# The present, the past and the future of TEDDY

Adriana Ceci

# The present, the past and the future of TEDDY

TEDDY
Task-force in Europe for Drug Development for the Young

**2005**

XTH FRAMEWOR
ROGRAMME

1°in Europe Network of Excellence to promote Paediatric Research and Paediatric Medicinals development

**2011**

Network of Excellence for Paediatric Clinical Research

Member of Enpr-EMA

Partners Agreement

**2018**

Legal Status

A Network with a legal status to be fully represented in the European paediatric research framework

TEDDY NETWORK
European Network of Excellence for Paediatric Clinical Research

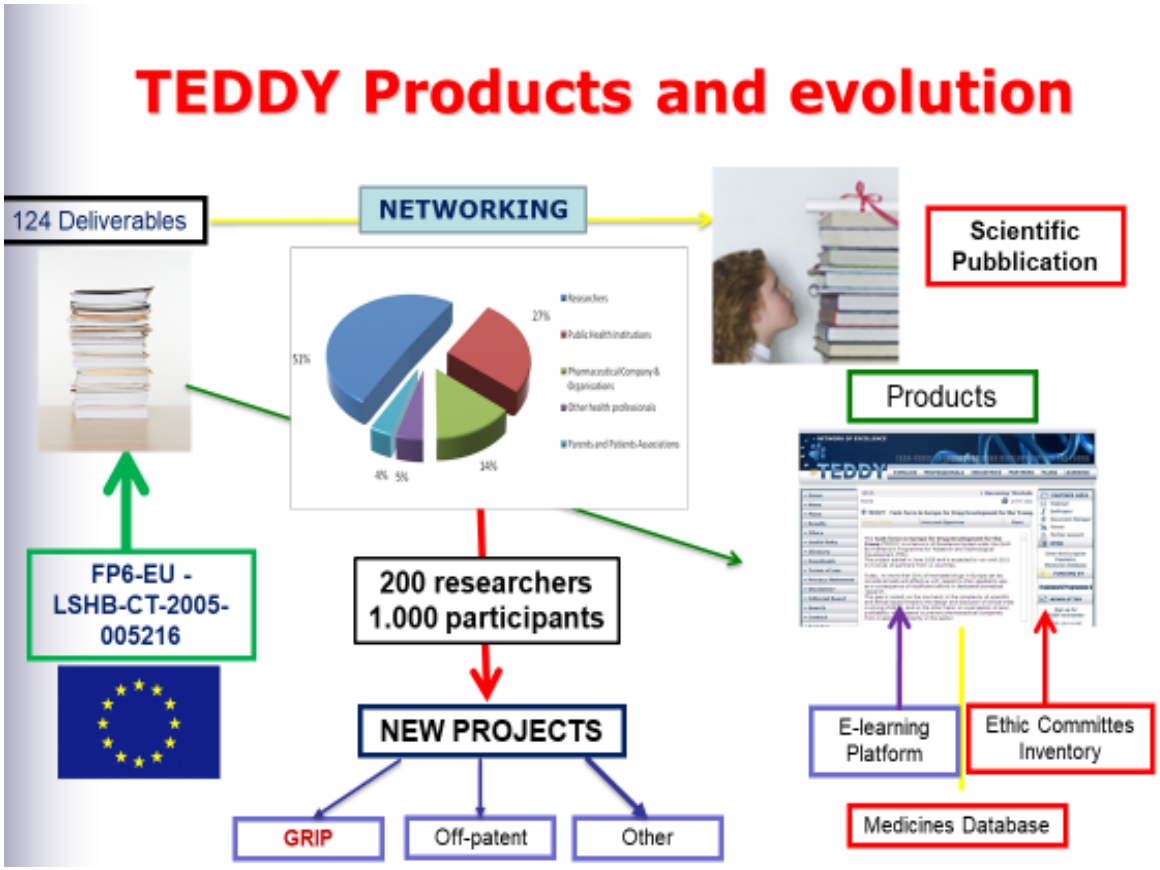
TEDDY
Task-force in Europe for Drug Development for the Young

# 1°in Europe Network of Excellence to promote Paediatric Research and Paediatric Medicinals development

## Main Topics

- *Life Science and Clinical research*
- *Ethics and methodology*
- *Drug uses in children*
- *Education in Paediatric Medicines*
- *Knowledge dissemination*

