EPTRI

EUROPEAN PAEDIATRIC TRANSLATIONAL RESEARCH INFRASTRUCTURE

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 777554

Paediatric Drug Development: Challenges and Opportunities

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EPTRI webinar: biotechnology to bring innovation in the paediatric drug development - Virtual Webinar - October 2nd, 2020

The event is part of the European Biotech Week 2020

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Summary

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Introduction

Notwithstanding the many progress made in the last decades, the lack of medicines still represents a **public serious health problem** both in term of: 1) no drugs available for some diseases (such as orphan) or some population (such as Paediatric) and 2) no drugs accessible to patients for economic and social reasons.

New EU pharmaceutical strategy aims to help ensuring Europe's supply of safe and affordable medicines to meet patients' needs. Revision of special legislations (ODA and P.R.) are included in the strategy.

People, **including children**, expect to benefit from equal access to efficacious, safe and affordable medicines as well as to innovative therapies as adults.

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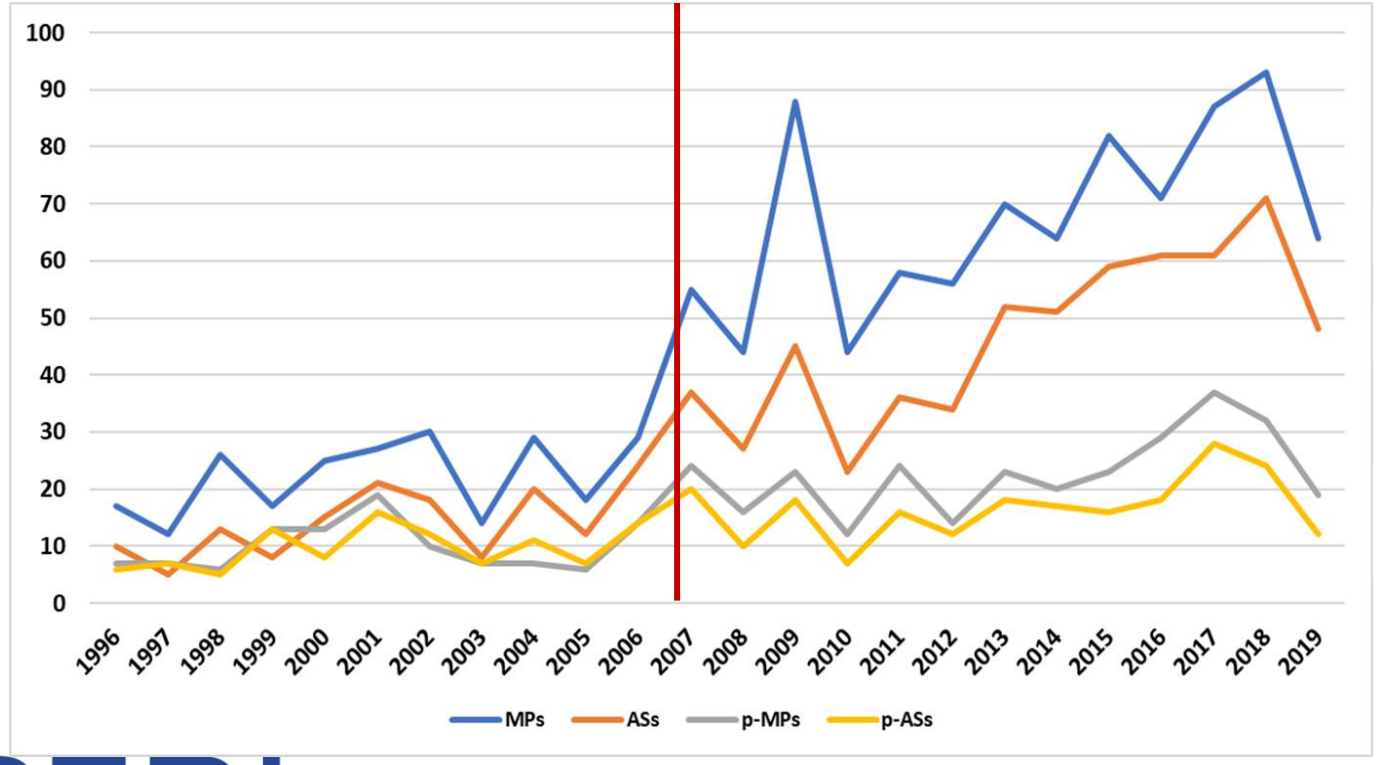
The state-of-the-art

In December 2019, a total of 1190 Medicinal Products were on the market in Europe, authorised under the Centralised Procedure: 34% of them were paediatric

BEFORE
Paediatric Regulation (EC) N° 1901/2006

AFTER
Paediatric Regulation (EC) N° 1901/2006



1190

843

405 (34%)

322 (38%)

