY experience with health data and database*
- *TEDDY participation as research resource in ENCePP WG3*

..THE FIRST ACTIVITY OF TEDDY WORKING GROUP ON HEALTH DATA COULD BE...

ENCePP WG3

Contribution to the concept paper:
*"Models for multi-database pharmacoepidemiologic studies"*

Different models identified for multi-database studies:

A) *Local data extraction and analysis, common protocol*

B) *Local data extraction and central analysis on patient-level raw data*

C) *Study-specific local data extraction in a common data model and central analysis*

D) *General local data extraction in a common data model and central analysis*

ENCePP WG3
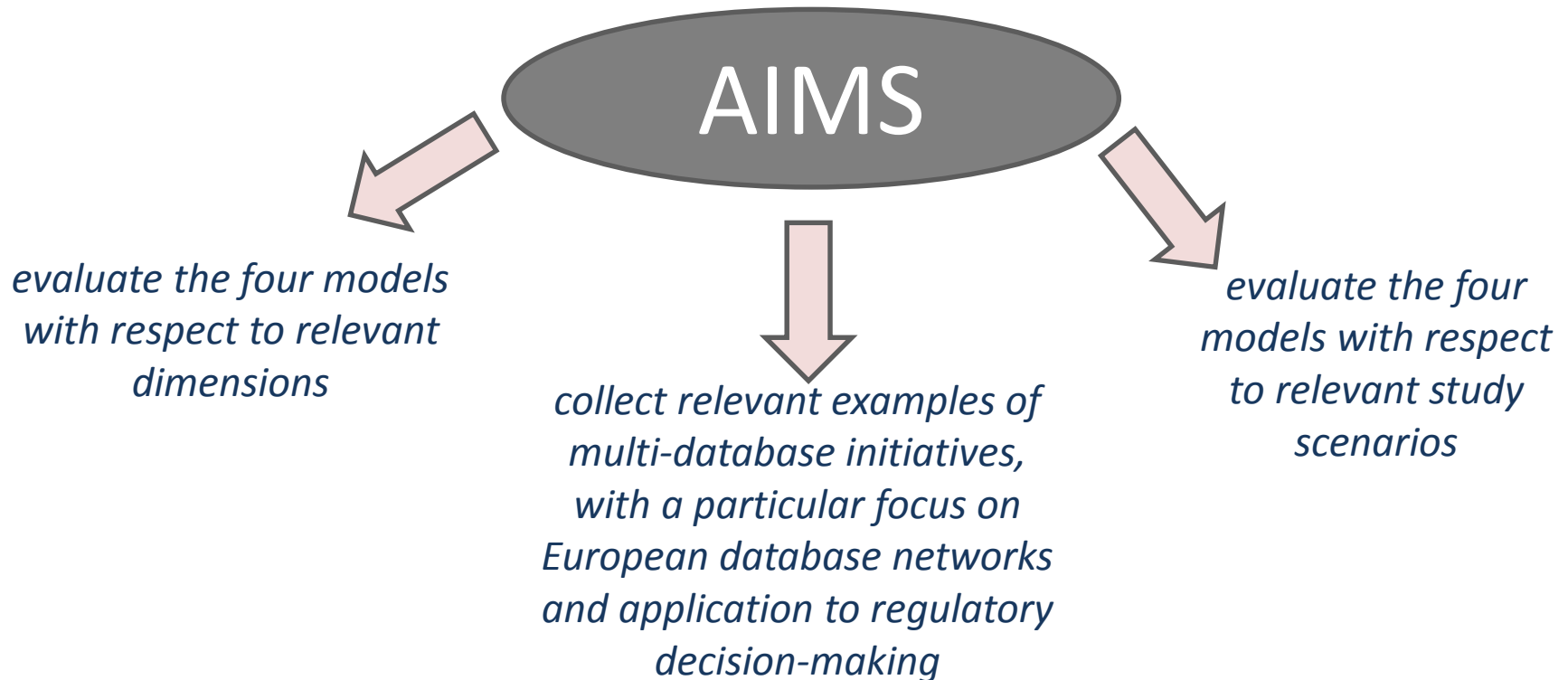
*The activity has been structured in different phases:*

> a) collection of relevant examples of multidatabase initiatives (**Nov-Dec 2017**, lead: Miriam Sturkenboom)
>   i.   use previous WG3 work
>   ii.   use recent systematic review

⬇
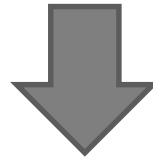
> b) evaluate the four models with respect to relevant dimensions (**Nov 2017 – February 2018**, lead: Rosa Gini)
>   i.   conduct systematic review of methodological literature on multi-database studies, to assess completeness of 4 models and identify relevant dimensions
>   ii.   conduct a consensus process based on the literature review to score the 4 models

ENCePP WG3

c) evaluate the four models with respect to relevant study scenarios (**Nov 2017 – February 2018**, lead: Gianluca Trifirò)

  i.   collect expert opinion via online questionnaire
  ii. explore EU PAS registry
  iii. survey of regulators
  iv. evaluate models across scenarios and dimensions
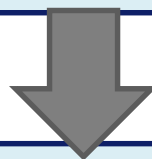
d) First draft of the concept paper and abstract ICPE (**mid-February 2018**, lead: TBD)
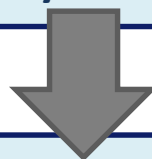
e) Final draft of the concept paper and manuscript for publication (**April 2018**, lead: TBD)

TEDDY *WG- Health data* proposal of work

1. Collaboration with ENCePP WG3

2. Collection of relevant examples of **paediatric** multidatabase initiatives

   (following the example of ENCePP)

   3. What else ?

Paediatric specificities

TEDDY
NETWORK
European Network of Excellence
for Paediatric Clinical Research

TEDDY Working Group members

- *Fedele Bonifazi (Italy)*

- *Madlen Gazarian (AUSTRALIA)*

- *Annalisa Landi (Italy)*

- *Kejla Musaraj (Italy)*

- *Valeria Pignataro (Italy)*

NEW MEMBERS ARE WELCOME!

TEDDY
NETWORK
European Network of Excellence
for Paediatric Clinical Research

Comments and proposals for discussion