i4KIDS EUROPE

i4KIDS-EUROPE White Paper:

Challenges and opportunities for effective paediatric innovation in Europe

eit Health

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EXECUTIVE SUMMARY

Paediatric innovation in Europe is significantly delayed compared to adult healthcare. New medicines are approved for children on average five years after their initial registration in adult indications. This delay affects a quarter of the population during life's critical phases of growth and development.

Children are our collective future; not sufficiently prioritizing the health and wellbeing of them has far-reaching consequences. Inadequately treated conditions that are not diagnosed or treated appropriately in children can result in long-term burdens on European healthcare systems and impair individuals' ability to fully participate as citizens and economic actors in our societies.

Fortunately, there are valuable lessons to be learnt from the examples we do have of successful paediatric innovation within the EU and beyond, which could help accelerate the integration of impactful solutions in children's healthcare in the future. Besides, the EU has been working to tackle some burden by implementing new regulations and fast-track processes in recent years; however, more needs to be done to achieve the desired impact and close the existing gap.

This White Paper, developed with insights from the i4KIDS-EUROPE consortium, provides an overview of the current landscape of paediatric innovation in Europe. It identifies the most difficult challenges faced by innovators and proposes a set of key recommendations, designed by experts, for overcoming them.

A clear call to action, supported by a detailed roadmap, is addressed to policymakers at both EU and national levels to boost the paediatric innovation ecosystem and ensure that the right technologies and care are available to all European children who need them.

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INTRODUCTION

BACKGROUND

Children's health differs greatly from that of adults. As a medical speciality, paediatrics deal with all aspects of development, wellbeing and illnesses from intrauterine life to the age of 18. Response to illness and stress varies by age, which is why effective treatment and care in the early years of life rely on strategic investment in adapted health interventions.

Childhood and adolescence are key life stages to achieve a healthy status and well-being in the long-term. Thus, reducing new-born, child, and adolescent morbidity and mortality remain key health priorities that all United Nations member countries have made a commitment towards.

Under the scope of the Sustainable Development Goals and the United Nations Secretary-General's Global Strategy for Women's, Children's and Adolescents' Health (2016–2030), member countries have agreed to engage in a transformative multisectoral action to improve the health and well-being across all ages, with innovation and partnerships as key levers to achieve this mission.

Research and Innovation in paediatric health is critical to ensure that children, regardless of their age, health condition, socio-economic situation, or place of birth, have access to the life-changing healthcare solutions they need to grow up stronger and contribute to a better society. To this extent, the development of efficient and sustainable paediatric healthcare relies on innovation.

However, paediatric innovation remains underemphasized in Europe and has opportunities potential for greater focus.

THERE ARE TWO MAIN CAUSES FOR THIS

1 A LACK OF SPECIFIC SOLUTIONS FOR CHILDREN

In Europe, health innovation still tends to focus more on the elderly than the young. This can mean that some young patients miss out on life-saving interventions, while others are treated with the **standard of care for adults, adapted ad hoc by their clinicians.** Due to limited options, clinicians must adapt innovation to children's needs – for example, by introducing adult-sized devices such as pacemakers into children's body – leading to poorer outcomes[i] for paediatric patient compared to adults.

The lack of suitable products for children often leads to off-label use[ii]. This means that products are used outside their approved indications, which typically exclude the paediatric population due to the absence of clinical studies assessing their safety and feasibility. The new Medical Device Regulation (MDR) currently active in Europe, can prevent manufacturers from utilizing off-label data to develop and market paediatric-specific sizes or versions of devices. As a result, adult devices and drugs are frequently adapted for use in children, despite lacking robust safety and efficacy data to support such applications.

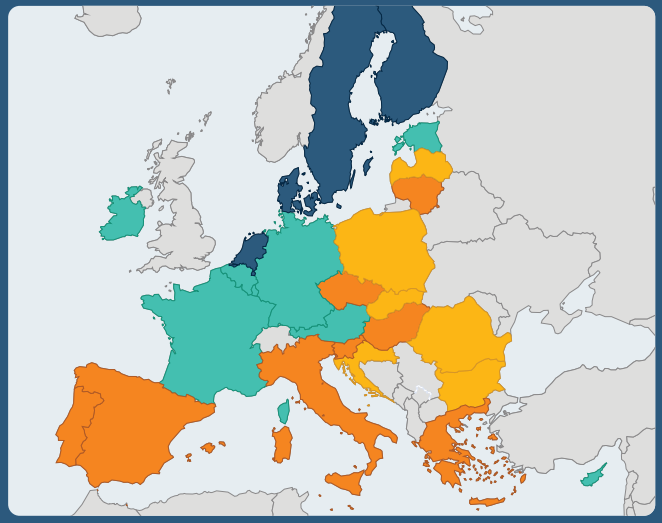
These inappropriate approaches to children's healthcare needs not only limit access to safe and effective treatments but also contribute to unnecessary anxiety and stress for young patients and their families.

2 A FRAGMENTED PAEDIATRIC ECOSYSTEM ACROSS EUROPE

One of the main reasons for the slow pace of paediatric innovation is that actors are scattered in a fragmented ecosystem across Europe.

Currently, innovation in the EU is driven by a few leading regions, creating a gap with moderate and emerging innovation ecosystems that lack the means to contribute extensively to progress in paediatrics *(European Innovation Scorecard).* This fragmented landscape leaves **best practices unshared and collaboration opportunities untapped,** to the detriment of all stakeholders. Limited connections among innovators, investors and regulators hinders the development of effective solutions to address unmet child health needs.