New paediatric medicines in Europe– EPMD, 2019

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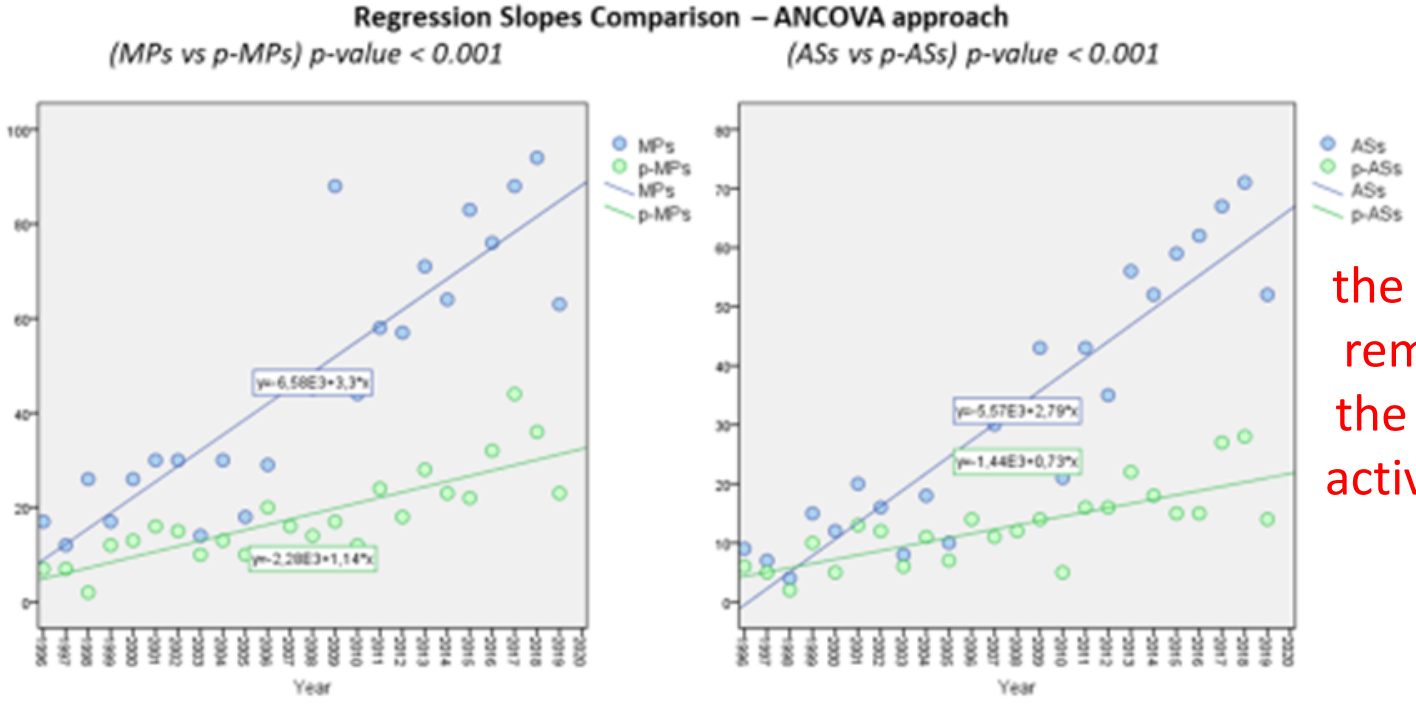
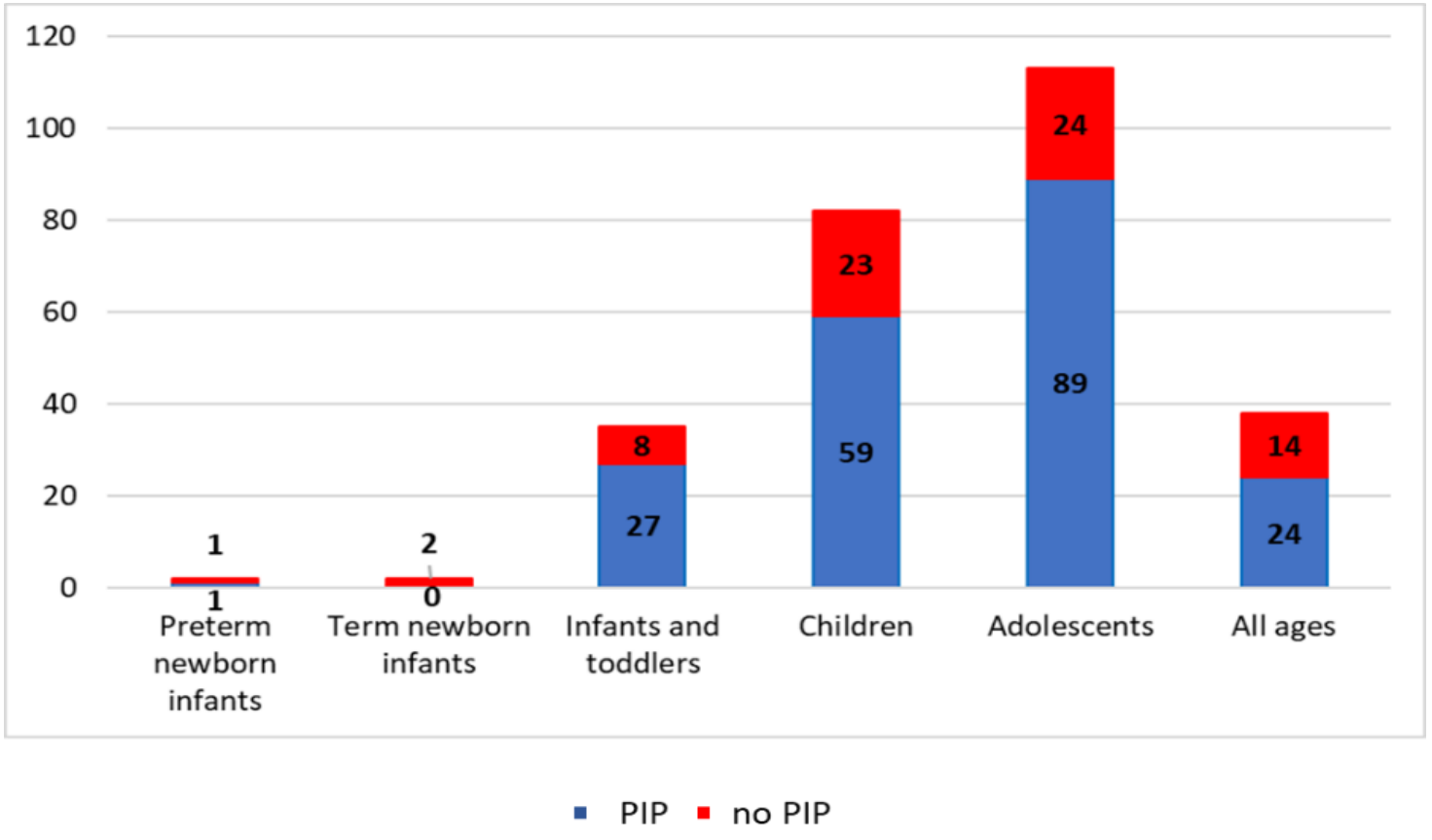
The state-of-the-art



