

EPTRI

European Paediatric Translational
Research Infrastructure

THE BIRTH OF EPTRI

The European Paediatric Translational Research Infrastructure (EPTRI) started as a **project** coordinated by **Consorzio per Valutazioni Biologiche e Farmacologiche** (CVBF – Clinical Validation from Biopharmaceutical Findings) and funded within the **H2020-INFRADEV-01-2017 programme, arising from the need to find answers to the serious lack of medicines for children in EU and worldwide.**

It aimed to **design the framework for the new research infrastructure (RI)** providing a conceptual design report (CDR) of EPTRI describing the scientific and technical requirements as well as the key components of the new RI. Five technical and scientific domains have been identified:

1. Human Development and Paediatric Medicines Discovery
2. Paediatric Biomarkers and Biosamples
3. Developmental Pharmacology
4. Paediatric Medicines Formulations and Medical Devices
5. Underpinning Medicines Development to Paediatric Clinical Studies

EPTRI AISBL



EPTRI (European Paediatric Translational Research Infrastructure) is a **non-profit research organisation** incorporated in the form of an Association Internationale Sans But Lucrative (AISBL) governed by Belgian law, **based at Leuven University**.

EPTRI is a **pan-European initiative** involving hundreds of research units gathered to **boost the paediatric research ecosystem** and **provide services to private and public stakeholders for the development of high quality and safe medicines, technologies and devices for children**.

EPTRI promotes processes allowing **stakeholders' engagement and knowledge translation by integrating the perspectives** of young patients and families, policymakers and payers, regulators and researchers, agencies and charities, academia and industries.

Our Vision



To increase knowledge on children growth and ontogeny characteristics relevant for the identification of novel therapies dedicated to children and to provide services for their development.

Our Mission



To implement competences, research strategies, access to key technologies, standardised models, and analytical tools, and to offer to public and private stakeholders qualified basic, preclinical and translational research services covering paediatric medicines discovery and development.

EPTRI FOUNDING MEMBERS



Belgium

- Catholic University of Leuven
- Hospital Association of Brussels - Queen Fabiola University Children's Hospital

Cyprus

- The Cyprus Institute of Neurology and Genetics

Czech Republic

- Fyziologicky ustav AV CR

Greece

- Athena Research and Innovation Center in Information, Communication and Knowledge Technologies

Italy

- Alma Mater Studiorum - Università di Bologna
- Consorzio per Valutazioni Biologiche e Farmacologiche
- Fondazione per la Ricerca Farmacologica Gianni Benzi Onlus
- Università degli Studi di Bari 'Aldo Moro'
- Università degli Studi di Milano-Bicocca
- Associazione "La Nostra Famiglia" scientific section IRCCS «Eugenio Medea
- Fondazione Penta ONLUS

