ID-EPTRI WP3 Survey – Main results and next steps

An online survey was delivered in April-May 2018 to collect different information clarifying the scientific and technological context for paediatric research in the European landscape and to identify potential service providers to be included in the future European Paediatric Translational Research Infrastructure. The survey was intended to investigate the existing competency and expertise in paediatric fields relevant for EPTRI, the perceived difficulties relevant for research activities, barriers and facilitators to allow paediatric research units to form research platforms to support EU Paediatric research and finally to declare the availability to deliver services in the framework of EPTRI.

More than 900 contacts were invited in this survey round to fill out the online questionnaire and 137 answers were got from 29 EU countries, with Italy, UK and Spain being the most represented countries (Figure 1).

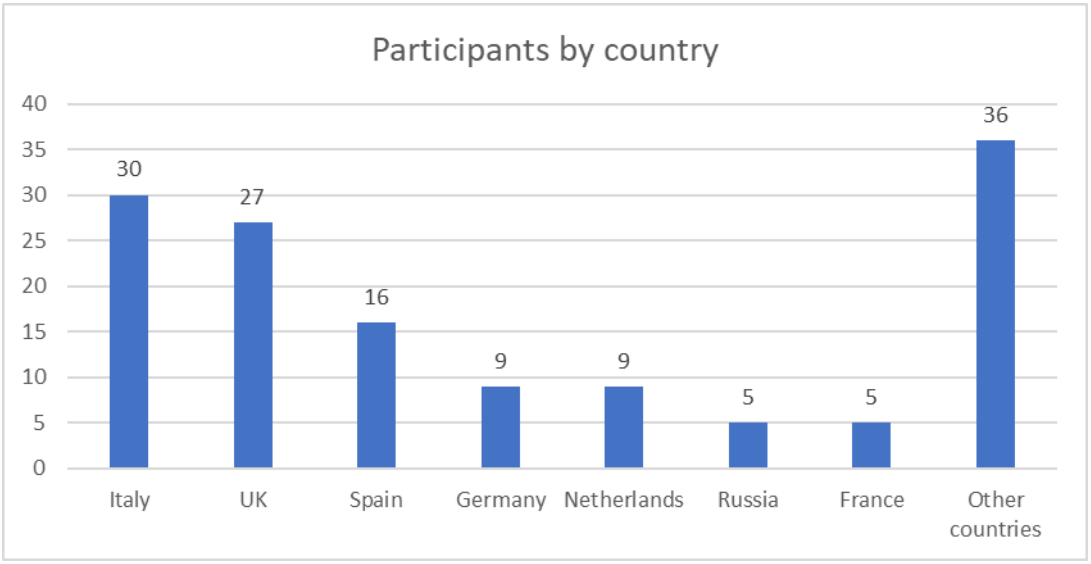

Figure 1. Geographical distribution of respondents

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1. Existing competency and expertise in paediatric fields relevant for EPTRI

The questionnaire was divided in four scientific domains, referring to the future EPTRI platforms.

a. Human Development and Paediatric Medicines Discovery

This area described the expertise of centres in mechanisms of human development that might be relevant in developing novel paediatric treatments and the study of specific targets and new emerging technologies with the intent of developing novel paediatric treatments.

Feedback from 81 respondents were got, with a prevalence of the following activities over the others: identification of novel drug targets of foetal/neonatal/paediatric populations (35), animal models (31), experimental validation of novel paediatric drug targets (29), study of paediatric development mechanisms relevant in oncology (27), immunology (26) and hormonal research (21).

Details on research activities related to this platform are available in figure 2.