the p-MP/total-MP rate remain quite similar in the time while the new active substances rate is lower

Medicinal Products (total and paediatric) and Active Substances (total and paediatric) approved by EMA

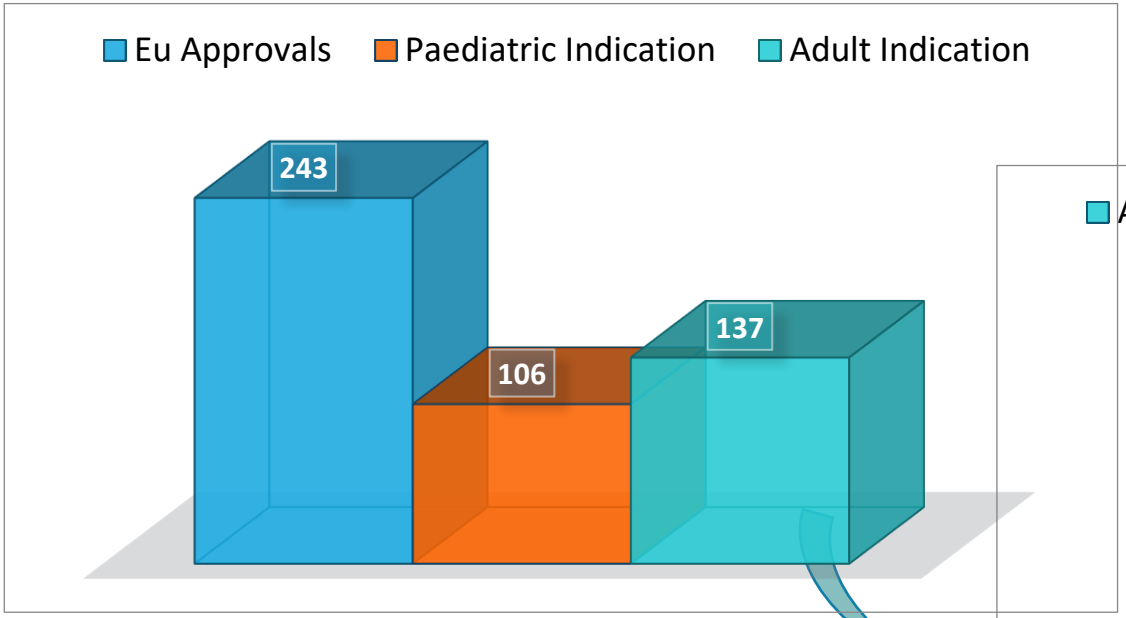
The state-of-the-art



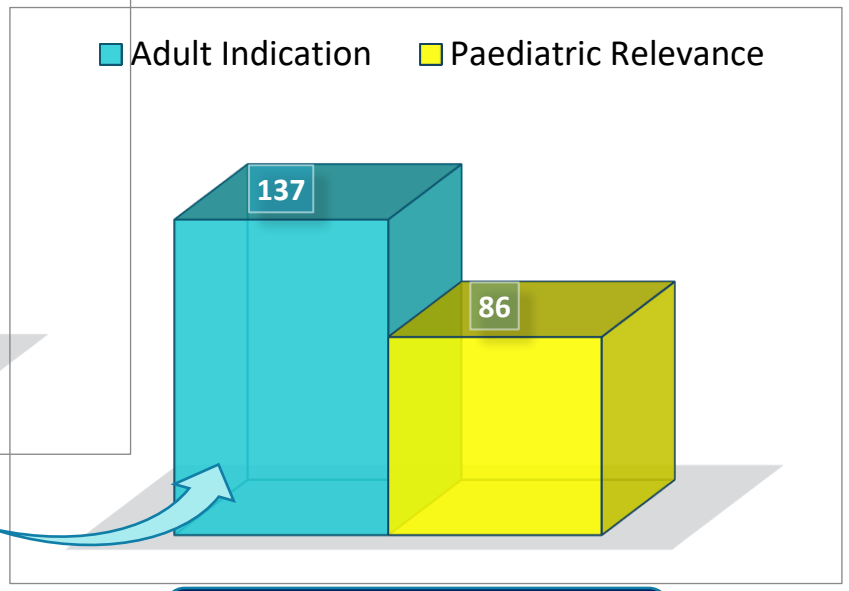
New paediatric medicines divided by age – EPMD, 2019