## Gained experience and Main Results

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European Network of Excellence for Paediatric Clinical Research

19 Partners (EU+ Israel); Coordinator CVBF; Scientific Coordinators Adriana Ceci & Carlo Giaquinto; Project Manager Fedele Bonifazi; EU Scientific Officer Fergall Donnelly

# Experience and tools from TEDDY NoE

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

| | | |
|---|---|---|
| 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 |

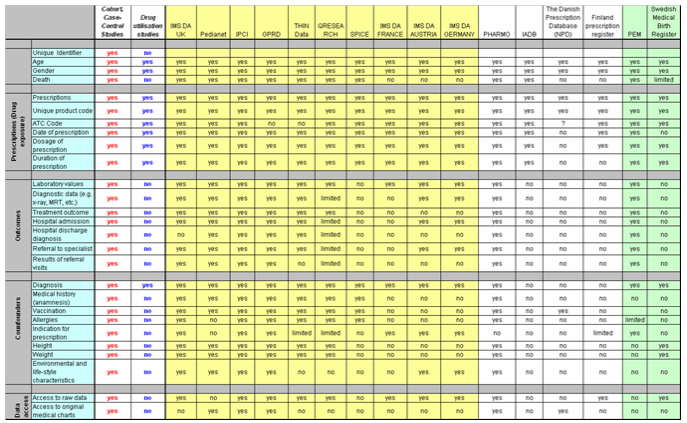
## Inventory of available Paediatric medicines and off-label use in Italy, UK and The Netherland

**One hundred-forty three** active substances corresponding to **269,590 prescriptions**

## European Survey on ethical and legal framework in paediatric research

27 European Countries
900 Ethic Committees identified
**770 Questionnaires** further circulated

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



| | | 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 | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes |
| | 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 |
| | Unique product code | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes |
| | ATC Code | yes | yes | yes | yes | yes | no | no | yes | yes | yes | yes | yes | yes | yes | ? | yes | yes | yes |
| | Date of prescription | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | no | yes | yes | no |
| | Dosage of prescription | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | yes | no | yes | yes | yes |
| | 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 |
| | 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 |
| | Treatment outcome | yes | no | yes | yes | yes | yes | yes | yes | no | no | no | no | yes | no | no | no | yes | no |
| | Hospital admission | yes | no | yes | yes | yes | yes | yes | limited | no | no | yes | yes | yes | no | no | no | yes | no |
| | Hospital discharge diagnosis | yes | no | no | yes | yes | yes | yes | limited | no | no | no | no | yes | no | no | no | yes | no |
| | Referral to specialist | yes | no | yes | yes | yes | yes | yes | limited | no | no | yes | yes | yes | no | no | no | yes | no |
| | 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 |
| | Medical history (anamnesis) | yes | no | yes | yes | yes | yes | yes | yes | no | no | no | no | yes | no | no | no | no | no |
| | Vaccination | yes | no | yes | yes | yes | yes | yes | yes | no | no | no | no | yes | no | yes | no | | no |
| | Allergies | yes | no | yes | no | yes | yes | yes | yes | no | no | no | no | yes | no | no | no | limited | no |
| | Indication for prescription | yes | no | yes | no | yes | yes | limited | limited | no | yes | yes | yes | no | no | no | limited | yes | no |
| | Height | yes | no | yes | yes | yes | yes | yes | yes | no | no | no | no | yes | no | no | no | no | yes |
| | Weight | yes | no | yes | yes | yes | yes | yes | yes | no | no | no | no | yes | no | no | no | no | yes |
| | 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 |
| | Access to original medical charts | yes | no | no | yes | yes | yes | no | no | no | no | no | no | yes | no | yes | no | no | no |

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# Successful Networking activities

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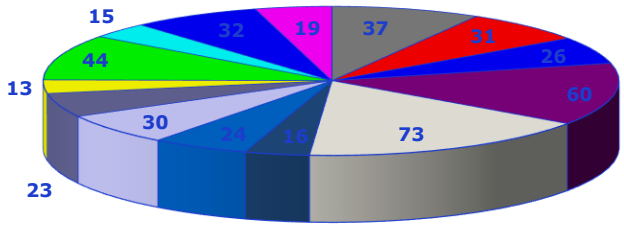


