



Integration of Paediatric Development into Drug Development - The Role and Benefit of a Centre for Paediatric Clinical Development

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Agenda

- Why Are Paediatric Centres Needed?
- Structure & Role of Paediatric Centres
- Benefits of Paediatric Centres
- Conclusion



Global Paediatric Market



The global paediatric drugs market was valued at USD 117.20 billion in 2021. It is expected to reach USD 300.70 billion by 2029, i.e., a CAGR of 12.5% for 2022 to 2029.

North America expected to dominate the paediatric drugs market due to:

- The rise in the volume of paediatric patient cases with children suffering from various autoimmune disorders, respiratory disorders, cerebral palsy, and muscular atrophy
- Steep rise in the adoption of advanced technologies in the US
- Rising healthcare expenditure
- The rise in government initiatives to create awareness in people for paediatric medicines, and early approvals with accelerated drug approval initiative by the US FDA to encourage the development of drugs for rare diseases and to decrease the rising paediatric burden are likely to create more opportunities in the market
- Rising number of research activities in NA and presence of major key players
- The rise in disposable income and improvements in healthcare infrastructure

Asia-Pacific expected to grow fast during the forecast period due to:

- Presence of generic manufacturers in this region
- Development of healthcare infrastructure
- Rising government initiatives and policy measures

Paediatric Regulations and Industry Adaptation



- Paediatric regulations enacted in the USA and Europe have affected the pharmaceutical and biotech industry, challenging the drug development processes and the organisational structures
- With science and innovation evolving, industry became proactive and invested in the set up of appropriate structures and capabilities to better handle the challenges and opportunities of paediatric drug developments
- Some pharmaceutical companies and contract research organisations have organised themselves to fulfill the regulatory obligations and optimise the paediatric drug development programmes

Pre-requisites for Safe & Effective Medicines for Children



Integration of paediatric aspects early in drug development is paramount

To make safe and effective medicines available for the paediatric population we need

- Timely development of evidence on the proper use of products in paediatric patients of various ages
- Specific tools, trial designs, methodologies, and adapted paediatric formulations
- To identify the patient population and its specific characteristics and medical needs, the environment where the medicine is likely to be used (e.g., hospital or community), the existing knowledge, and the medicine's acceptability/palatability

Paediatric Specificities

Paediatric studies require unique strategies that differ from adult studies

Considerations which must have paediatric-specific approaches to ensure study success:

- Study Protocol & Design
- Study Sites
- Recruitment & Retention
- Consent/Assent
- Investigational Product
- Formulation/Device Considerations

The evolution of paediatric regulations, a growing commitment to paediatric studies by sponsors, have increased demand for timely, high-quality, cost-effective paediatric clinical trials. To meet this mandate, will be required

- a sustainable research infrastructure, efficient regulatory processes and review systems, and a **knowledgeable workforce** able to
- generate robust data that can be used for regulatory approval, labeling of products for children, and decision-making in clinical practice
- address strategic, operational, medical and scientific challenges presented by the small, widely dispersed patient populations that characterize paediatrics

Rationale for Creating a Centre for Paediatric Clinical Development

Complexities of paediatric drug development

Paucity of available paediatric patients

Highly competitive therapeutic domains

Minimal financial returns on investment (the 6-month reward)

These elements have

- Hampered optimal investment and operational implementation
- Led companies to assess whether existing internal structures and processes tailored to address adult drug development were also fit for purpose to address the unique needs of paediatric drug development
- Led companies to evaluate whether centralising paediatric expertise will address a drug developer's organisational needs

Outcome: To address the challenges and opportunities of paediatric drug development, some pharma and CROs, have invested in building appropriate structures and capabilities as part of their business strategy, i.e., created a Paediatric Expert Group / Paediatric Centre of Excellence / Centre for Paediatric Clinical Development

Paediatric Centre - Optimisation of Drug Development



Before starting the clinical development of a compound, **guidance** should be sought from **paediatric therapeutic experts**, especially those with clinical research expertise

Close collaboration between adult and paediatric therapeutic experts is strongly encouraged to ensure **maximal alignment between the adult and paediatric programmes**

The centre for paediatric development can help ensure these collaborations are established in an effective and timely manner