The state-of-the-art

The lack of paediatric medicines is also affecting highly Innovative drugs, as in the group of marketed Orphan Medicinal Products(200-2020)



16 OMPs from RNA recombinant



2 OMP advanced therapy

- ✓ 243 OMPs out of a total of 1819 (13,5%) are to date approved for the MA in Europe
- ✓ 106 OMPs out of a total of 243 (55%) are paediatric

Orphan paediatric medicines– EU-ORPHAN, 2020

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R&D in paediatrics medicines limitation

Age subsets: physiologic characteristics are different from the adults and extremely variable by days, months and years of age.

PK/PD variability makes very difficult to standardise drug activities measures, and in particular impacts on the right dose definition.

Maturational processes due to enzymes/receptors ontogeny have impact on effects measures including biomarkers (**ontogeny linked pharmacogenomic variability in children**)

Paediatric drugs must be developed in children using ad hoc methods and technologies

To *adequately* study drugs in paediatrics!

- ⇨ **to evaluate efficacy and safety**
- ⇨ **to assess correct dosages and formulation**

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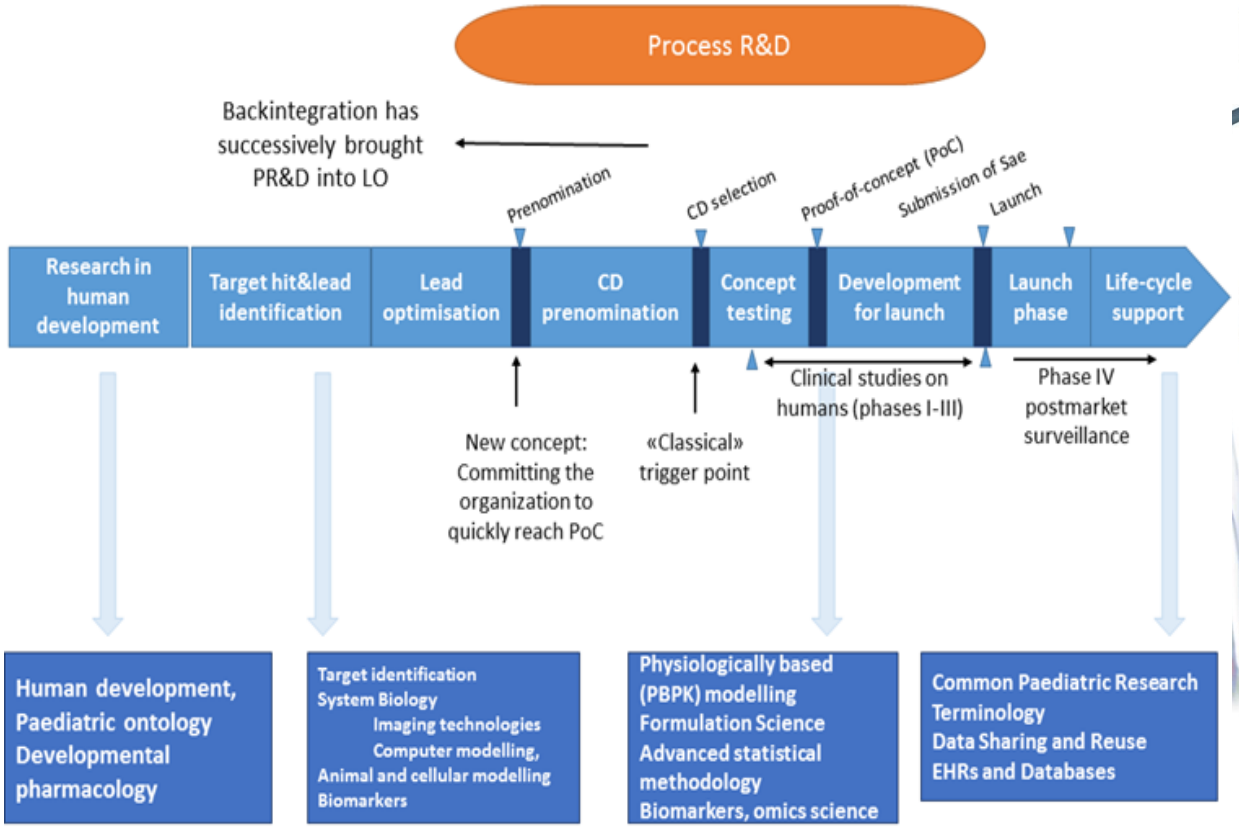
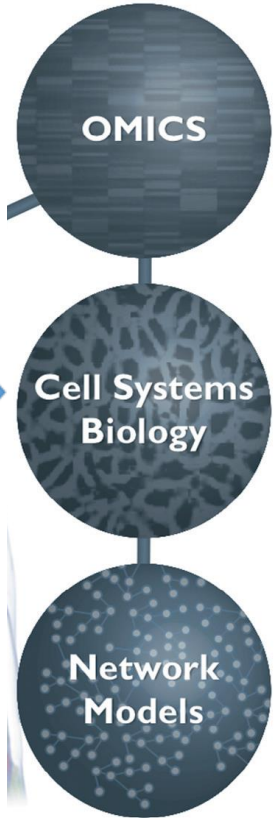
Challenges in drug discovery and development process