- Anaesthesiology
- Infectious Dis.
- Respiratory Dis.
- Cardiology
- Oncology
- Diabetes
- Epilepsy
- Gastroenterology
- Immunology
- Migraine
- Nephrology
- Pain
- Psychiatry
- Rheumatology

## 14 Therapeutic areas 'Experts Groups'

Data collected on 443 drugs of interest for children

- paediatric status in different countries
- availability on the market
- therapeutic needs
- available/ongoing trials and studies

All data stored in TEDDY Database (EPMD)

channel and reimbursement

| OMP trade name | Number of countries where OMP is available | Ranges of first availability | Number of countries where OMPs are distributed by pharmacies | Number of countries where OMPs are 100% reimbursed |
|---|---|---|---|---|
| Aldurazyme | 5 | 2003–2004 | 2 | 4 |
| Busilvex | 6 | 2002–2005 | 1 | 4 |
| Carbaglu | 4 | 2002–2006 | 0 | 2 |
| Fabrazyme | 7 | 2001–2006 | 2 | 5 |
| Glivec | 7 | 2001–2006 | 2 | 6 |
| Onsenal | 2 | 2002 | 1 | 3 |
| Replagal | 4 | 2001 | 2 | 2 |
| Somavert | 5 | 2002–2004 | 1 | 3 |
| Tracleer | 5 | 2002–2003 | 1 | 3 |
| Trisenox | 3 | 2002 | 1 | 2 |
| Ventavis | 6 | 2003–2004 | 2 | 3 |
| Zavesca | 5 | 2003–2005 | 1 | 3 |
| Litak | 4 | 2004 | 1 | 3 |
| Lysodren | 4 | 2004–2005 | 1 | 4 |
| Orfadin | 3 | 2005 | 1 | 1 |
| Pedea | 3 | 2004 | 1 | 1 |
| Photobarr | 0 | not available | not available | not available |
| Prialt | 0 | not available | not available | not available |
| Xagrid | 2 | 2005 | 1 | 1 |
| Wilzin | 2 | 2004–2005 | 0 | 2 |

Source: our elaboration.

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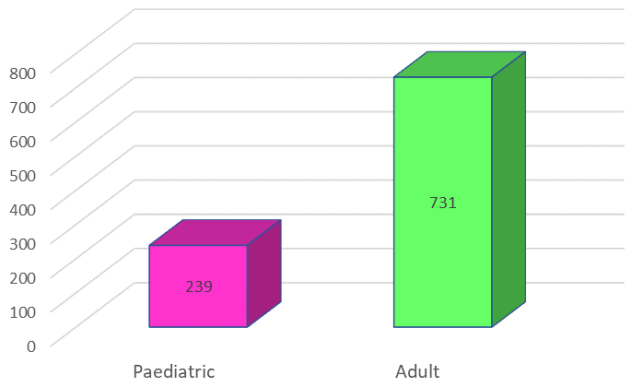
# Experience and tools from TEDDY NoE

*A database containing information on paediatric drugs authorised by the European Medicine Agency (EMA) under the centralised procedure. It is aimed to create a* ***harmonised, integrated and reliable European source of information*** *on paediatric medicines in Europe*

After 10 years from the entry into force of the Paediatric Regulation, the number of paediatric medicines has tripled, but they remain ˜ 1/3 of all the centrally authorised medicines

