DEFERIPRONE EVALUATION IN PAEDIATRICS

SEVENTH FRAMEWORK PROGRAMME

FP7 Health Program supporting paediatric initiative: the DEEP multinational and multicultural experience

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DEFERIPRONE EVALUATION IN PAEDIATRICS - FP7 PROJECT - SP1 - COOPERATION HEALTH-F4-2010-261483

DEEP -DEFERIPRONE EVALUATION IN PAEDIATRICS

DEEP is a 4-year multinational project aimed to make available reliable treatments to children with **beta-thalassaemia, sickle cell disease and other congenital haemoglobinopathies** which represent the most severe forms of anaemia in the world with specific reference to the ***Mediterranean Area***

A large research-driven network covering the **'area' to which the disease belongs to**

- 16 Partners
- 18 recruiting centres from 7 Countries:
  EU: Cyprus, Greece, Italy, (UK)
  non-EU: Albania, Egypt, Tunisia

The DEEP project: what's new

Starting from an **old drug**, the project aims to perform paediatric studies in order to develop a new liquid formulation specific for the paediatric population and a new paediatric indication

The Project develops around a full drug developmental Plan (PIP) approved by the European Agency-PDCO that includes:

- **Liquid Formulation preparation**
- **2 Clinical Trials:**
  - PK trial providing appropriate dose definition (DEEP-1)
  - efficacy-safety multicentre, comparator controlled trial (DEEP-2)
  - long-term safety non-interventional study (DEEP-3)
- **1 post-marketing study**
  - pharmacoeconomic study

A new Marketing Authorisation (PUMA)

The DEEP project: what's Innovative

- Innovative approaches in CTs: ***DEEP-1*** **PK modeling/simulation** study to define drug exposure and appropriate dosage of deferiprone for children aged < 6yrs
- Inclusion criteria based only on number on **transfusional Fe** intake without **any age threshold**
- First time comparison between the **two oral available comparators**: deferiprone vs deferasirox
- ***DEEP-2****:* the **larger RCT** in *paediatric patients*
- **New, more reliable endpoint based on magnetic resonance:**

Cardiac **MRI T2*** included as **co-primary endpoint** for children above 10 year and liver **MRI-R2** included to measure **LIC instead of liver biopsy** in all patients not requiring sedation.

The DEEP Project: what's Challenging

Paediatric population (involves children of different ages)

'Registrative' CTs with

- Economic burden
- Ethical stringent provisions
- GCP-ICH E11 obligations

A rare and disperse population involving different Rare Congenital Anaemia

Multi-ethnic population

with different cultures and laws

The DEEP strategy deals with COMPLEXITY

THE DEEP MULTISTEPS APPROACH

1. To organize a 'trials management plan and infrastructure' including SOPs, data management, drug management, pharmacovigilance, monitoring, etc