For effect of the biological revolution the entire drug developmental paradigm has been changed and today it requires **the inclusion of relevant innovative technologies** (enabling technologies) into the development process to be translated in innovative drugs





Drug Discovery Today

The paediatric sector should be enabled to respond to these very rapid advancements

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How to cover the paediatric medicines' gap

Ad hoc research instruments *are absolutely needed in light of the largely recognized principle that in research as well as in clinical settings* ***children cannot be addressed with adults instruments****.*

TWO MAIN PILLARS

Networks

Paediatric CTs Networks remain the corner stone of the chain of efforts necessary to make available to children new medicines and appropriate treatments

Infrastructures

RIs are needed to provide structured and stable research services and to implement innovative technologies and methods tailored for these ages' groups

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EPTRI - European Paediatric Translational Research Infrastructure

EPTRI is proposed as a a new infrastructure, dedicated to paediatric research, aimed to cover **some critical gaps** using the instrument of the EU-RIs (ESFRI)

EPTRI aims to provide

- **structural support** to researchers
- access to **specific paediatric research services**
- research platforms for **collaborative work**
- **increased knowledge** on many scientific topics related to preclinical and translational paediatric research

FOUR THEMATIC PLATFORMS

- **Paediatric Medicines Discovery**
- **Paediatric Biomarkers and Biosamples**
- **Developmental pharmacology**
- **Paediatric formulations**

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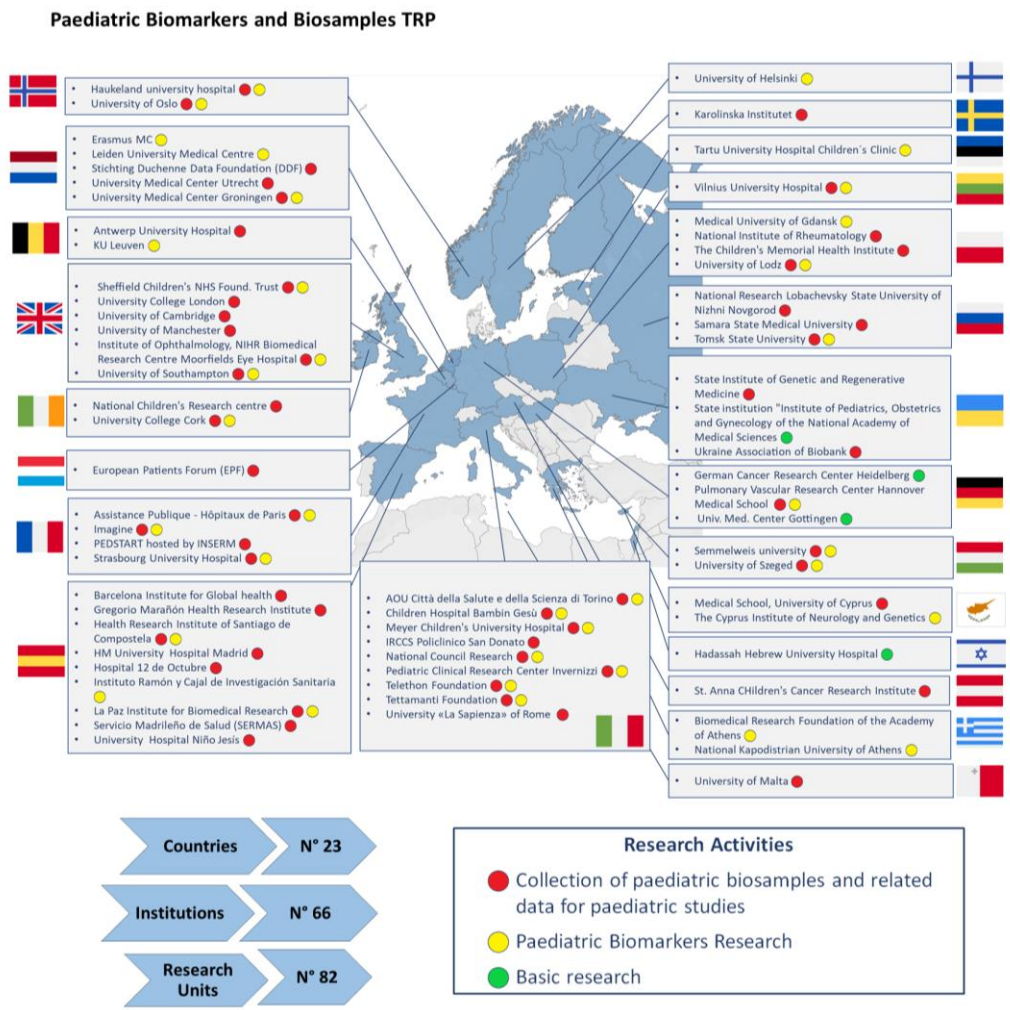
Biomarker and Biosamples Platform



The RUs participating in this platform are mainly dedicated to research activities in the field of biomarkers identification and validation steps.
The TRP will also aim to give access to large quality controlled biosamples collection suitable for research on paediatric medicinal products.