While a few sector-specific initiatives have been implemented with some success such as *ECHO* for children's hospitals and *c4c* for clinical trials, paediatric innovation needs to be pushed harder to break down barriers and unlock existing opportunities that supports health equity across all EU members.



THE EU NEEDS TO PLAY A KEY ROLE IN BOOSTING AND SPEEDING UP PAEDIATRIC INNOVATION

i4KIDS-EUROPE is a European paediatric network for innovation funded by the European Union and led by Sant Joan de Déu Barcelona Children's Hospital. Established in 2023, it builds on the successful national i4KIDS initiative in Spain and is expanding its activities across Europe to strengthen their collaboration and bring new paediatric solutions to the European market. This consortium of eight multidisciplinary partners from five different countries stands for Inclusive and Interconnected Ecosystem to Boost Paediatric Innovation in Europe (i4KIDS-EUROPE) and aims to connect, enhance and promote a European paediatric ecosystem. It is made up of:

- *Sant Joan de Déu Barcelona Children's Hospital (Spain)*
- *Children's University Hospital Latvia (Latvia)*
- *HUS Helsingin yliopistollinen sairaala (Finland)*
- *Rigshospitalet, Mary Elizabeths Hospital (Denmark)*
- *K.I.D.S. Children's Hospitals Innovators' Club (Poland)*
- *Inveniam Group (Spain)*
- *EIT Health Spain (Spain)*
- *Fundació de Recerca Sant Joan de Déu (Spain)*

i4KIDS-EUROPE aims to improve children's health across healthcare settings by creating an efficient, sustainable and inclusive European paediatric innovation ecosystem that integrates all relevant stakeholders from emerging, moderate and strong innovator countries. Enabling synergies, preventing redundant efforts, and offering the necessary services and resources to improve the paediatric innovation capacity of the EU Member States, i4KIDS-EUROPE stimulate Europe's competitiveness and economic growth in this area and directly impact the health of European societies today and in the future.

Katariina Gehrmann
Director of Digital and Innovation Services, Department of Children and Adolescents at HUS (Finland)

"i4KIDS-EUROPE is an excellent initiative to support innovation within paediatrics. We need to work together to ensure that the barriers hindering innovation and research in paediatrics are tackled. Children are our future – as adults, we have the responsibility to support children on their growth journey."

OBJECTIVES OF THIS WHITE PAPER

This White Paper compiles the many insights gathered in the course of the i4KIDS-EUROPE project (2023-2024) and proposes a clear roadmap towards a pan-European paediatric ecosystem, including actionable recommendations for all stakeholders who can shape the implementation of new policies and tools to pave the way for a more efficient paediatric innovation: regulatory agencies (e.g. EMA), funding bodies (e.g. European Innovation Commission, investors), European umbrellas organisations (e.g. EFPIA, Medtech Europe), among others.

EXPECTED ACTIONS THE WHITE PAPER SHOULD TRIGGER:

Boost Public Funding dedicated to paediatrics while raising awareness about the need for private investment as a societal impact for the future of the society.

Develop incentives for companies investing in paediatric solutions, promoting Open Innovation and education programs to enhance collaboration and visibility in children's health.

Facilitate the peadiatric regulation navigation by implementing fast-track and adopting best practices from across Europe and beyond.

Foster a strong culture of paediatric innovation in hospitals by allocating more resources, particularly in moderate and emerging countries, while strengthening exchange practices with the EU ecosystem.

APPROACH

This White Paper will be structured around two sections:

Diagnosis: From key data on the specificities of paediatrics to opportunities and successful initiatives facing similar challenges, we are proposing a landscape of paediatric innovation in Europe. The analysis builds on the work of i4KIDS-EUROPE, which includes a needs and challenges assessment report based on questionnaires and interviews with emerging and leading innovators in Europe, as well as deep-dive working groups with experts.

Call to action: Designed as a clear roadmap for decision-makers, this section will propose key measures in the form of actionable recommendations for creating a more competitive European paediatric innovation market and making a meaningful, lasting impact on children's health.

Please note that this White Paper focuses on innovations that benefit paediatric patients, encompassing both medicines and medical devices. While we combine these two industry sectors in our call to action, we fully recognize the fundamental differences in their development processes and pathways to market, including distinct legislation, clinical trial requirements, HTA assessments, and reimbursement frameworks.

LIMITATIONS

This White Paper reflects the information and views gathered from all actors involved in i4KIDS-EUROPE, acknowledging that some stakeholers may be underrepresented. The analysis is based on the current state of paediatric innovation and seeks to respond to the ecosystem's needs. Consequently, current regulation it should be periodically reviewed to integrate evolving challenges, rapidly advancing technology, and changing frameworks such as the ongoing revision of the EU's legislation.

CHAPTER 1

THE CURRENT LANDSCAPE OF PAEDIATRIC INNOVATION IN EUROPE

The history of paediatric innovation in Europe is marked by major advances driven by both the public and private sectors, such as the introduction of crucial vaccines (i.e. meningococcal B) or better neonatal intensive care units that have seen their mortality rates drop thanks to better technologies and public policies.

Notwithstanding these breakthroughs in improving children's health, paediatric cancers, respiratory diseases and a rising prevalence of mental illness remain serious, even vital threats to children and adolescents' health that need to be more effectively addressed.