2. To implement a unique procedure and a unique CTA 'trial submission package'

3. To develop a 'patients tailored approach' involving children, families and association

THALASSEMIA PROGETTO GUARIGIONE

THALASSEMIA INTERNATIONAL FEDERATION MEMBER

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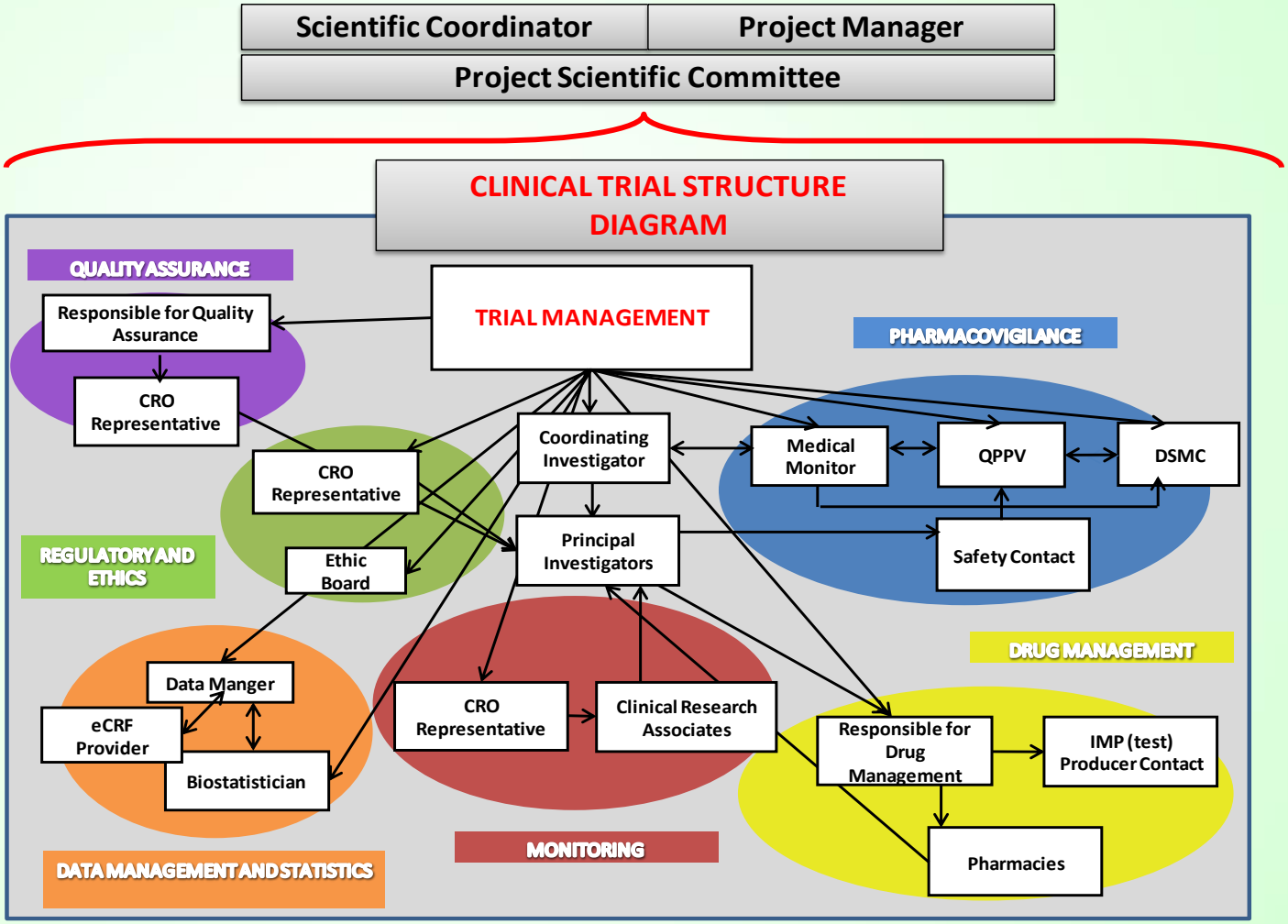
The DEEP strategy deals with DIVERSITY

STEP 1:

A COMPLEX (AND EXPENSIVE) ORGANISATIONAL INFRASTRUCTURE HAS BEEN SET UP



The legislative context: national rules in DEEP countries

- In **EU Countries (Italy, Cyprus and Greece)** the Competent Authority authorisation and the Ethics Committee approval is ruled by the **Directive 2001/20/EC** in terms of CTA form, IMP documents, insurance, informed consent Specific rules for the paediatric population PIP, EMA 2008 recommendations, ICH-E11, etc)

This 'gold standard' is to be applied in all centers modified according to the national rules

- In Albania specific rules on CTs are lacking; a special decision from the Ministry of Health is needed
- In Egypt the CTA is largely similar to Europe, but informed consent procedures are different (i.e. consent from only one parent is accepted- sending samples abroad is regulated)
- In Tunisia the Ministry of Health, the National and local ECs shall authorise a paediatric trial