## Medicines approved up to 2017




*European Paediatric Medicines Database, October 2017*

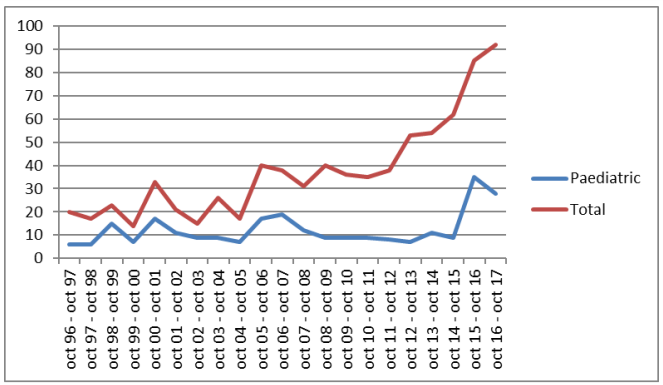
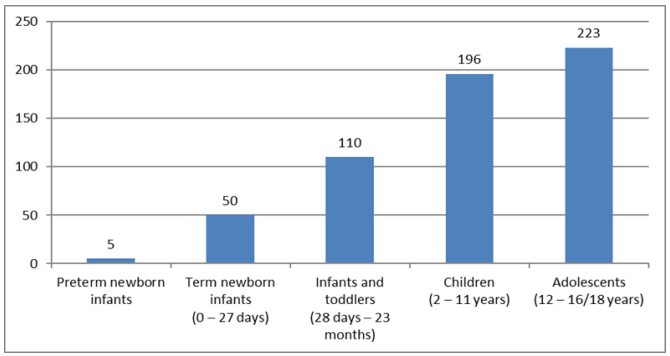



Figure 1 - Medicinal products authorised by EMA divided by year (Oct. 1995 – Oct. 2017)

Not a constant increase for paediatric medicines approval




Still few medicines approved for term and preterm newborns

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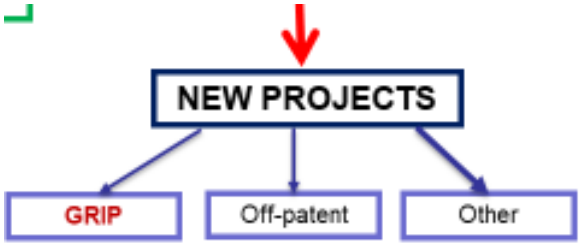
# Network of Excellence for Paediatric Clinical Research

## (on Voluntary Agreement basis)





After expiring, the funded period TEDDY has consolidated its activities in the field through a research Consortium Agreement among 41 partners from 14 countries

From 2014 TEDDY was Member of EnprEMA, Category 4 while from 2016 TEDDY is Member of EnprEMA category 1.

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**Focus on Ethics and Regulatory**

- **SOPs**
- **Inventory of the applicable procedures for trials and studies in EU/non EU countries**

**Focus on paediatric trials governance and management**

- **Sites Inventory**
- **Sites preparedness**
- **Pharmacovigilance**
- **Trials Management**

**Focus on children empowerment and awareness**

- **Trials informative documents tailored for children and adolescent**
- **1° Italian YPAG promotion and setting up**

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## SOPs Availability

***RATIONALE***

The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with *written SOPs to ensure that trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s).*

The TEDDY Network has produced some procedures in the context of the FP7 trials that have been conducted with the involvement of many TEDDY partners.


A plan for SOPs update is now ongoing.

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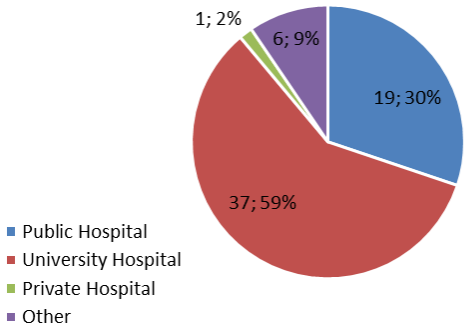
## Sites Inventory

Expertise of centres performing paediatric clinical trials, available services, equipment and the centralised services supporting clinical trials in each site


### *Preliminary experience*

Answers were got from 63 centres belonging to 11 Eu and non-Eu countries (Ireland, United Kingdom, Italy, Albania, Norway, Iceland, Denmark, Austria, Switzerland)

### *Respondents*




### PROs and CONs

- *Completeness of the information to be collected*
- *Possibility to reach all Eu countries through national contacts*
- *Easy-to-use online system*

- *Length of the survey*
- *Difficulty to check mistakes in the completion*
- *Self-report*
- *Need for help-desk service*

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## Informative documents and YPAG

**The GAPP (GAbapentin in Paediatric Pain) project intends to improve the therapeutic perspectives of children who suffer from chronic pain, providing them with the drug " Gabapentin"**

- **3 different BOOKLETS for each study** (GABA-1 e GABA-2) for different age groups
- **2 different ASSENT FORMS** for patients from 7 to 11 and from 12 to 17 years of age

*Available in the 7 languages of the project ( Albanian, French, Greek, English, Italian, Dutch and German)*


