EPTRI

European Paediatric Translational Research Infrastructure

"Legal and Regulatory issues dealing with pediatric translational research in the EPTRI (European Paediatric Translational Research Infrastructure) framework"

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EPTRI framework

EPTRI project → ***need to find answers to the serious global lack of medicines targeted for children.***

26 partners from 19 EU/Associated countries.

Coordinated by Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF).

EPTRI
EUROPEAN PAEDIATRIC TRANSLATIONAL RESEARCH INFRASTRUCTURE

EPTRI framework

- **Funds**: Horizon 2020 EU Research and Innovation programme
- **Budget**: 3,071,250 euros
- **UE Grant**: 3 million euros
- **Period**: 2 years
- **Coordinator**: Consorzio per Valutazioni Biologiche e Farmacologiche (CVBF)
- **Start date of the project:** 1 January 2018

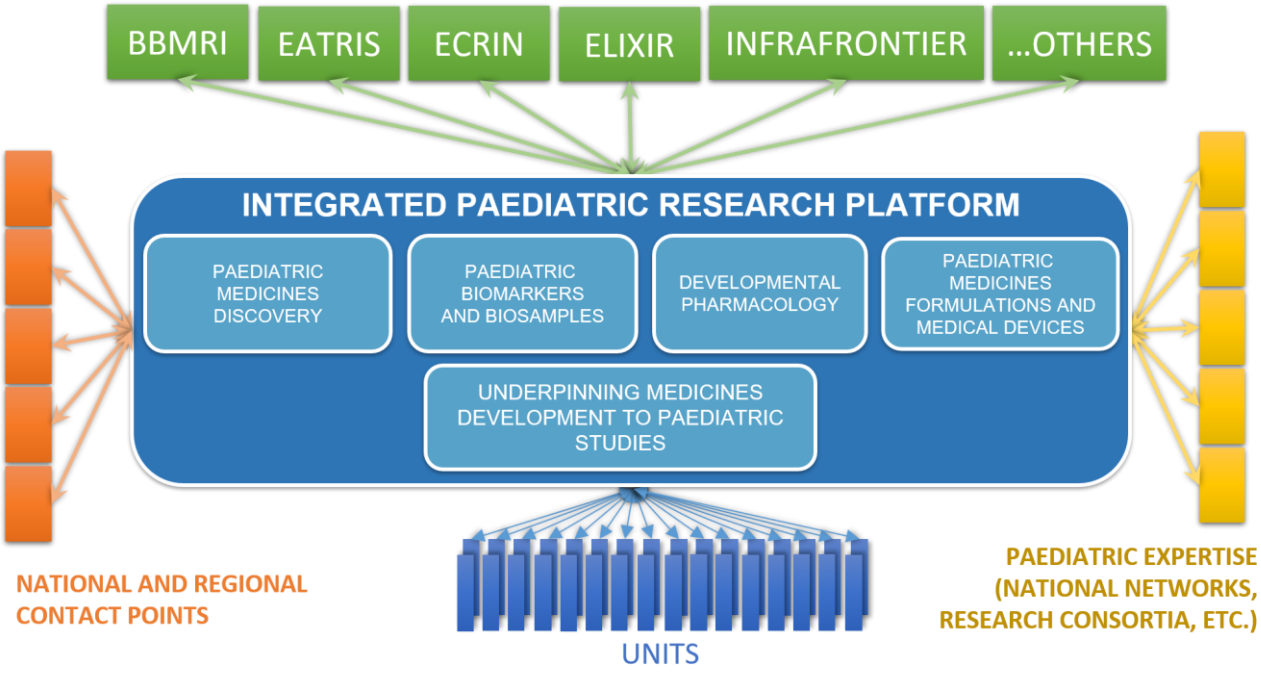
EPTRI framework will be created by the generation of a **Conceptual Design Report (CDR)**, describing the scientific and technical requirements as well as the key components of the new RI

- Design of a virtual space for all dispersed paediatric research
- Identification of critical gaps in paediatric medicines research
- Planning of the integration of the proposed RI with existing RIs

EPTRI framework

The project will cover five technical and scientific domains including:

- 4 research platforms:
  - Pediatric Medicines Discovery
  - Pediatric Biomarkers and Biosamples
  - Developmental Pharmacology
  - Pediatric Medicines Formulations and Medical Devices



- the scientific domain “Underpinning Medicines Development to Pediatric Studies”, integrating key technologies into the medicines development process in children and acting as a bridge between EPTRI and other RIs and pediatric clinical trials networks.