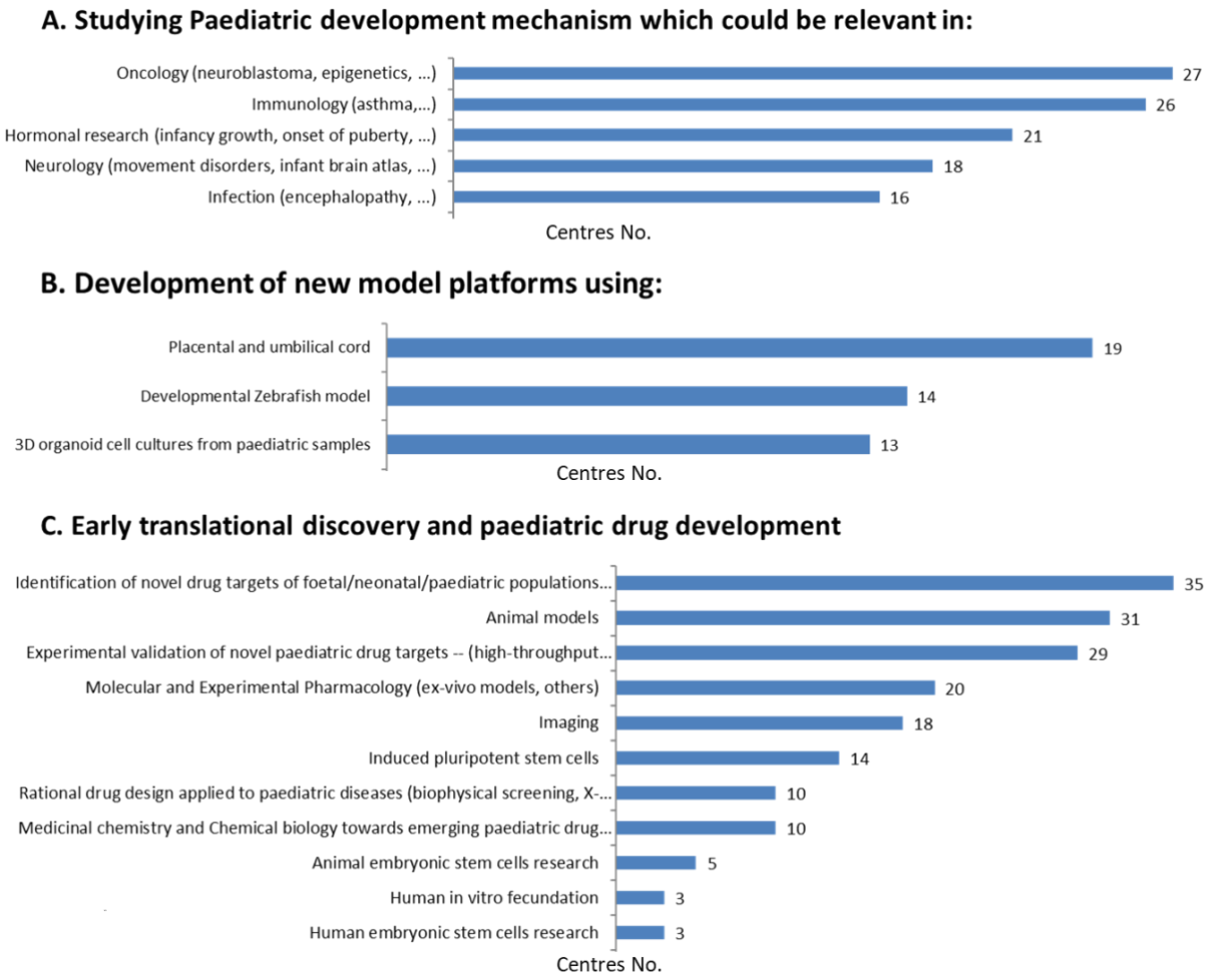

Figure 2. Research activities on Human Development and Paediatric Medicines Discovery (WP5)

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b. Paediatric Biomarkers and Biosamples

49 respondents performed research activities in the field of paediatric biomarkers, mostly referring to identification, characterisation and validation of biomarkers used as diagnostic and prognostic tools. Identification and characterisation of predictive markers in response to therapy was also well represented (Figure 3).