**Patient diary for each study (GABA-1 and GABA-2)**


**The objective of the DEEP project is the marketing of a new formulation of deferiprone for the treatment of iron overload in paediatric patients affected by congenital anaemias**

- 3 different BOOKLETS explaining CTs aims and procedures and what they are going to experience
- 2 different ASSENT FORMS

*Available in the 6 project languages (Albanian, Arabic, English, French, Greek, Italian)*

**Two animated videos have been developed:**

- presenting general information on clinical trials for young children
- presenting general information on clinical trials for teenagers


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## Informative documents and YPAG

**YPAG (Young Persons Advisory Group)**

**A Young Persons Advisory Group, or YPAG**, is an organization composed of youths, patients, carers and people interested in a health condition or in research, actively participating as partners, advising researchers and their teams in a full range of activities in various research projects and initiatives.

CVBF in collaboration with the TEDDY Network and the paediatric University Hospital Azienda Ospedaliero-Universitaria Consorziale Policlinico di Bari – Ospedale Pediatrico "Giovanni XXIII" promotes the first italian YPAG in Bari corresponding to a new chapter of iCAN, named "KIDS Bari".

Launch event on 7th June 2017 in Bari

KIDS Objectives:
Peer support for young patients;
advocacy for children, patients and participants in clinical trials;
advise young people on research;
raising public awareness;
fundraising.

Consorzio per Valutazioni Biologiche e Farmacologiche – Dege e shoqerise se huaj, Albanian Branch Office in collaboration with the TEDDY Network and University Hospital Center Tirana "Mother Teresa", Service of Paediatrics), promoted the first YPAGin Albania, named KIDS Albania.

Launch event on 15th September 2017 in Tirana

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## Participation in public consultations/contribution in other initiatives

Survey of Young Persons Groups (YPAG) in Europe (January 2017)

blic consultation on "Summary of Clinical Trial Results for Laypersons" (August 2016)

Survey for Enpr-EMA networks regarding Young Persons Groups (April 2016)


Guideline on Conduct of Pharmacovigilance for Medicines used by the Paediatric Population (2006)

Draft guidance on 'specific modalities' for non-commercial clinical trials (2006)

Reflection Paper on the use of Pharmacogenetics in the pharmacokinetic evaluation of medicinal products (2006)

EMA Assessment of paediatric needs and Priority-List of Off-patent medicinal products for paediatric studies (2007, 2008)

Enpr-EMA request for information to develop a Global Paediatric Clinical Trials Network (October 2014)
Contribution to the topic of transition from paediatrics to adults clinical care settings by (May 2015)

ICH E11 (R1) guideline on clinical investigation of medicinal products in the pediatric population (April 2017)

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## Participation in public consultations/contribution in other initiatives


Ethical Considerations for Clinical Trials Performed in Children (2007)

Public consultation on the revision of "Ethical Considerations for Clinical Trials on Medicinal products conducted with Minors" (August 2016)

ICH E11 (R1) guideline on clinical investigation of medicinal products in the pediatric population (April 2017)

Public consultation to gather stakeholders' experiences of the EU Paediatric Regulation (February 2017)

Public consultation on the concept paper on the Revision of the 'Clinical Trials Directive' 2001/20/EC (February 2011)

Contribution to amendments proposed by GRiP to the draft Regulation on Clinical Trials on medicinal products for human use (May 2013)

Stakeholder consultation for Horizon 2020 Societal Challenge "Health, demographic change and wellbeing" for the programming exercise 2016/2017 (September 2014)

Evaluation of the legislation on medicines for children and rare diseases (medicines for special populations) (January 2018)