Poland

- Children's Memorial Health Institute

United Kingdom

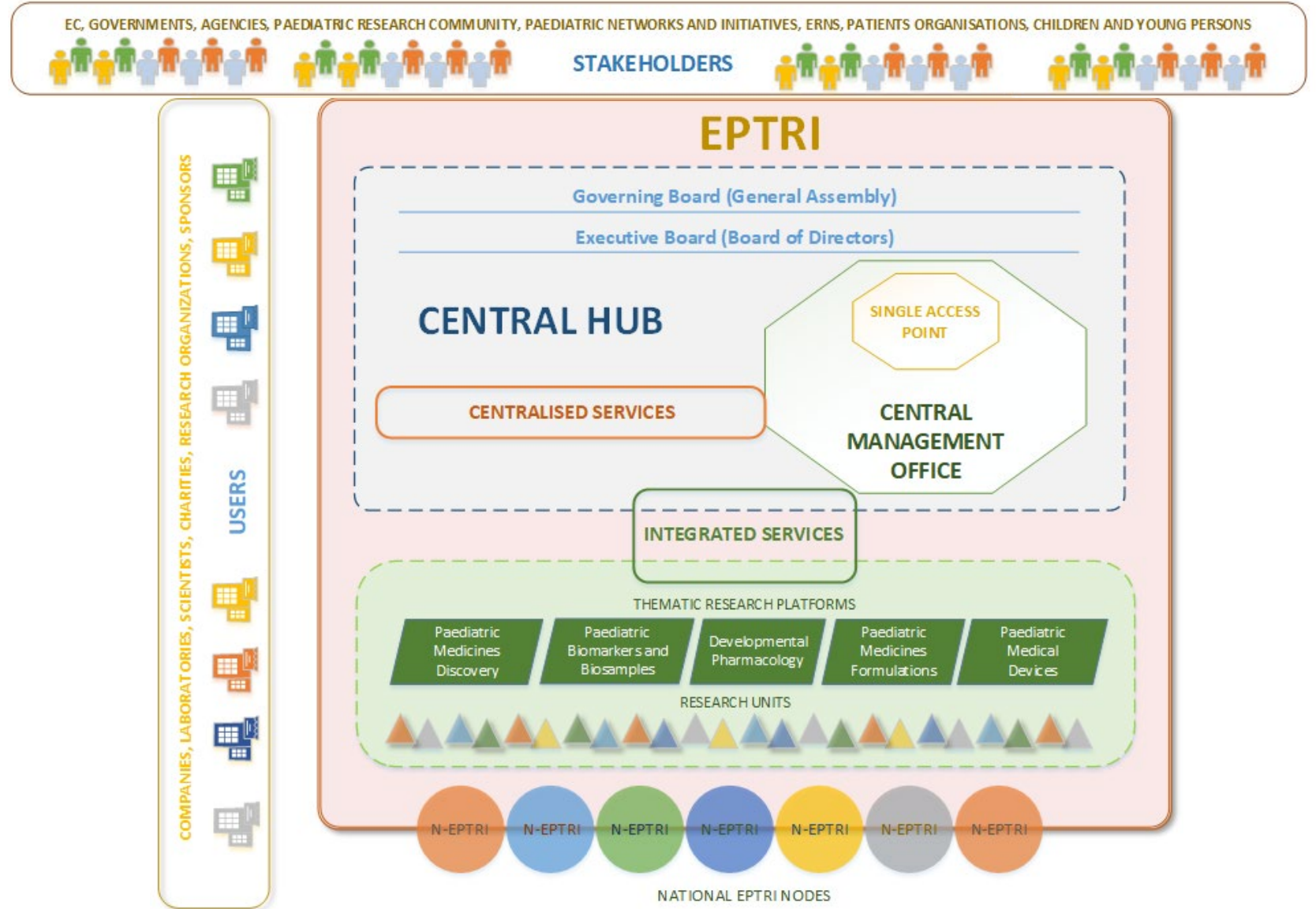
- Sheffield Children's NHS Foundation Trust

Israel

- ALYN Hospital

Governance

EPTRI is organized as a distributed Research Infrastructure according to a Hub and Spoke model, with a Central Management Office, interconnected with the distributed research units, grouped within Thematic Research Platforms (according to their area of expertise), and National Nodes (according to their location)



Paediatric Research Services

Integrated Services



provided by the five **Thematic Research Platforms (TRPs)**



Paediatric Medicines
Discovery



Paediatric
Biomarkers &
Biosamples



Developmental
Pharmacology



Paediatric Medicines
Formulations



Paediatric Medical
Devices

Centralised Services

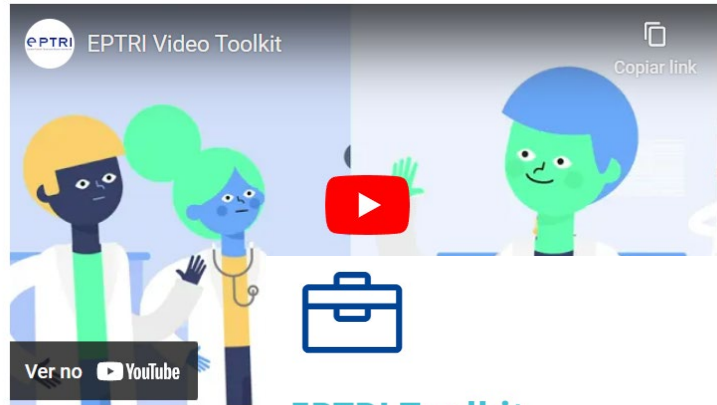


provided by **Central Management Office (CMO)**

- Providing access to paediatric patients' cohorts.
- Providing access to paediatric samples and related data.
- Advice on in-vivo / in-silico clinical study design.
- Advice and Document preparation for regulatory and ethic procedures.
- Advice on preparing HTA reports for paediatric medicines, diagnostic and MDs.
- Advice on Data and sample sharing preparation.
- Supporting application to (public and private) funding opportunities.

The EPTRI Centralised Services are **advice or hands-on activity transversal to the TRPs** and intended to **support any step of the paediatric research conducted in the basic, pre-clinical and translational settings.**

EPTRI Research Engagement & Educational Resources



Toolkit

EPTRI Toolkit

On Basic and Translational Paediatric Research for Patients and Families

Webinars



Surveys



Paediatric Manifesto



EPTRI Special Issue

EPTRI has launched the research topic collection "Supporting the Pediatric Drug Development: From Basic Research to Clinical Studies and Technological Advancements"

Clinical Studies

Safety and Efficacy of MSC-EVs in the Prevention of BPD in Extremely Preterm Infants (EVENEW)

Biogenera's multi-center Phase 1 clinical trial of the anti-cancer drug BGA002 for aggressive pediatric cancers

Gabapentin in Paediatric Chronic Pain study (GAPP Study)

EPTRI Manifesto: Obstacles to paediatric research

WHY do we need a Manifesto?