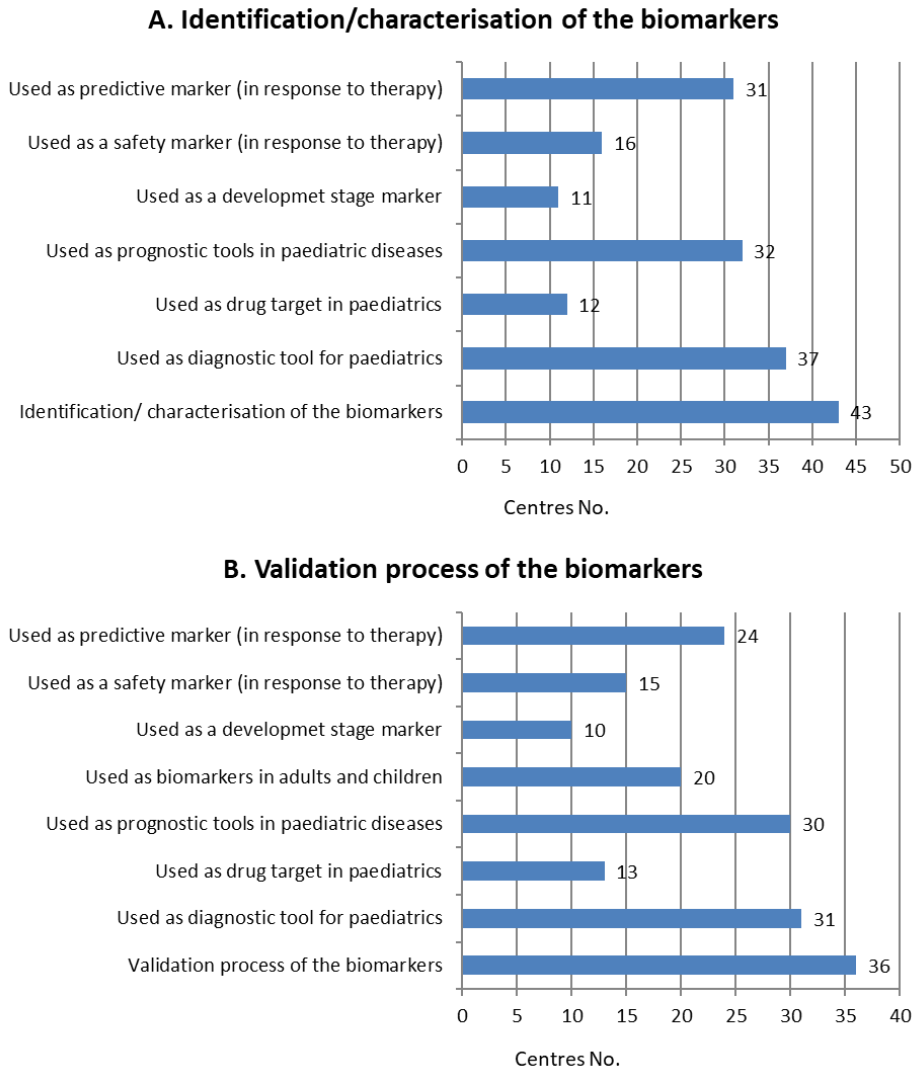

Figure 3. Research activities on Paediatric Biomarkers and Biosamples (WP6)

As main and original result in this research framework, the survey has identified a relevant number of research unit (a total of 34) active in biobanking biosamples of paediatric interest, with 13 centers declaring to have biobanks exclusively dedicated to paediatric biosamples representing all the paediatric ages (from neonates to adolescents and young adults) and many therapeutic areas and specific diseases from cancers to genetic and rare diseases. Details on these biobanks are available in table 1.