1.1 EXISTING GAPS IN PAEDIATRIC INNOVATION

ACCESS TO PAEDIATRIC MEDICINES

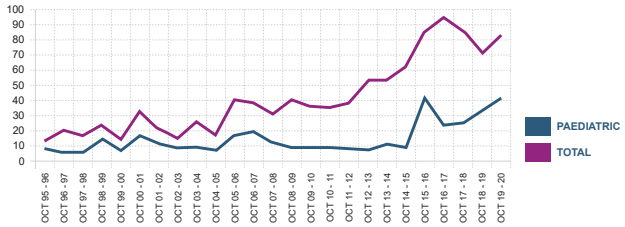
Significant progress over the past decade has led to safer, more effective drugs for children. Regulatory initiatives like the EU Paediatric Regulation and the US Pediatric Research Equity Act have also encouraged greater focus on developing medicines specifically for young patients.

However, many drugs are administered off-label, with approximately **50% of off-label medications used in children**[iii], reaching around 90% for newborns in ICU[iv], despite not being specifically tested or approved for pediatric indications. This can lead to dosing inaccuracies and the increased risk of side-effects or reduced efficacy that come along with them, thus compromising the safety and health outcomes of paediatric patients.

Progress has been made in recent years, as over **260 new medicines were authorized**[v] **for use by children in the EU between 2007 and 2016**, along with 43 new paediatric-appropriate dosage forms. In **2020 alone, 41 new medicines were approved for use in children.**

- The obligation created by the EU Paediatric Regulation to submit a Paediatric Investigation Plan (PIP) with any new drug approval application contributed significantly to improving the availability of paediatric treatment options and consequently reduced off-label use. By 2017, more than 1,000 PIPs had been agreed upon, indicating a clear upward trend, with 60% of them finalised between 2015 and 2017.
- Accordingly, the number of clinical trials in paediatrics has **increased by 50% (2007-16) and now represents 12% of all clinical research.**
- Despite these positive trends, a 10-year report from the European Commission indicated that the increase in available medicines for children was only in the range of 5-10%[vi] for children. Particularly in therapeutic areas such as oncology and neonatology, challenges remain and developments for children are still insufficient.

MEDICINAL PRODUCTS AUTHORISED BY EMA DIVIDED BY YEAR (OCT. 1995 - OCT. 2020) [vii]



In the US, from 2007 to 2023, 180 drugs were granted paediatric exclusivity, with 15 of these designations awarded in 2023. Over the same period, 929 labelling changes were made for drugs now available for paediatric use. (i.e. new paediatric indications or the addition of safety and efficacy data).[viii]

- Today, the time interval between a medicine's initial approval in adult and its approval in paediatric indications is estimated at 5 years in the European Union, versus 9 years on average in the US.[ix]

ACCESS TO PAEDIATRIC MEDICAL DEVICES

There is a **significant lag in the development of children's medical devices,** compared paediatric drugs, with also very few medical devices in orphan devices (for rare diseases). Therefore, off-label use For instance, pediatric cardiology often relies on the off-label adaptation[x] of adult devices to meet the clinical needs of children. Experts argue that lack of profitability and high development costs are major barriers[xi]. Paediatric patients are continuously growing, and rapidly, so the device must be adaptable in size to suit a wide age range. This presents a significant challenge and limits the devices that can be used. Meanwhile, many patients and families express a **substantial unmet need for new paediatric devices for their conditions.**
Children suffer from this limited access to medical devices, as evidenced by the fact that the US Food and Drug Administration (FDA) approves **far fewer health technologies for use in children** each year than for adults:

59 premarket device applications were approved for paediatric use in 2021[xii]. This means that paediatric specialists do not always have access to the advanced tools they need to address the unique healthcare needs of their young patients.

The situation is arguably even more challenging in Europe and faces significant gaps. While the FDA has been reporting the number of devices approved for paediatrics since 2008, there is **no data available about how many medical products** (biotech, pharmaceutical, digital or medtech) **have entered the EU market with a specific paediatric indication** in the last years.

The average delay in the approval of medical devices in paediatrics compared to adult care is also considerable. In the US, it is estimated that the **availability of paediatric devices are about 10 years**[xiii] **behind the standard of care for adults.**

INEQUITIES IN FUNDING AND SOLUTIONS ADOPTION IN PAEDIATRIC HEALTHCARE

Significant disparities in access to paediatric healthcare services exist across Europe. An important reason for this is the underinvestment in commercialisation and adoption of new solutions for children, especially in countries with moderate and emerging innovation ecosystems. These inequities lead to delayed diagnosis and treatment, poorer health outcomes, and increased morbidity and mortality among children.

INVESTMENT IN PAEDIATRICS

1.6%
of total venture capital in US healthcare

Investment in paediatrics is not only heterogeneous across different countries, it is also insufficient overall. In the US, for instance, only **9.4% of the total funding** provided by the National Institutes of Health (NIH) is allocated to paediatric research, although children represent 25% of the global population.

In the private sector, venture capital in paediatric healthcare innovation has declined over the past decade, accounting for just **1.6% of total venture capital investment in healthcare in the US**[xiv] in 2020. Pharmaceutical development of medicines for paediatric use continues to represent a minority when compared to the population that paediatrics represent.[xv]

Janene Fuerch
Paediatrician & Co-Director at Stanford Impact 1 (USA)

"Industry spends more money to develop health technologies that address the last month of life than on technologies that can transform a lifetime"

START-UPS

188
European start-ups

Start-ups are key actors in any innovation ecosystem and their need for investment is particularly acute in the healthcare sector, where the commercialisation of new solutions relies on the development of prototypes, feasibility analysis, and the conduct of clinical trials. Despite limited data and difficulties to identify "paediatric-only" start-ups, we nonetheless identified as many as **188 European start-ups** (November 2024) that focus on developing healthcare solutions for children.