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Research technologies gaps
(data from users' survey, last update 2020)

The major problem in the identification of paediatric biomarkers as well as in the progression from a candidate biomarker to a validated paediatric biomarker is that, **due to the ontogeny linked pharmacogenomic variability in children**, we cannot assume that adults' biomarkers have the same level of significance in a paediatric process. The second issue is that to produce valuable results, **access to paediatric samples is necessary**

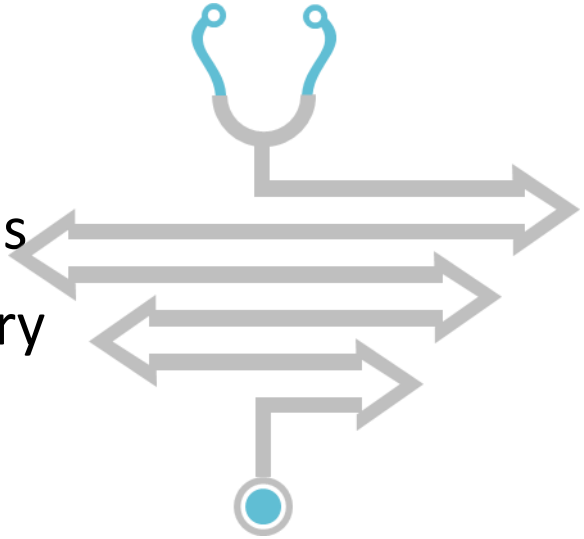
- **Biobank:** few biobanks and organized samples collection dedicated to children available and accessible.
- **Genetic factors** are part of the significant covariates that may influence pharmacokinetics. Ad hoc study are needed.
- **Polymorphisms:** Among the 'omic' sciences (pharmacogenomic, m-RNA, Transcriptomics, Metabolomics and Proteomics) only a small number have been studied to identify or validate paediatric biomarkers.
- **Personalized medicines relevant application are expected** in children but limited implementation.
- **IT technologies:** to provide integration and synthesis of evidence.
- **AT (gene and cell):** as for other products paediatric approach is needed.

Areas for research

Research activities and services cover the performance of studies aimed at the identification, characterisation and validation of paediatric biomarkers.

Many RUs (25 RUs) in this platform develop basic research activities aimed to identify prognostic/diagnostic/predictive biomarkers of high paediatric interest for:

- ✓ Pre-term infants
- ✓ Rare Genetic Diseases
- ✓ Allergy and respiratory diseases



- ✓ Neurological disease
- ✓ Early growth and pubertal development
- ✓ Multifactorial diseases

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Paediatric Drug Development Biomarkers Platform expected contribution

EPTRI contribution is expected in term of provision of:

- ✓ **well-annotated biological materials** of paediatric origin currently not easily accessible,
- ✓ **biomarkers identification and validation with reference to paediatric diseases and age groups**

Based on

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Biomarker and Biosamples Platform Outline