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Hosting institution	City and Country	Range of human development stage covered	Main topics
Hospital Universitario Niño Jesús - Pediatric Hematology & Oncology	Madrid, Spain	infants to adolescents	Acute leukemias
Health Research Institute of Santiago de Compostela - GENVIP- Biopharma - Innopharma GENVIP-GENPOB	Santiago de Compostela, Spain	newborns -18 years old	diagnostic and prognostic footprints associated to paediatric diseases
National Children's Research Centre	Dublin, Ireland	NA	immunology including Cystic Fibrosis, IBD, Dermatology, Rheumatology, Obesity/Endocrinology; cardiology; paediatric cancer
Oslo University Hospital Department of Pediatric Research	Oslo, Norway	NA	Paediatric cancers, liver disease. Production of hepatic organoids
AOU Città della Salute e della Scienza di Torino Stem Cell Transplant and Cellular Therapy Laboratory - Paediatric Oncohematology Unit	Torino, Italy	0-18 years	biological samples pre and post hematopoietic cells transplantation
Tomsk State University The Institute of Biomedicine	Tomsk, Russia	genetically informative studies of child development	Sample collection and biomarkers analysis; Infromative features extraction; Creation of classification rules
St. Anna Children's Cancer Research Institute	Wien, Austria	up to young adults	Paediatric cancers
University College London Great Ormond Street Institute of Child Health	London, United Kingdom	children	Wilms tumour
		birth-18years	Different diseases (rare inherited diseases, rare skin diseases), newborn samples
Children‘s hospital, Vilnius University Hospital Santaros klinikos Centre of Competence and Biomedical Research	Vilnius, Lithuania	newborns, infants, children, adolescent	n.a.
Children’s Memorial Health Institute	Warsaw, Poland	n.a	n.a
University of Cambridge, Department of Paediatrics	Cambridge, United Kingdom	birth to adolescence / young adulthood	Type 1 diabetes; Paediatric cancers - germ cell tumour; Rare neurological disease; Neonatal brain injur; Early growth and pubertal development; Reproductive development / Disorders of sex development
University Medical Center Groningen Department of Laboratory Medicine, Laboratory of Metabolic Diseases	Groningen, The Netherlands	n.a.	n.a.

Table 1. Details on paediatric biobanks hosted in institutions answering to the EPTRI survey

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c. Developmental Pharmacology

27 answers were got for this field of expertise, mostly referring to drug dosage – development of analytical methods adapted to low volumes (15), PK/PD modelling and simulations in the different age groups, different diseases, different ethnic groups (14) and dosage calculation for first in child pharmacokinetics (13). Other items were less represented, like studies on placental drug transfer (4). Further details on research activities in Developmental Pharmacology are available in figure 4.