COMPARISON OF PAEDIATRIC INNOVATION LANDSCAPE IN DIFFERENT ECOSYSTEMS: EU, US AND ISRAEL

	EU+UK	US	ISRAEL
Number of paediatric startups*	188	250+	46
Start-ups per million kids	1,4	3,42	17,6
Investment in paediatric innovation	N/A	N/A	$193M
Drugs approved for paediatric use	41 (2020)	15 (2023)	N/A
Approved medical devices for children	N/A	59 (2021)	N/A
Healthcare spending (% of GDP)	10,9%	18%	8%

** According i4KIDS-EU consortium database in November 2024 – it can be partial in some cases.*

ADOPTION

20%
Adoption in children's hospital

The adoption of paediatric innovations by hospitals is another area in need of support. According to a survey of European healthcare professionals, only **22% report having access to the latest paediatric medical devices and technologies.**[xvi]
The situation in paediatric imaging illustrates the lack of investment in children, resulting in poor uptake and missed potential solutions for children: while approximately 800 AI imaging tools have been approved by the FDA, **only 20 have regulatory approval for kids.**[xvii] Of those without paediatric approval, over 80% could be beneficial for children.[xviii]
Children are no little adults and have unique needs - AI tools designed for adults often fail or perform poorly when applied to paediatric cases.

1.2 MAIN STAKEHOLDERS IN PAEDIATRIC INNOVATION

THE ESSENTIAL FAMILY'S ROLE IN PAEDIATRIC PATIENT-CENTRIC HEALTHCARE

The role of paediatric patients and their families in health research should be considered an integral part of the research and innovation process, with opportunities for them to be a partners and play a meaningful role. Their involvement can begin with identifying unmet medical needs and continue through the various phases needed to bring innovative solutions to market.

Despite widespread recognition of the value that children, young patients, and their caregivers add to paediatric innovation, this involvement is still not standard practice. The European Clinical Trials Regulation (No. 536/2014) encourages patient involvement in clinical trial protocol design (Annex 1, Article 17, Section e), as well as the Medical devices clinical investigations (MDR article 62) and requires research teams to provide evidence of patient input within the dossier submitted to regulatory agencies.

In recent years, several initiatives have been established that now enable a meaningful and ethical involvement of children, young people, and caregivers in health research. Two notable examples include Connect4children, a pan-European clinical trial network funded by the Innovative Medicines Initiative (IMI), which provides the logistical and operational structure for multi-country health research initiatives; and eYPAGnet (European Young Person's Advisory Groups Network), a network of experts in paediatric patient involvement, founded in 2017, with over 15 experts and more than 30 youth advisory groups across Europe.

Involving children is essential for designing patient-centred innovation. Their contributions must be guided by experts and uphold ethical principles and children's rights at all times. Health innovation demands a shift to frameworks that place the patient at the centre and ensure their meaningful contributions. I4KIDS promote these frameworks to drive real progress in paediatric innovation.

In addition to the vital role of families in paediatric innovation, other key stakeholders significantly contribute by establishing regulatory frameworks, developing robust research infrastructures, or fostering collaboration. Numerous parties, including caregivers, clinicians, therapists, schools, payers and policymakers, must coordinate across various organisations to ensure children's health and safety throughout various life stages.

STAKEHOLDERS MAP OF MAIN PLAYERS IN PAEDIATRIC INNOVATION IN EUROPE

"It really does take a village to raise a child"