The DEEP strategy to deal with diversity

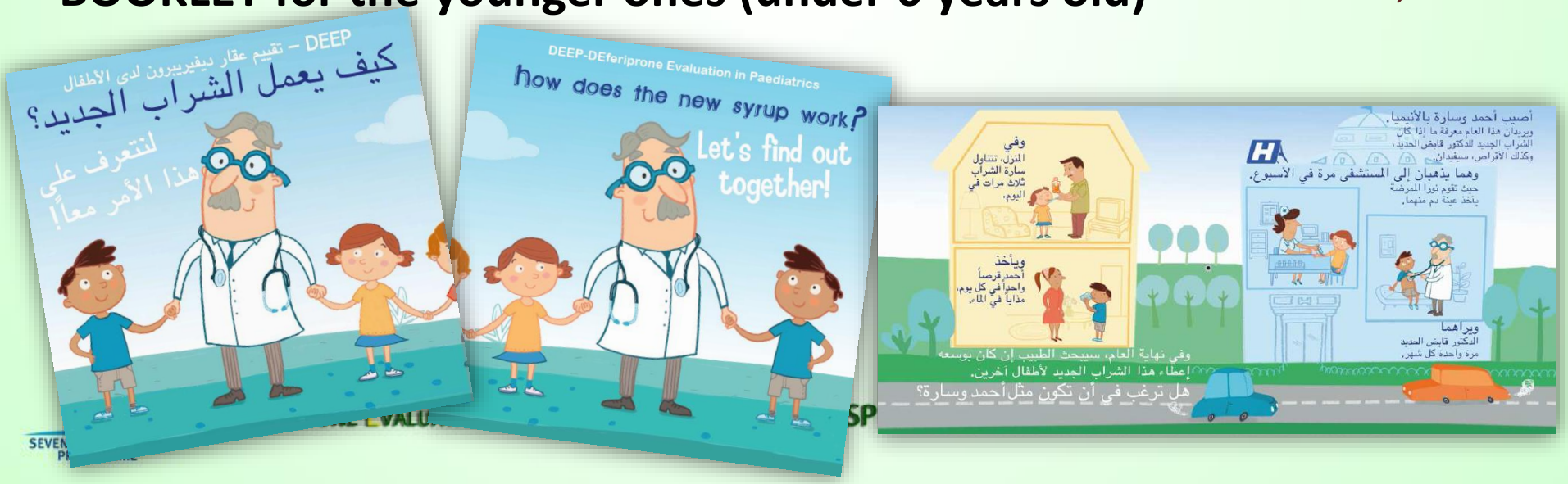
STEP 3: PATIENTS EMPOWERMENT IN DEEP

Patient-tailored communication model:

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

Translated in the national language: available in Arabic, Albanian, French, English, Italian, Greek

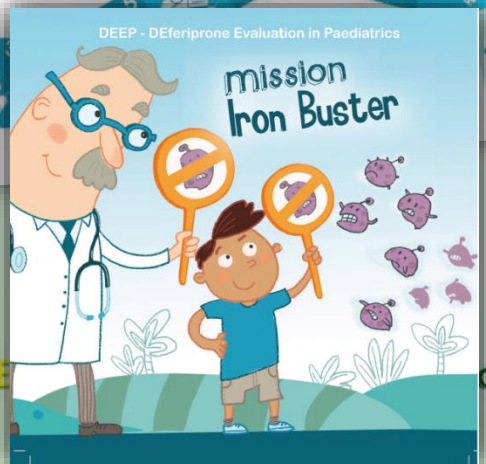
BOOKLET for the younger ones (under 6 years old)



The DEEP strategy to deal with diversity

STEP 3: PATIENTS EMPOWERMENT IN DEEP

BOOKLET and ASSENT FORM for 6-10 years old children



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The DEEP strategy to deal with diversity

STEP 3: PATIENTS EMPOWERMENT IN DEEP

BOOKLET and ASSENT FORM for 11-17 years old adolescents

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Recruitment and approval: the state of the art