Centre for Paediatric Clinical Development - Responsibilities



Support the process of paediatric drug development

Structure, roles and responsibilities of a paediatric centre vary depending on the company

Drivers and Role of Centre for Paediatric Clinical Development

Two main drivers for a company when establishing a paediatric centre

- First priority: Develop medicines for paediatric patients to fulfill unmet medical needs and reduce off-label use
- Fulfill regulatory requirements

A paediatric centre is to

- Enhance internal company functioning and
- Facilitate or establish interactions externally to enhance the quality and efficiency of paediatric medicines development, e.g., through
 - External paediatric research networks
 - Collaboration with academic institutions, public private partnerships
 - Collaboration with patients' organisations

Paediatric Centres – Differences between Companies



Survey among nine global pharmaceutical companies with established internal paediatric centres showed that the structures, roles and responsibilities, and scope of work deviates significantly from company to company

The range of structures spans from a **looser aggregation of subject matter experts** who meet on an ad hoc basis to **paediatric-specific departments** with governance function

The mandate varies substantially, with some paediatric centres having **consultative capacity** only, while others **have strategic ownership and full accountability** for the paediatric development programme (*from paediatric plan (s) to drug approval*)

Paediatric Centres Structures in the Pharmaceutical Industry

Pediatric infrastructure (Model)	Model 1 (Department like)	Model 2 (Medical chair)	Model 3 (Regulatory chair)	Model 4	Model 5
Ownership for the strategic plan of a pediatric program and accountability towards senior management	Pediatric development team (e.g., for specific pediatric indications such as oncology)	Adult project team	Adult project team	Adult project team	Adult project team
Pediatric Strategy across projects tasks ^b /Pediatric Portfolio management	Separate strategic team and portfolio management	Within core expert team	Within core expert team; portfolio management separate	Within core expert team; portfolio management separate	By project teams
Dedicated Pediatric Clinical Expert	Full time ^a	Full time	Full time (some indications part time)	Full Time (some indications part time)	Part time
Regulatory	Full time	Full time	Full time	Full time	Part time
R&D/CMC/Tox	Technical development team lead is part of core expert team	Separate, not part of core	Pharm Dev, DMPK part of core	CMC/Tox	Separate
Clin Pharm, Pharmacometrics and Biostats	Full time (Clin Pharm) in core expert team	Separate, not part of core	Full time in core expert team if focus is on quantitative functions ^c	Part time in core expert team	Part time in core
Other functions	Communication specialist, healthcare, law, finance, real world data, project manager in core team	None	Project manager, patent, and translational science in core expert team	None in core expert team	None in core expert team

^aFull-time employee; full to $\geq 50\%$.

^bE.g., pediatric biomarker; palatability; bio-distribution; extrapolation; adolescents in adult program.

^cQuantitative functions: Clinical Pharmacology, Pharmacometrics/Modeling & Simulation/Quantitative System Pharmacology, Biostatistics.

Factors Influencing Structure of Paediatric Centres

Company's portfolio influences size, mandate, and diversity of paediatric centre

- Companies with strong focus on oncology mainly opt for a structure where the paediatric centre is responsible for the programme strategy
 - FDA: RACE for Children Act; EMA: considers broader condition to require paediatric development

Paediatric development is in many companies part of the overall product strategy driven by the adult project teams

Key mandates of paediatric centres

- Provision of **specific expert consultative advice** on all aspects of paediatric development
- Collaboration with external academic experts and paediatric research networks, advice from regulatory bodies, participate to external paediatric initiatives that serve to keep the paediatric centre infrastructure up to date

Common to all paediatric centre structures

- An emphasis on **medical functions**, with expert paediatricians, appointed to the centre or working closely with the paediatric centres

Additional Common Functions in the Paediatric Centres



- **Regulatory Experts:** No consistency in the given role
 - Responsibility only for the paediatric strategy and interactions with the regulatory authorities
 - Actively engaged in shaping regulatory policy both specific to paediatrics and to other development topics such as e.g., access, pricing and reimbursement, or innovative analytics
- **Pharmacometrician**
 - Provide expertise in quantitative clinical pharmacology, clinical and nonclinical Modeling & Simulation, bioinformatics, Health Technology Assessment, and payer's evidence as well as in translational science
- **Clinical Operations:** An essential part of paediatric centres
 - Number of clinical operation experts and their level of dedication differs in whether they only support paediatric studies or are also responsible for adult clinical development programmes