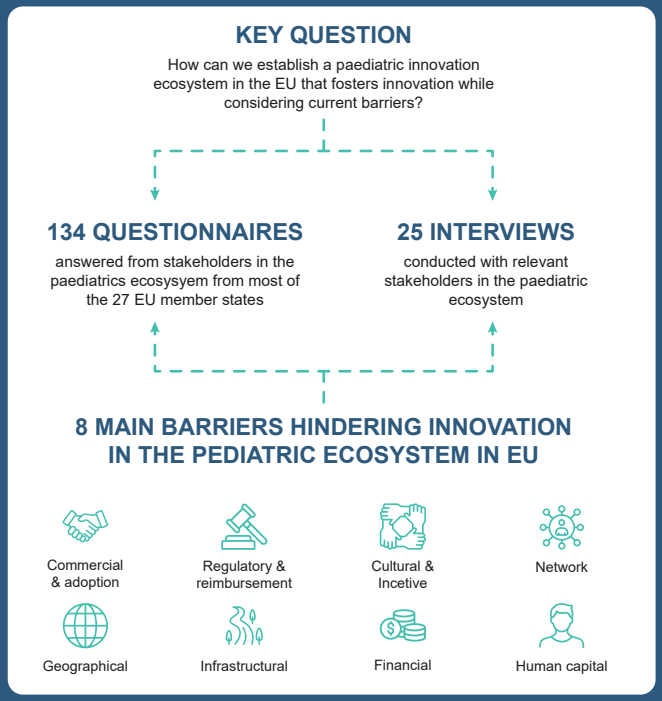
METHODOLOGY

EUROPE PAEDIATRIC INNOVATION SITUATION REPORT AND NEEDS ANALYSIS

ANALYSIS

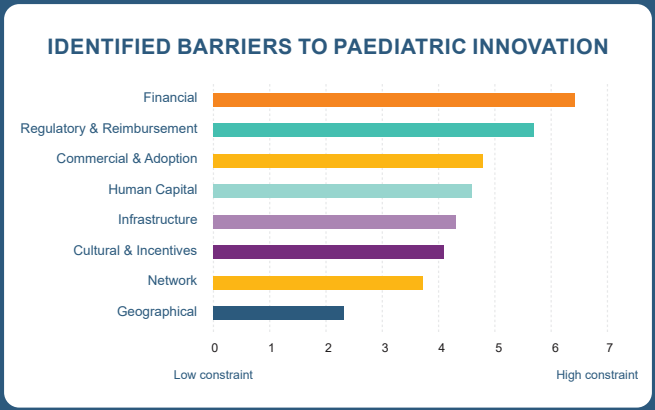
The first milestone of the i4KIDS-EUROPE consortium was a fact-finding effort to diagnose gaps and identify barriers, reflected in *"Europe Paediatric Innovation Situation Report and Needs Analysis"* published in March 2024.

This large study was undertaken on the basis of a questionnaire answered by 134 diverse stakeholders (32% of healthcare providers, 25% of start-ups, 20% research institutions, 7% of large companies, 7% of patient organisations, 5% of investors and 4% of government and regulators) at a European level and completed by 25 in-depth interviews with key actors of paediatric innovation to better understand the barrier faced by each respondent's stakeholder group and also depending on its level of innovation he is evolving.



RESULTS

Based on the results obtained, it became apparent that the paediatric innovation ecosystem faces several barrier that have yet to be overcome, as evidenced by the numerous barriers perceived as an high obstruction to innovation.



Our findings revealed a broad consensus on the barriers to pediatric innovation, indicating an unmet need at the European level that prevents the ecosystem from operating at full capacity. Highly innovative regions, compared to emerging countries, prioritize certain obstacles to innovation differently. The in-depth interviews offered valuable insights:

- The **key barriers are financial and regulatory.** Europe-wide support and solutions should be considered to overcome these and create a new framework.
- **Commercialisation, reimbursement and adoption are perceived as an additional pain point,** especially for paediatrics start-ups and industry that encountered hurdles in developing their solutions due to the delays in gaining market access that affect their competitiveness compared to bigger markets with unified frameworks.
- **Human capital is perceived as significantly more important in lower innovation areas** than in leading innovation areas. Interviews emphasised the importance of commercial skills for healthcare providers to shift mindsets towards innovation. Similarly, infrastructure barriers are more important in lower innovation regions, where IT systems and data sharing within hospitals may still be underdeveloped.
- While network barriers are not considered as a key impediment, networking was cited by many interviewees as potential solutions to overcome other barriers.

DELVING DEEPER INTO THE STATE OF PAEDIATRIC INNOVATION: THE EXPERT WORKING GROUPS

Despite the broad range of responses from participants in the report, there was consensus on the need for further exploration of the impediments and potential solutions within the innovation ecosystem. This holistic approach should expand the pool of participants in terms of stakeholder groups and geographic diversity. Consequently, the formation of specialised working groups was necessary to delve into the roots of these challenges and develop effective strategies to address them.

OBJECTIVES & APPROACH

The working groups aimed to formulate a series of recommendations addressing the four major barriers of the ecosystem. Composed of 68 leading experts, each group engaged in open discussions, focusing on critical aspects essential to shape the future of paediatric innovation in Europe, such as funding, regulation, commercialisation, and human capital. They focused on establishing priorities, identifying necessary resources and outlining actionable steps to transform current hurdles in tomorrow's opportunities.

CHAPTER 2

DIAGNOSIS AND RECOMMENDATIONS

This section outlines the roots of the challenges existing in paediatric innovation and offers potential solutions and recommendations to improve the situation at a European level. It highlights numerous successful initiatives that have been launched on various scales, within and outside of Europe, alongside unsuccessful endeavours, to distil lessons learned and best practices. Actionable recommendations are proposed for overcoming each individual hurdle.

2.1 AVAILABLE FUNDING FOR PAEDIATRIC INNOVATION

FINANCIAL BARRIERS

Financial barriers are the main hurdle for paediatric innovation, due to the specificity of the funding in the sector: a large part of paediatric innovation in hospitals has historically been funded by donations from philanthropists. Unfortunately, this funding does not provide sufficient support on the commercial side for start-ups from origin to exit. There is an overall lack of available money from the buy and sell-side in the paediatric innovation ecosystem, signaling a strong need for an injection of cash.

There is an overall scarcity of financial resources on both the buy and sell-side of the paediatric innovation ecosystem, signaling a strong need for an injection of cash (public, but also private with only 1,6% of total venture capital investment in healthcare invested in paediatrics in 2020).[xix]

Securing funding is a well-known burden for start-ups, research institutions and healthcare providers, all of whom have less access to financing than large companies. 89% of interviewees from the situation report stated the difficulty in obtaining financing for early-stage projects in paediatrics, from both public and private funding sources.