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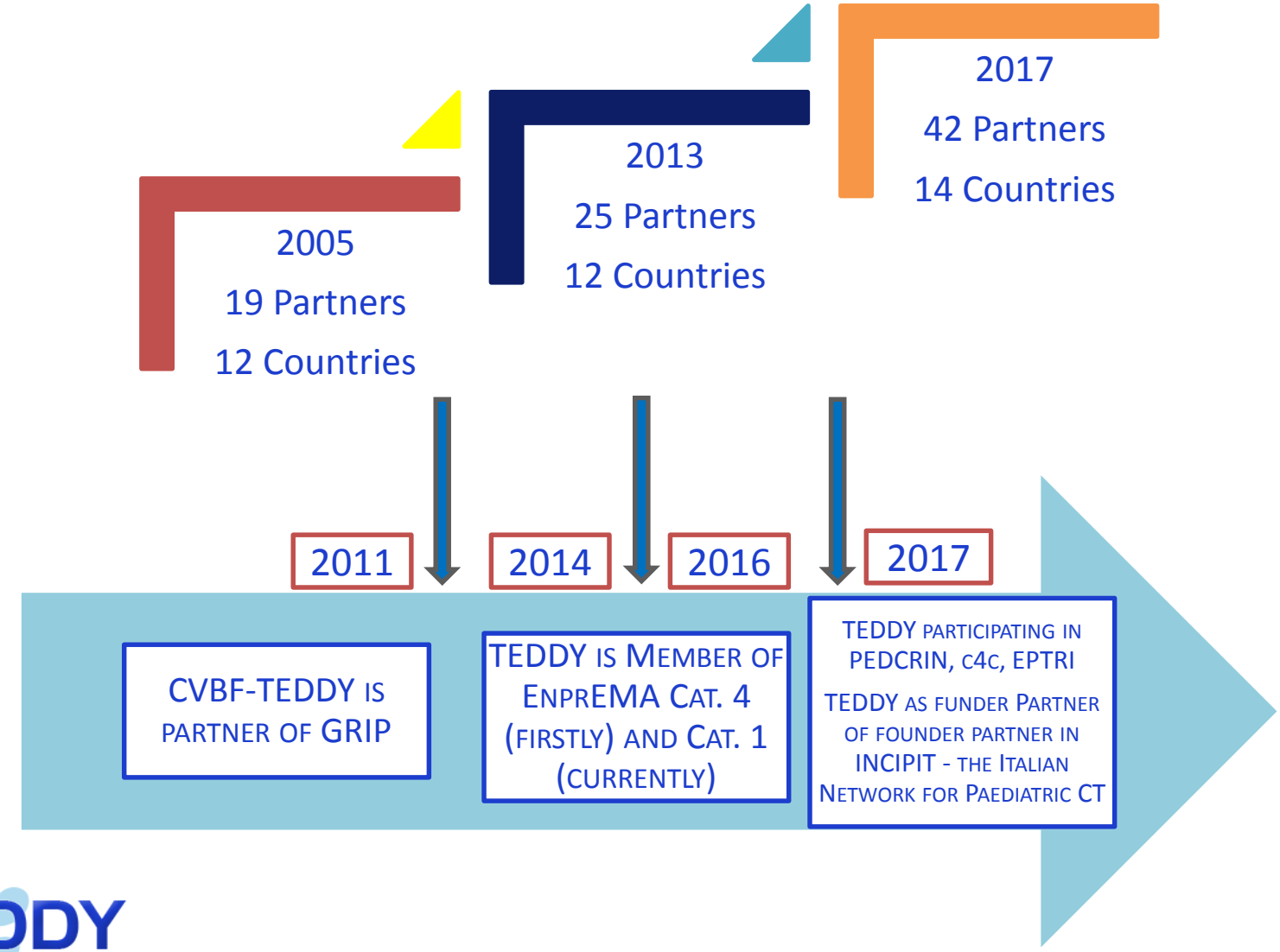
# TEDDY Step by Step

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# TEDDY future plans and ambition

## WHY to provide TEDDY with an autonomous legal status?

**To consolidate the work carried out up to date**

to expand the future perspective of the Network


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# TEDDY future plans and ambition

| | |
|---|---|
| PARTNERS | • Up to 42 partners<br>• Up to 14 countries |
| CURRENT PRODUCTS | • EPMD annually updated<br>• CTs Sites Inventory<br>• EU/non-EU Regulatory Procedures<br>• Communication Tools for children |
| WORKING GROUPS | • CTs SOPs/ Ethical Issues/Off-label<br>• Regulatory/CTs facilities/Health Data<br>• Children engagement/ATMPs for children |

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**WHICH** resources to be committed in this effort?

# TEDDY future plans and ambition

Through an **autonomous representativeness we aim to**

Have a **consolidated role** in the European paediatric research community framework

Enlarging the participation of its Members **actively taking part in new EU projects**

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