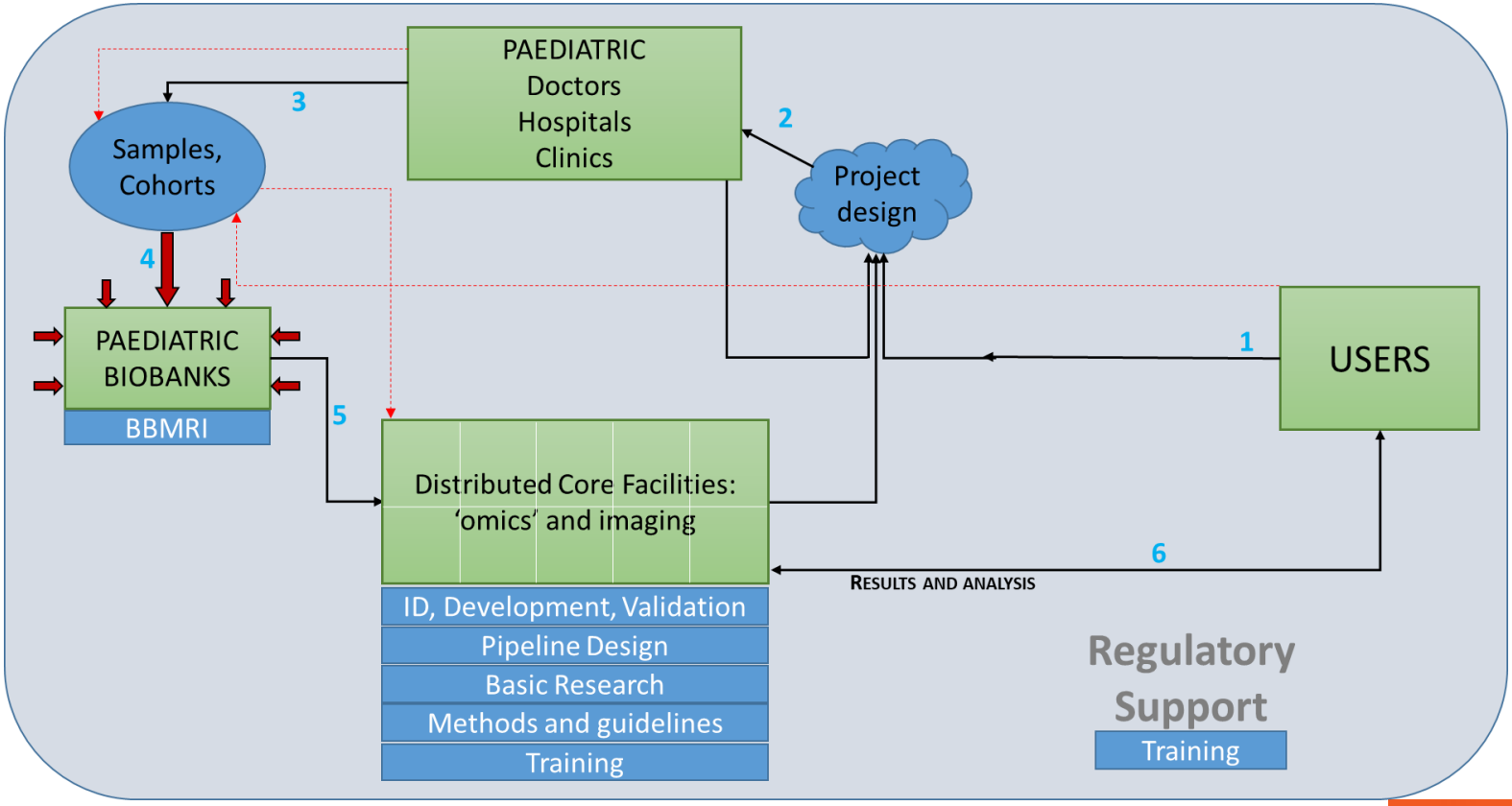
Country	RUs	Paediatric samples collections from normal and pathological conditions available in the institution
Cyprus	The Cyprus Institute of Neurology and Genetics –	Foetal, Preterm newborn, Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager, Parent (or family members)
France	PEDSTART hosted by INSERM	Preterm newborn, Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager, Parent (or family members)
France	Imagine, Institut des maladies génétiques	Foetal, Preterm newborn, Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager, Parent (or family members)
Greece	Biomedical Research Foundation, Athen	Foetal, Preterm newborn, Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager, Parent
Hungary	Semmelweis University - I. Clinic of Pediatrics	Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager
Italy	AOU Città della Salute e della Scienza di Torino -	Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager
Italy	National Research Council (CNR) – ITB	Children (6 to puberty), Teenager, Parent (or family members)
Malta	University of Malta - Center for Molecular Medicines	Term newborn, Parent (or family members)
Poland	National Institute	Toddler (0-5 year), Children (6 to puberty), Teenager, Parent (or family members)
Russia	National R Lobachevsky State University of Nizhni	Toddler (0-5 year)
Spain	University hospital Niño Jesís	Toddler (0-5 year), Children (6 to puberty), Teenager
Spain	La Paz Institute for Biomedical Research	Foetal, Preterm newborn, Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager
Spain	HM University hospital Madrid	Toddler (0-5 year), Children (6 to puberty), Teenager
Spain	Health Research Institute of Santiago de Compostela	Preterm newborn, Term newborn, Toddler (0-5 year), Children (6 to puberty), Teenager, Parent (or family members)

RUs in EPTRI Biomarkers Platform hosting biobanks and paediatric samples collections, by type of biosamples collected