As described by **WHO** *Global reproductive, maternal, newborn, child and adolescent health policy*

"Investing in children is one of the most important things a society can do to build a better future"

FUNDING SYSTEMS

BARRIERS	SUCCESS CASES	RECOMMENDATIONS
PUBLIC FUNDING		
Lack of public funding and gap of specific calls for paediatric innovation: Public funding is present in Europe, but on general calls, that are not dedicated to paediatrics. The unique needs of children have been underrepresented in the Framework Programmes of the EU one year more. To date, only two calls have specifically targeted children under Horizon Europe in Cluster 1 (Health). [xx] Most national and European grants are targeted at health conditions with society-level prevalence (e.g. obesity and cardiovascular disease), making them difficult to access for innovations designed for the smaller paediatric population. Within the scope of more general grants (e.g., medtech, digital or pharmaceutical innovations), paediatric healthcare solutions can be eligible. However, competing within more general categories against solutions targeted at the adult population creates similar problems. Thus, there is a clear gap in specific public funding allocated to paediatrics. **Underfunding of some steps in the innovation process (TRL 3-5):** Steps in the development pathway that appear underfunded are the proof-of-concept and prototyping stages. This leads to difficulties in turning an idea to a viable product, scaling up and attracting private funding to actually reach patients. Innovative companies end up failing in this "Innovation Valley of Death".	**PEDIATRIC DEVICE CONSORTIA (PDC) GRANT PROGRAM[xxi] (US):** The PDC program is a funding initiative by the FDA, existing since 2009, to support the development of medical devices for children. Paediatric devices often represent a smaller market segment, which can discourage investment from the medical device industry. The PDC helps to mitigate these risks by providing financial, logistical, and expert support to encourage practical innovation, directly beneficial to patient care. Besides, the PDC also **provides critical funding ($6.75 million** for 5 years, approximately **$1.5 million per consortium**) to fund advancements in paediatric medical devices. For 2023-2027, the PDC have funded 5 different consortia over the US. These consortia, once selected by the FDA, offer **expertise and support to innovators and companies** by assisting in device development, including prototype development, clinical testing, commercialization strategies and navigating FDA approval process. These awards include commitments to improving clinical trial infrastructure, advancing diversity and health equity as well as real-world evidence. **Outcomes:** Since 2009, the PDC has supported over 1,000 medical device projects, resulting in 26 pediatric devices reaching patients by 2023.	Increase focus on paediatrics at all levels of fundings: • **Support the creation of paediatric-specific Research & Innovation (R&I) calls.** • **Set-up an intermediate financing system** to bridge the gap once grant public funding has ended, to allow successful project's implementation. Despite often receiving less attention than the initial discovery and innovation stages, this stage a determinant of success and is key to reach final users with activities such as stability testing, scaling up production, ensuring the product is actually viable in the proposed environment, etc. • **Articulate new private investment funds at a EU level. Generate incentives such as** tax breaks for funds that earmark funding for and more grants for private companies supporting research in the paediatric space. • **Implement a European PDC,** replicating the Paediatric Device Consortia Grant Program of the FDA, selecting specific children's hospitals across Europe that could benefit from funding and support for medical devices.

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS
PRIVATE FUNDING		
Perception of a small market with lower Return On Investment (ROI): Private funding is clearly under-invested in paediatrics, as investors see projects in this field as having a higher risk-reward ratio and longer timelines. Investors have often been uninterested in paediatrics due to the business model: the perception of a small market with complexities in the regulatory pathways compared to adult products, make it as more risky to ensure a high ROI. In general, there is simply a lack of private paediatric-focused funds, with only about a dozen funds that are actively investing in paediatrics (in Europe and the US combined.) **Comparison to the adult market:** Investors are reticent to enter the field of paediatrics due to its smaller market, more complex clinical trials, and more stringent regulatory pathways. Most investors typically prioritise dual-focus technologies that apply to adults first and children later, but this often results in a maladaptation to children's needs. HCPs that serve both adults and children prioritise their internal budget for what they consider the larger need (usually adults). The same happens in industry: companies with diverse product portfolios struggle to internally defend a paediatric business case when competing for the same budget as adult products. **Lack of flexibility of fundraising rules:** Paediatrics has often been crowdfunded, receiving money from individuals that seem to have more emotional connection to paediatrics than traditional investors. However, fundraising is subject to strict rules that do not allow "crowd-like" funding, meaning that individuals or organisations willing to invest need to be registered as "investors" in order to join a Venture Capital (VC) fund. Likewise, it can be legally challenging for non-profit organisations to invest directly into ventures and seek a ROI. This hinders investment by actors that would otherwise be candidates for investing in paediatric innovation as they are more likely to be driven by a social mission than many VC funds that merely seek economic ROI.	**EXISTING INVESTORS IN PAEDIATRICS:** **Montana Impact Fund (EU):** The private equity firm Ship2B Ventures, Dr. Marc Ramis and Sant Joan de Déu Hospital together created the Montana Impact Fund dedicated to paediatric health. The fund has a first round of €30M to invest in start-ups, either in early-stage development or more mature, which are currently working on the prevention of childhood illnesses, developing personalised treatments for paediatric patients or promoting solutions to improve the quality of life and monitoring of side-effects in children who have overcome disease. This kind of venture provides another investment model beyond the traditional path for paediatric healthcare. **Thinking of Oscar (UK)** mission is to 'Bring the Future of Healthcare to Children', through the funding of innovative projects that focus on improving the experiences of sick children.	• Make a **European priority for investing in the first years of life** and incentivize the gatekeepers (funders, industry and academic Technology Transfers Offices (TTOs) to promote solutions for paediatric indications, conveying the message that healthy children become healthy adults, and that this benefits all of society. • **Create more flexible rules for fundraising in paediatrics** that could include individuals, families and philanthropists to increase the diversity of the investment pool. Standalone investments should be facilitated to allow easier fundraising. • Encourage **early stage merging of projects,** if possible, before companies are created, or shortly thereafter. This would optimise the use of resources, reduce duplication of efforts pursuing comparable solutions and improve the quality of deal flow for investors.
MINDSET SHIFT TOWARDS IMPACT FUNDING		
Low ROI in paediatrics comes from a lack of social impact measurement. The limited market size, less competitive business cases and competition with the adult market make paediatrics appear less economically attractive: for companies, establishing a new commercial division requires substantial investment and paediatrics does not offer promising returns. **The core issue in paediatrics is the prevailing mindset:** financial returns are frequently prioritised over social impact. Paediatrics needs to shift towards emphasising social impact to improve KPIs, making the field more attractive to investors and promoting greater commercialisation and social impact.	**NATIONAL SOCIAL BONDS (UK)** National social bonds are considered a best practice in risk-sharing, as an instrument to fund a need that a hospital can have. It is focused on value-procurement and provides an alternative purchasing framework: for instance, it focuses on the success of avoiding adverse events in children, rather than on the number of visits of the patient to the hospital. **Social Impact Bonds (SIBs)** are innovative financial instruments designed to fund public projects through private investment. They aim to achieve positive social outcomes and cost savings for governments. These bonds allow private investors to finance projects that address social needs, and if the projects meet predefined outcomes, the government repays the investors with a return on investment. The UK pioneered the SIBs model in social sectors, launching the world's first **SIB** in 2010. In healthcare, several SIBs have been implemented targeting different areas, such as in mental health services. They have been funding interventions that support people with mental health issues, reducing the burden on the healthcare system and improving patient outcomes. The UK's success with SIBs stems from a supportive ecosystem of government support, experienced intermediaries, and a well-established community investing in impact.	• **Launch a social impact bond initiative in paediatrics** to address a social unmet need, with a mix of public and private funding through a competitive call. • **Shift mindsets away from seeking immediate returns,** towards emphasising long-term value and cost reduction through paediatric innovation (provide data on cost savings over time). This shift should also include adopting value-based pricing models that integrates the outcomes and benefits of paediatric innovation, generating evidence. • **Launch working groups on ways of measuring health economic outcomes** and how to measure the results of actions in preventive care.