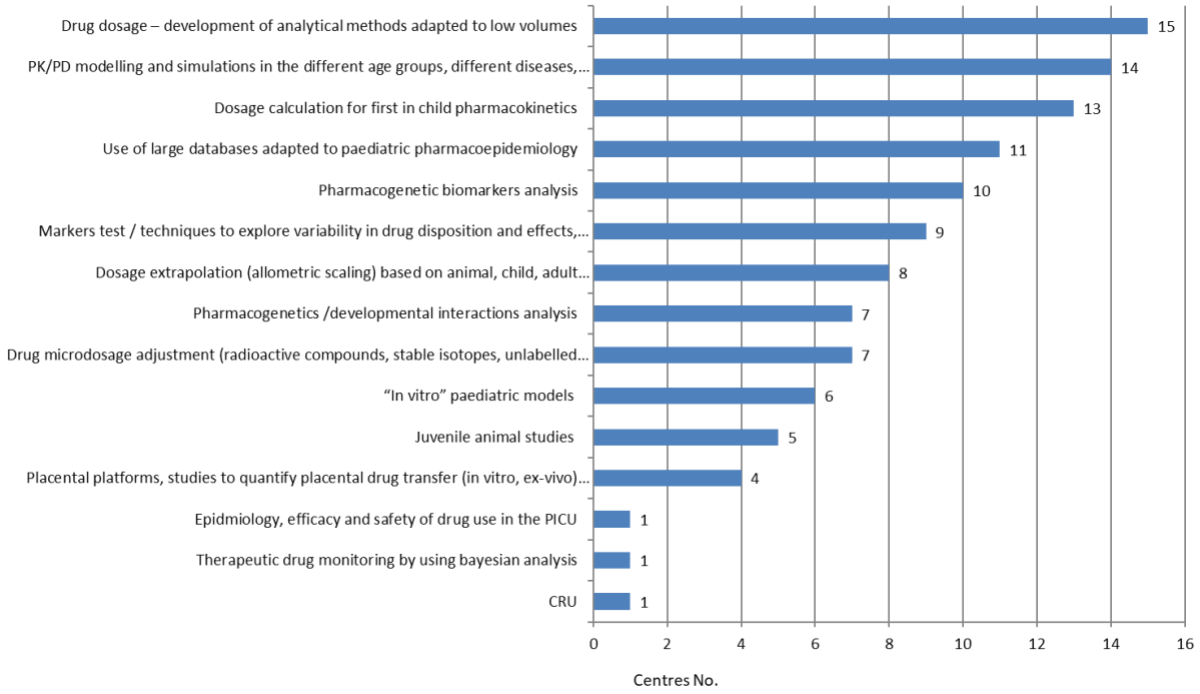

Figure 4. Research activities on Developmental Pharmacology (WP7)

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d. Paediatric Medicines Formulations and Medical Devices

A lower number of centres (22) declared expertise in this field, mostly referring to the development of paediatric formulations/drug delivery design for enteral (17) and non-enteral (14) routes of administration. Research on taste-masking technologies (12) and biopharmaceutics (9) was also performed. Other items were less represented. 7 units declared to be able to perform end user assessment of medicines administration devices. Among them, 4 units also performed research and development activities of new devices. Full details are indicated in figure 5.

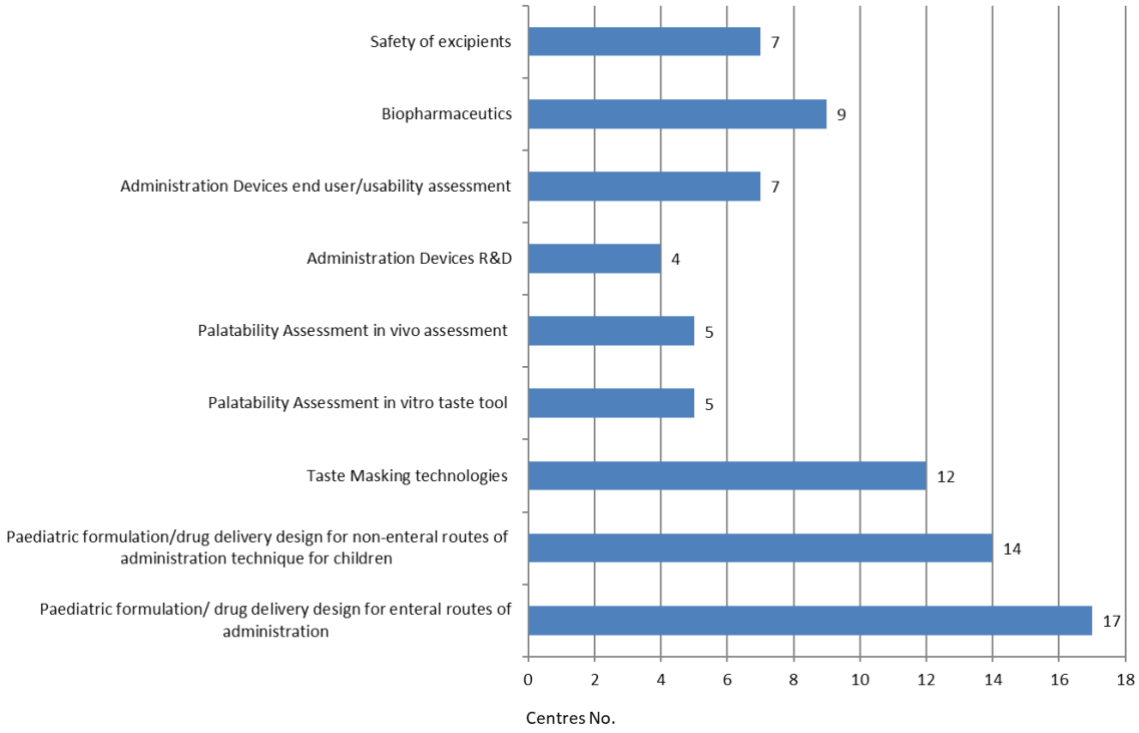

Figure 5 Research activities on Paediatric Medicines Formulations and Medical Devices

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2. Availability to deliver services in the framework of EPTRI

Respondents were asked to detail the services they were able to offer in the framework of the future Research Infrastrucuture. Some general services were listed (table 2) including scientific and IT facilities, ethical and regulatory expertise, training and management know-how.