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EPTRI framework

- Promote a translational approach from the bench side to the bedside
- Accelerate pediatric drug development processes
- Include most relevant technological innovations in research for children's health

Translational research…many definitions

- Bench-to-bedside enterprise of harnessing knowledge from basic sciences to produce new drugs, devices, and treatment options for patients. For this area of research—the interface between basic science and clinical medicine—the end point is the production of a promising new treatment that can be used clinically or commercialized (“brought to market”). (Woolf SH. JAMA. 2008)

- It is defined by a process that starts with fundamental research (genes, molecular processes, biochemical pathways) and ends at a macro level (social healthcare, access to healthcare, access to education, and so on) (Waldman SA et al. Clin Transl Sci. 2010)

EPTRI expected results

Overcome paediatric research **fragmentation** in Europe

Link researchers to groups interested in the **same scientific issues or therapeutic areas**

Promote an **integrated approach** to paediatric medicines development: innovation + clinical trials

Enhance paediatric research both globally and in the European scenario

Orient researchers when they conduct their research having in mind the implementation of the full chain of **translation**

Bridge the existing paediatric initiatives with the outcomes of the new RI

Influence the efforts made by the existing biomedical RIs when they deal with paediatric research

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EPTRI phases

CONTEXT ANALYSIS PHASE	OPERATIONAL PHASE	FEASIBILITY PHASE
Performed in all the technical and scientific domains identified, the perceived value and the possible gaps to be covered will be estimated by enquiring the scientific Communities, the concerned national Authorities and many other Stakeholders	The different components of the new RI will be planned, including governance model, strategies for interaction with national Authorities and the existing RIs, the IT-architecture model, services to be provided and a business plan	Develop virtual exercises simulating the operations of the RI to work with: - Scientists - Governments - Patients (YPAGs) - Other RIs

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Ethical, Legal and Regulatory issues in the pediatric drug development process

Different phases of the drug development process in paediatrics raise different legal and regulatory issues:

- Data protection and confidentiality (General Data Protection Regulation)
- Storage of samples and biobanking
- Preclinical studies (research on animals)
- Societal Issues (access to medicines & healthcare, trials in developing, emerging countries, prioritizing health needs…)
- Research including emerging technologies and advanced therapies (tissues and cells, gene therapies, gene-editing)

Accelerating Translation to Pediatric Needs

"Safe and effective pharmacotherapy in pediatric patients requires the timely development of information on the proper use of medicinal products in pediatric patients of various ages and, often, the development of pediatric formulations of those products."

(Clinical Investigation of Medicinal Products in the Paediatric Population, Guidelines, EMA, E 11)

Accelerating Translation to Pediatric Needs

Pediatric formulations can be difficult and time consuming, the development of these formulations must be considered early in medicinal product development!

- Medicinal products for diseases predominantly or exclusively affecting pediatric patients (trials on pediatric population except for initial safety and tolerability data, usually obtained by adults).

Accelerating Translation to Pediatric Needs

- Medicinal products intended to treat serious or life-threatening diseases, occurring in both adults and pediatric patients, for which there are currently no or limited therapeutic options.

- Medicinal products intended to treat other diseases and conditions (Testing of these medicinal products in the pediatric population would usually not begin until Phase 2 or 3).

Uppsala & Leiden Reports

The respect of core human rights from a child's perspective has been recently analyzed in two reports Commissioned by the Committee on Bioethics of the Council of Europe:

1. *The rights of children in Biomedicine: challenges posed by Scientific Advances and Uncertainties*, 2017 (Uppsala Report).
2. *From law to practice: Towards a roadmap to strengthen children's rights in the Era of Biomedicine, 2017* (Leiden Report).

Bioethics Principles

Human Rights (Leiden Report)

1. **Human dignity**: Individuals must be able to live their own lives (However the concept of dignity is not always clear according the Convention on Human Rights and Biomedicine).
2. **Autonomy**: Right to make own choices (free choice and informed consent). Competence is Prerequisite.

Informed consent

"Children or adult" debate – "Children are not little adults"

Parents or Legal representative are entitled to give informed consent on their behalf.

Consent / Assent

Payments to children!

Bioethics Principles

3. Integrity: physical and mental integrity. Individual must decide itself on interferences with his/her integrity. Additional protection for children by restricting beforehand a number of biomedical interventions (e.g. participating in biomedical research, living organ transplantation and genetic testing)

4. Equal treatment and non-discrimination: Council of Europe issues a "*Recommendation on the Participation of Children and Young People*" (**CM/Rec(2012)2**).

Bioethics Principles

5. Access to justice: Specifically addressed for children (Convention on the Rights of the Child, UN,1989).

States should establish legal protection for cases of violation of rights also for children (e.g. right to receive information in relation to transplantation, right data protection).

Bioethics Principles

- Declaration of Helsinki
- United Nations Convention on the Rights of the Child
- Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine.

Risks & Benefits

- National legal orders have the competence to provide safeguards for balancing the risks and benefits of children in health care.
- Direct Benefit can be defined as progress in treatment, for the group of children.
- The **European Convention on Human Rights and Biomedicine** states in its **Article 17.2** that exceptionally and under the protective conditions prescribed by law, where the **research has not** the potential to produce results of **direct benefit** to the health of the person concerned, such research **may be authorized** subject to specific **conditions.**

Risks & Benefits

1. The research has the aim of **contributing**, through significant improvement **in the scientific understanding** of the individual's **condition, disease or disorder**, to the ultimate attainment of results capable of conferring benefit to the person concerned or to other persons in the same age category or afflicted with the same disease or disorder or having the same condition.