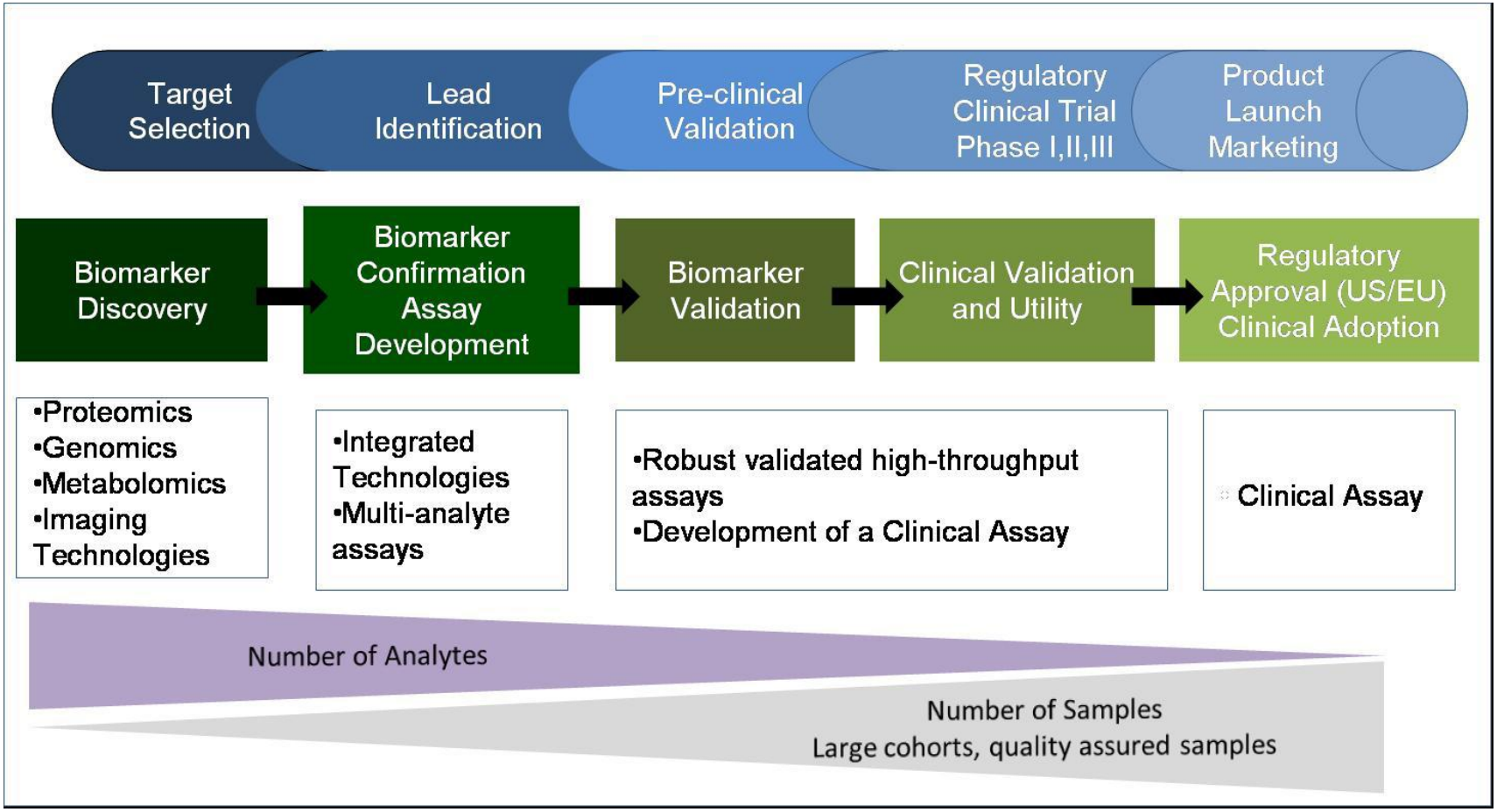
For both research and clinical use

Biomarker and Biosamples Platform Outline

A close relationship with clinical facilities is extremely beneficial since these organisations, represent not only a source of sample collections but also the sites where newly identified and characterised paediatric biomarkers should be validated and proposed for future clinical studies.



Areas for research in the Platform

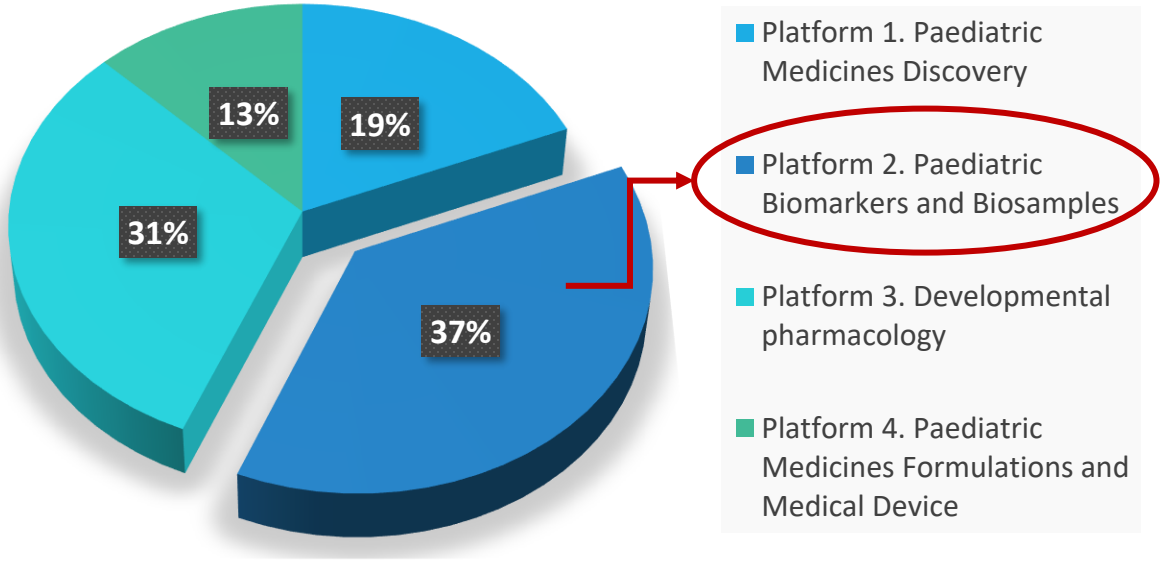


http://education.molecularmedicineireland.ie/page/g/s/91

Feasibility Studies

Services required:

- ✓ **Identification and validation of biomarkers**
- ✓ **Omics applications**
- ✓ **Biobanking**
- ✓ **IT tools and data interoperability**



10 FS proposals were received from 6 internal and 4 external users

Six proposals were related to Paediatric Biomarkers and Biosamples Platform

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INFRAIA-02-2020 for Integrating activities

Joint research activities aimed to develop resources enabling research, to be selected according to criteria of excellence, expected impact, feasibility and cost.

7 partners in 5 Countries

JRA3 – Biosamples collections and paediatric research models the ELSI service will identify and evaluate data processing activities to be carried out within the project and will provide ad-hoc recommendations on the processing of personal and special categories of data for research purposes.

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