Further Functions Appointed to the Paediatric Centres



Safety Experts: Included in some paediatric centres

- Others rely on the expertise provided by the project team or included in specific safety knowledge groups, e.g., to provide expertise on the impact on the liver, cardiac, or immune system

Nonclinical and Quality/CMC functions: Frequently included in the core paediatric centres although

- They may serve as part of a separate expert group, e.g., a nonclinical paediatric expert group, and functioning mostly through their respective project teams

Epidemiology, Real World Data, Legal Advice/Patent Experts

- Either included in the core of paediatric centres or consulted on an ad hoc basis

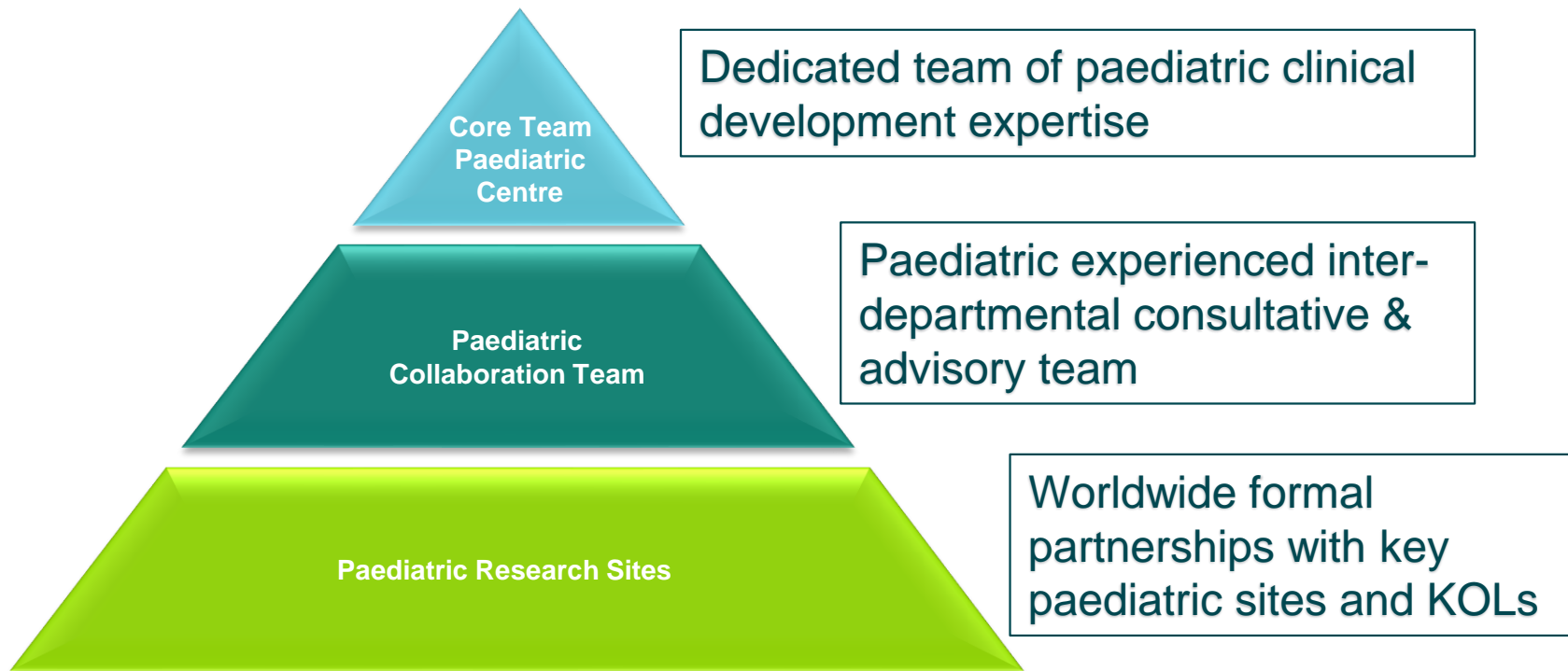
Example of Pharma Company “Paediatric Centre”

Johnson & Johnson’s ‘Child Health Innovation Leadership Department’