LACK OF AWARENESS OF PAEDIATRIC PROJECTS

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS

PAEDIATRIC PROJECTS ARE PERCEIVED AS RISKY AND SUCCESSFUL CASES ARE LACKING VISIBILITY

Lack of visibility of paediatrics success cases:
Paediatric innovators are challenged in conveying the high need and large potential societal impact given that the paediatric population appears as small, segmented by the high number of paediatric diseases, with a minimum of 7000 rare paediatric diseases. Indeed, there is a perception that paediatrics projects are too risky compared to adult projects. This perception is potentially due to the shortage of paediatrics success cases existing in Europe that is creating less argument to convince VCs for a first investment. Successful projects in paediatrics exist in Europe, but they are suffering from a lack of visibility that is not empowering and pushing the paediatric market forward.

New investment theme for Venture Capitals: Although impact investing is gaining traction, paediatrics is still a relatively new investment theme for VCs. It takes time to gain awareness from the investors' point of view and to see the reward that investment in paediatrics can bring to improve children's life. Industrial (corporate VCs) funds better understand the impact of paediatrics but are still few players in the market.

The **Patient Innovation platform** is an online community where patients, caregivers, and healthcare professionals can share and develop innovative solutions for health challenges. It connects users to collaborate, provides resources and support for advancing ideas and encourages feedback to improve solutions. The platform aims to empower those with firsthand health experience to contribute to better patient care globally.

• **Create a collaborative platform/data sharing initiative** that collates all paediatric related opportunities e.g. funding calls, relevant investors, success cases, networking events to match different stakeholders (like Patient Innovation). This digital infrastructure in which local, regional, and national (potential) projects could be shared would provide oversight of the ecosystem and maximize synergies with limited resources. Private investors could see first-hand the success of investment in paediatric innovations, strengthening the validation of such innovations, and connect with start-ups from emerging innovation regions.

• Identify **Champions and promote paediatrics as an investment area,** highlighting its potential for societal impact. This could include the identification and support of large companies interested in investing in pediatric healthcare, helping to raise visibility and drive momentum in the sector.

• **Involve hospital-specific programs for investigator-initiated paediatric studies,** as a good opportunity for nonprofits/foundations to support a company. Legally, it is often easier for these groups to fund hospitals working on early or clinical-stage innovation rather than investing directly in a company.

TRAINING NEEDS FOR PAEDIATRIC INNOVATORS

LACK OF KNOWLEDGE ON PUBLIC AND PRIVATE FUNDING

How to win a public grant as a paediatric-start-up:
Questionnaire respondents highlighted that a better leverage and knowledge of EU R&I funding programs is extremely relevant for early-stage innovation projects, typically housed within research institutions, healthcare institutions or start-ups. This inability to access funding stems from two sides: (i) lack of awareness of paediatric grants; and (ii) lack of knowledge, experience, and support in how to successfully apply for such funding. While paediatric and R&I grants might exist, their accessibility is not effectively communicated to the relevant stakeholders in emerging innovation groups.

How to build an attractive business case and prepare for fundraising:
Investors don't always see value in paediatric business cases in terms of economic rewards. There is a need to learn how to build a business plan that is sustainable and attractive for both public and private fundings, while including the social impact.