2. The research **entails only minimal risk and minimal burden** for the individual concerned.

Risks & Benefits

Risk assessment => evaluation of the risk of the medicinal product tested. In case of conflict between the children's interest and research interest, the first must always prevail.

- **Potential Harms**: A genetic diagnosis might decrease individual in opportunities and freedom of choice. Violation of privacy is considered as potential harm.
- The unavailability of **age-appropriate** pediatric **formulations** may also incur a level of **risk**. Pediatric patients should be given medicines that have been appropriately evaluated for their use.

Risks & Benefits

Determination of the levels of risk in Member States differs.

European Medicines Agency, UK (2001)

Risks should be i) **minimized** and ii) **reasonable** in relation to the expected benefit (including knowledge gained). Analysis should take into consideration risks of short term as well as long-term risks including delayed occurrence of such risks.

Risks & Benefits

US Department of Health and Human Services Regulations examples of risk

(in all cases assent and parental consent!)

Title Public Welfare 45, Code of Federal Regulations § 46.404

No more than minimal risk.

Title Public Welfare 45, Code of Federal Regulations § 46.405

More than minimal but potential for direct benefit

Risks & Benefits

Title Public Welfare 45, Code of Federal Regulations § 46.406

Minor increase over minimal risk without direct benefit, but research is likely to yield generalizable knowledge about subject's disorder or condition.

Title Public Welfare 45, Code of Federal Regulations § 46.407

Not otherwise approvable, but presents an opportunity to understand, prevent or alleviate a serious problem affecting health or welfare of children.

Legal framework

Regulation 1901/2006 on medicinal products for pediatric use and amending Regulation ECC 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) 726/2004.

Encourages the pharma industry to perform research able to address the specific therapeutic needs of children.

Establishment of the **Pediatric Committee** within the European Medicines Agency. (Article 6).

Legal framework

General Data Protection Regulation 679/2016

Informed consent of data subjects to the data controller for their sensitive data processing.

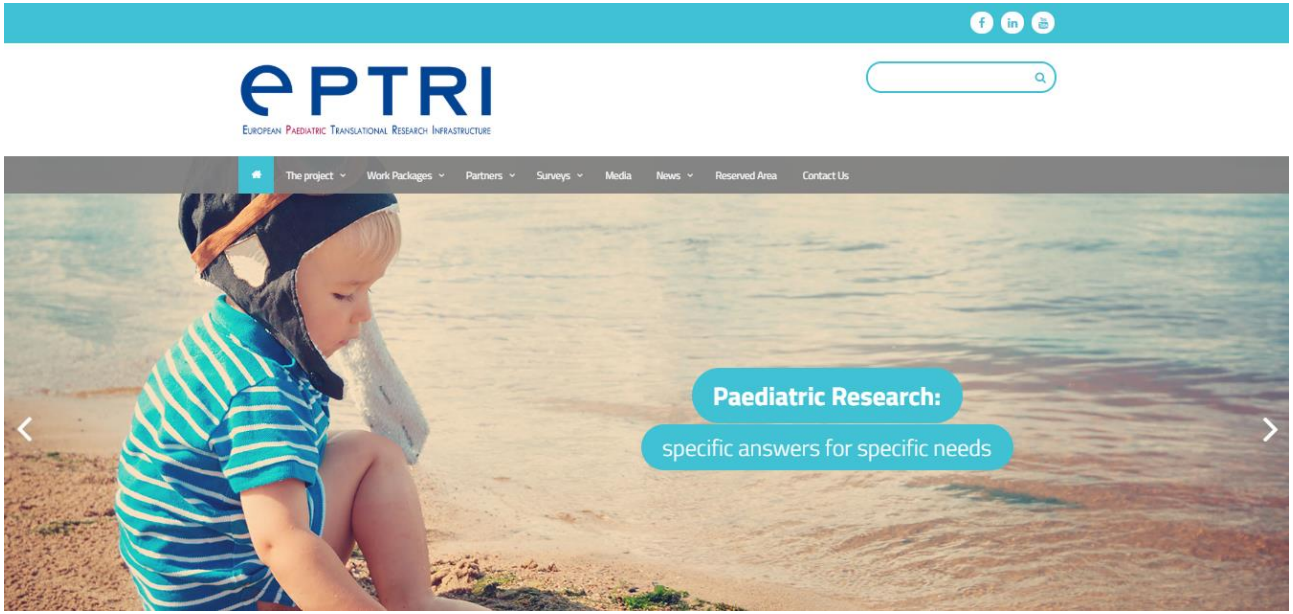
Guidelines

- CHMP Guideline on conduct of Pharmacovigilance for medicines used by the pediatric population, EMA/CHMP/235910/05.

- Clinical Investigation of Medicinal Products in the Pediatric Population (E 11), CPMP/ICH/2711/99.

- Confederation of European Specialists in Pediatrics (CESP) guidelines.

Be in contact with EPTRI



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