- A core paediatric department formed almost exclusively by paediatricians to guide the company’s paediatric portfolio
- Paediatricians act as key contact to
 - Principal investigators
 - External clinical experts
 - Paediatric hospitals
 - Medical societies
 - Paediatric research networks
- Paediatricians support other functions, where needed, on paediatric drug development, e.g., when it relates to policy, clinical plans, formulation



Example of CRO Centre for Paediatric Clinical Development



Paediatric Centres to be contacted Early in Drug Development



For most of the surveyed companies, it is mandatory to **reach out to the paediatric centres early for discussion on the paediatric drug development strategy** and review of regulatory documents such as Paediatric Investigation Plan (PIP), Pediatric Study Plan (PSP), or clinical study protocols; for others, such an approach is voluntarily

In most companies surveyed paediatric centres are used to develop **internal guidance documents**, best practice standards, and template documents and to provide **regulatory intelligence expertise** to help project teams designing their paediatric development programme

Recommendations for Paediatric Centre

No one type of paediatric centre works for all companies

Important success factors

A structure that is fit for purpose: ensure that the paediatric structure is designed to meet organisational needs and support the integration of paediatric aspects early in drug development

A cross-functional group for project team support and external network interface with a group chair, at least partially dedicated to paediatrics (full time or at least 20%) to ensure objectives are met

Senior management endorsement demonstrating a commitment within the company mindset to support paediatric development, not only as an obligation but also as an opportunity

Use the adult programme to better inform the paediatric strategy, e.g., support the development of an extrapolation concept, of an additional biomarker, or of paediatric clinical endpoints prior to their incorporation into the paediatric programme

Key Success Factors: Fit-for-Purpose Paediatric Centre

Questions to Address for a Fit-for-Purpose Paediatric Centre

1. What organisational culture change is required for the paediatric centre and the utility it may offer to be “bought into”? Is organisational information, advocacy, and training on paediatric needs required?
2. Is there a champion within the company’s management structure? Are they engaged and successful as an influencer?
3. What is the mandate for the individual paediatric centre?
 - Delivering on efficiency in regional regulatory requirements? <– >Driving innovation for paediatric drug development?
 - Is the mandate region specific or is it intended to address global paediatric drug development needs?
4. What function and role will the paediatric centre serve organisationally?
 - Internal consultancy to operationalize paediatric programme development?
 - Will the paediatric centre serve any governance function (e.g., sign off on strategic planning or protocol review)?
5. What composition is required to deliver on each organisational mandate? Clinical and clinical operations only or cross-functional programme strategy including e.g., discovery and technical development?
6. Are there critical foundational start-up activities that are required (e.g., paediatric data standards, paediatric assent templates, paediatric protocol templates) before the paediatric centre can focus its deliverables on the organisational mandate?
7. What is the resource commitment (personnel and financial) that is needed to credibly deliver the organisational mandate?
8. What are the deliverables the paediatric centre can credibly deliver to the organization in 1 year, 3 years, 5 years, or 10 years?
9. What is the estimated impact organisationally (e.g., efficiency, quality) and societally?
10. Is there senior management support?

Importance of a Paediatric Centre - Now and for the Future



Precision medicine and tissue agnostic development approaches continue to emerge, disease pathophysiology knowledge increases, hence, more opportunities will be seen in early phase development for investment in innovation for rare/ultra-rare paediatric diseases

Global markets continue to shift and impact investment in innovation, so it is becoming increasingly important for a paediatric business case to consider common paediatric morbid-mortality in the third world such as neonatal sepsis, childhood respiratory infections, diarrhea, malnutrition, or parasitic infection

A paediatric centre may be a prerequisite to be prepared for the new opportunities, and to meet any new demands

Conclusion

- Irrespective of how they are implemented, “paediatric centres” constitute a valuable resource for sponsors pursuing paediatric drug development
- “Paediatric centres” have been shown to provide value to project teams
 - They offer the opportunity to strengthen clinical research
 - They develop solutions for important issues
- Paediatric structures and expert groups are paramount to support optimisation of the development of paediatric medicines
- Companies who are not in a position to have their own paediatric centre can work with a paediatric centre from a contract research organisation for their paediatric strategy and paediatric development

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- **Consider paediatric development early in drug development**
 - **Liaise with “paediatric centre” early**



Thank You

For questions, please contact us:

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