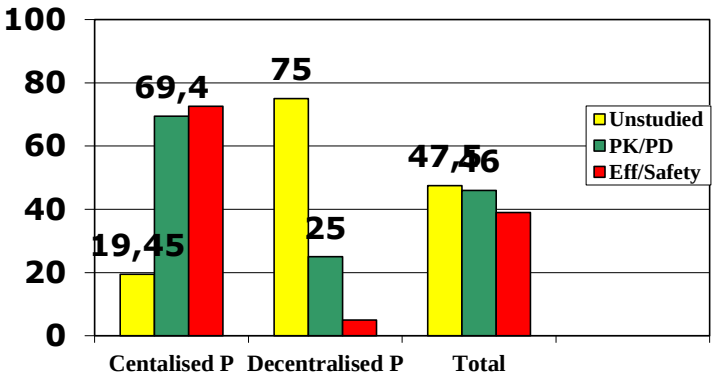
- *New formulation* is available to the investigational sites and used in the trials
- *DEEP-1* is concluding recruitment with success
- *DEEP-2* approved by the 80% of the Ethics Committees and Competent Authorities and the recruitment is now starting
- *DEEP-3* observational study is on-going

DEEP is a succes story in the EUROMED perspective

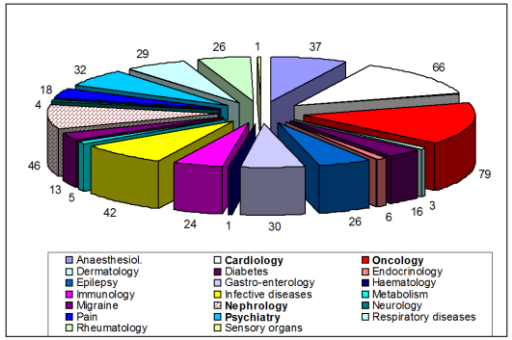
What makes DEEP project so special in the contest of FP7 Projects Framework?

*DEEP is aimed to **respond to a specific need** from the European Union Policies and rules on Paediatric Medicines as stated in the Paediatric Regulation*

Less than 30% of Medicines on the market are approved for children. Unapproved drugs are used 'off-label' because uncovered therapeutic needs.



Ref. EMA: All the needs: ~ 20 therapeutic classes
~ 400 active substances



DEEP is responding to a real therapeutic need.

This need is a common need in european and no-european MEDITERRANEA REGIONS

The DEEP project: based on scientist excellence located to European/no-European countries

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DEEP demonstrate to be able

FP7 application

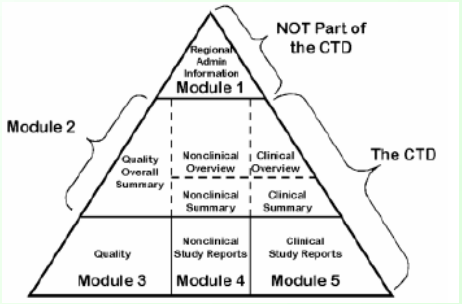
- Project considered on the basis of scientific excellence (no paediatric needs)
- No mention to the trials conduct
- Very few preclinical studies funded

PIP application

- Research Consortia having no experiences in regulatory process
- A whole **research & development plan requested.**
- All paed. subsets should be covered
- Details of timing & measures including preclinical, formulation
- Efficacy, Safety

PUMA Applications

- Commercial Sponsor
- Intellectual Property



The lesson learnt from these projects

- ***In response to the EC Research policies***
  - ***Networking action:*** a very large scientific community is sharing competencies and skills.
  - **Pubblic-private** integration and support to **SMEs**
- ***In response to the specific topic (Paediatric Medicines:***
  - ***Development of Paediatric Plans (PIPs available*** for **15** Active Substances)
  - ***Consistent number of paediatric patients,*** *also* ***neonates,*** in the trials
  - An appropriate drug for treating **iron overload in children**
- ***In response to the Scientific Community expectations***
  - ***Innovative elements*** included in the trials: pharmacogenetic studies
  - **New competencies** acquired (Regulatory, trials managements, Ethics, Communication with parents/patients, etc)

Conclusions

Is DEEP Research CONSORZIUM qualified to apply for?

Health, demographic change and wellbeing

- Excellent Science
- Industrial Leadership
- Societal Concerns