Topic	Centres No.
Training courses	45
Ethical/legal issues, informed consent data protection and confidentiality	40
Biomarker regulatory validation	38
Data repositories (access/management/deposition)	36
Accredited/certified facilities (ISO certified, GLP, GMP, GCP)	36
[-omics technology platforms]	34
Assessment of projects impact and innovation potential	30
Data management expertise	30
Access to/management/deposit of chemical compounds	16

Table 2. General research services that might be offered in the framework of EPTRI

More in detail a panel of specific services and facilities to make available within EPTRI, as derived by the competences declared is reported in table 3. It will be implemented and updated after a second survey step will be completed.

Reference platform	***Specific services***
Human Development and Paediatric Medicines Discovery (WP5)	Research on human development mechanisms relevant for paediatric diseases
	Rational drug design applied to paediatric diseases (biophysical screening, X-ray protein crystallography, protein biochemistry, molecular modelling, virtual screening, Chemo-informatics, ADME/Tox predictions)
	Access to/management/deposit of chemical compounds
	Novel paediatric drug targets (high-throughput biochemical screening assays, cell-based screening, other)
	Stem cell biology, regenerative medicine/tissue engineering approaches
	Molecular and Experimental Pharmacology (ex-vivo models, others)
	Animal models focused on paediatric diseases
	Human in vitro fecundation
	Imaging
Paediatric Biomarkers and Biosamples (WP6)	Identification/ characterisation of the biomarkers for paediatric use
	Validation process of the biomarkers for paediatric use
	Biobank organisation (targeted on paediatrics)
	Access to/deposit of human paediatric biological samples (biobanks)
	Data on biological paediatric samples repositories (access/management/deposition)
	High-throughput screening for biological paediatric use
	Omics technology platforms to be used for paediatric drugs development

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Developmental Pharmacology (WP7)	"In vitro" models
	Juvenile animal studies
	Sensitive biofluids assays – development of analytical methods adapted to low volumes
	harmacometrics in the different age groups, different diseases, different ethnic groups
	Markers test / techniques to explore variability in drug disposition and effects, including
	Adverse drug reactions
	Microdosing
	Paediatric pharmacogenetics
	Use of large databases adapted to paediatric pharmacoepidemiology
	Placental platforms, studies to quantify placental drug transfer (in vitro, ex-vivo) tools for systematic use of small biological samples (gut, liver, kidney and brain)
Paediatric Medicines Formulations and Medical Devices (WP8)	Paediatric formulation/ drug delivery design for enteral routes of administration
	Paediatric formulation/drug delivery design for non-enteral routes of administration technique for children
	Taste Masking technologies
	Biopharmaceutics
	Medical Devices end user/usability assessment
	Safety of excipients
	Palatability Assessment in vitro taste tool
	Palatability Assessment in vivo assessment
	Administration Devices R&D

Table 3. Specific services to be provided in each EPTRI platform

3. Conclusion and next steps

This survey provided a comprehensive overview on the facilities and knowledges available in the various thematic platforms addressed within the EPTRI project.

On its basis, more information about research areas, available paediatric research services and facilities of units and potential service providers to be included in the future European Paediatric Translational Research Infrastructure will be got through direct contacts between the platform leaders and the units.

A new survey round has been started, to enrich the data collection for some specific fields of expertise, reach additional units that in these months were informed about EPTRI, increase the coverage of European countries and describe the panel of services that the research units might offer (as detailed in table 3).

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