20% of the EU population are **children**.

However, paediatric drugs research is neglected due to low industrial interest in such a limited market.

Only 30-50% of medicines are available for children at different ages/diseases.

CHARTER OF FUNDAMENTAL RIGHTS OF THE EUROPEAN UNION (2000/C 364/01)
SOLIDARITY Article 35 - Health care

Everyone has the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities.



Lack of:

- Sufficient pre-clinical information on paediatric medicines based on innovative discovery tools such as molecular targets, paediatric cellular lines models, biomarkers variability, animal juvenile models, etc.
- Paediatric clinical studies covering all the paediatric ages, also considering the influence of physiological maturation of biological functions on study conduct and results**
- Innovative study design applications like modelling, use of existing data, artificial intelligence applications, etc.**
- Tools to translate R&D into specific paediatric and orphan therapeutic approaches
- Fragmentation of expertise, scattered knowledge, and intradisciplinary technologies
- Low capacity of data/information sharing among institutions
- Limited participation of patients and caregivers in drug and therapies development as well as clinical phases
- Poor interest on children's fundamental rights on health care and safe medicines
- Unsolved and uncovered ethical as well as legal issues on paediatric research from preclinical phases to access policy and education

EPTRI involvement in Clinical Studies: BIOGENERA

Phase I Study in paediatric patients affected by Neuroblastoma

Interventional, open label, single arm, non-randomised **Phase I** clinical trial aimed to investigate safety, tolerability and PK of BGA002 in paediatric patients affected by Neuroblastoma with MYCN amplification/expression.

- 1) **DOSE RATIONALE:** use of a **model-based approach** for the integration of preclinical in vitro and in vivo data to support the clinical dose rationale. PK-guided approach through drug exposure measurements for the adjustment of dosage to reach the target AUC.
- 2) **STUDY DESIGN:** adaptive trial, with PK-guided dose escalation and efficient within patient dose escalation. Multicentric study enrolling up to 18 patients with refractory or relapsed metastatic or localized disease.

Innovative methodological approach:

A model-based approach allows effective integration of pre-clinical data, providing a robust basis for the dose rationale. The use of clinical trial simulations in conjunction with adaptive procedures allows for the identification of informative protocol designs in early paediatric oncology trials.

EPTRI involvement in Clinical Studies: EVENEW

Phase I/II Study in preterm newborns

Phase I single arm, dose escalating and Phase II double blind, randomized, placebo-controlled, dose finding Clinical Trial assessing safety and efficacy of intratracheal administration of allogeneic umbilical cord mesenchymal cells-derived Extracellular Vesicles in preventing Bronchopulmonary Dysplasia in **extremely preterm newborns**.

- 1) **DOSSIER FOR CTIS:** participation in the preclinical phase and the preparation of the dossier for CTIS submission and involvement in the group of Scientific Advisors for the product development.
- 2) **STUDY DESIGN:** contribution for the implementation on an innovative study design using the seamless approach (Phase I/II trials), a dose-escalation stage to select the **maximum tolerated dose (safety)**, followed by an expansion cohort to investigate its **activity/efficacy**.

Innovative methodological approach:

Seamless trials improve efficiency by combining multiple trial phases, reducing time and resource use, and allowing adaptive modifications based on interim data. They maximize the use of small patient populations by enabling continuous data collection and minimizing recruitment challenges.

EPTRI involvement in Clinical Studies:

GAPP

**Adaptive design
in children from 3 months to
less than 18 years of age**

To evaluate Efficacy, Pharmacokinetics, and Safety of Gabapentin in **children from 3 months to less than 18 years of age** experiencing moderate to severe chronic neuropathic or mixed pain: an Adaptive-design Prospective Cohort Study (GAPP Study).

1) **DOSE RATIONALE:** contribution for the calculation of the dose rationale for gabapentin using as tools pharmacokinetic (PK) modelling and clinical trial simulations (CTSs) to optimize doses and protocol design for a prospective investigation in paediatric patients with chronic pain.

2) **STUDY DESIGN:** contribution for the implementation on an innovative study design with the advantage to include prospectively planned opportunities for modifying study design elements and hypotheses based upon interim data analyses.

Innovative methodological approach:

Adaptive designs can make clinical trials more flexible by utilising results accumulating in the trial to modify the trial's course in accordance with pre-specified rules. Trials with an ***adaptive design*** are more efficient, informative and ethical than trials with a traditional fixed design.

3) **PIP:** contribution for PIP modification and resubmission.

EPTRI: ACHIEVED MILESTONES & FUTURE GOAL