EIT Health Innovators Community Mentors and Coaching Network is a european leading pool of over 200 healthcare industry experts, in any topics. A specific pool for paediatric mentors has been built and identified as part of i4KIDS-EUROPE project.

The Green Room is a free space for founders to practice their pitch, risk free, in front of current investors and subject matter experts. A panel provides advice, answers questions and highlights areas of opportunities to gain confidence and help innovators/start-ups to prepare for fundraising.

Agency for the Promotion of the European Research in Italy (APRE)
Horizon Europe colaborative with National Contact point, such as APRA in Italy. This network has been appointed by the European Commission to provide free-of-charge assistance for the participation in the EU Framework Programmes for R&I.

• **Build support systems for scouting and writing R&I grant proposals,** for both paediatric-specific grants or best presenting a paediatric innovation in a non-paediatric grant (i.e., strong market, high impact).
This would include training modules to help innovators effectively articulating their value proposition when applying for funding, upskilling their business case modelling and integrating the standard of care vs. the innovative solution value.

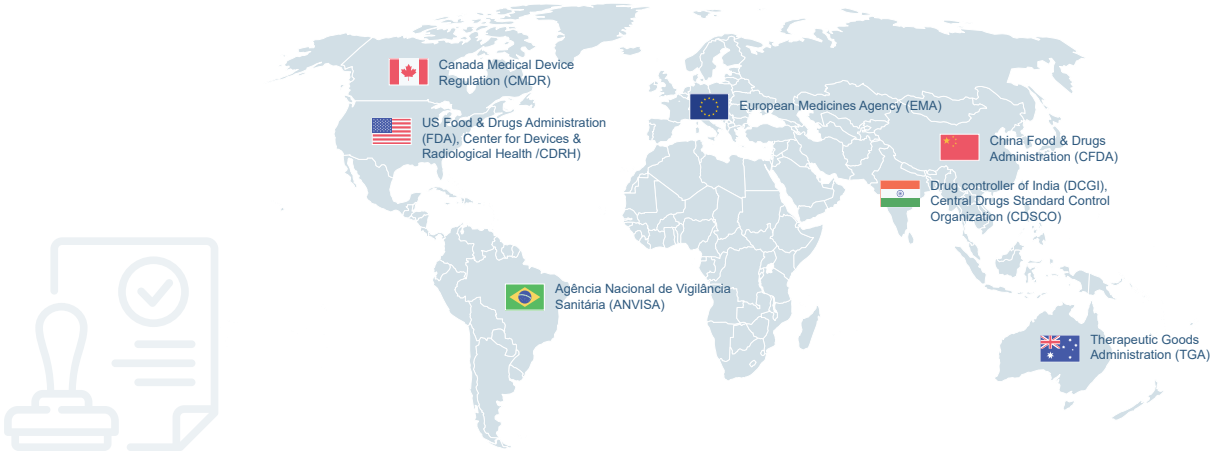
• **Mentorship for start-ups in paediatrics** to better understand the requirements of private investment and how to create a proper business plan, such as pitching opportunities e.g. the Green Room.

2.2 REGULATORY PATHWAYS FOR PAEDIATRIC INNOVATION

REGULATION FRAMEWORK IN EUROPE AND BEYOND

GLOBAL REGULATORY FRAMEWORK AND APPROACHES TO PAEDIATRICS

The regulatory landscape for paediatric medicines and medical devices is shaped by various international agencies, each adopting unique strategies to ensure safe and effective diagnosis and treatments for children. Key global players include the US Food and Drug Administration (FDA), the European Medicines Agency (EMA for medicines), the European Comission)Notified Bodies for medical devices) and the World Health Organization (WHO), among others.



UNITED STATES (FDA)

The FDA mandates specific paediatric studies through initiatives like the Pediatric Research Equity Act (PREA) and the Best Pharmaceuticals for Children Act (BPCA). These laws incentivize paediatric research and require the inclusion of children in drug development processes.

The FDA promotes pediatric device innovation through the **Pediatric Device Consortia (PDC) Grant Program,** funding non-profit consortia to advance pediatric device development. **The Premarket Approval (PMA)** and **510(k)** pathways are used with specific pediatric guidance, while the **Humanitarian Device Exemption (HDE)** pathway allows for a faster, less stringent approval process for pediatric orphan devices, requiring only evidence of probable safety if the device poses no significant risk.

Since the 1960s, the FDA's regulatory framework has significantly influenced pharmaceutical regulation worldwide. Countries like Australia, New Zealand, and Canada[xxii] have system recognition partnerships with the FDA, while nations like India and Qatar align their regulations closely with the FDA. This alignment simplifies market entry for start-ups and innovators.

The **Mutual Recognition Agreement (MRA)** between the European Union and the United States aims at aligning pathways for the approval of medical products (specifically in the **Pharmaceutical Annex** (which also impacts certain medical products)). It focuses on reducing the conformity assessment procedures.

EUROPEAN UNION (EMA AND EUROPEAN COMMISSION)

The **EMA** implements the Paediatric Regulation for the approval of **medicinal products,** which necessitates a Paediatric Investigation Plan (PIP). The regulation aims to improve the availability of paediatric medicines and ensure that they are appropriately adapted for children's use.

However, not all products are available in every EU country market. The industry determines which markets to enter and decides on the formulations and package sizes offered in each country, leading to considerable variation. Each country conducts its own Health Technology Assessment (HTA) and makes independent decisions regarding pricing and reimbursement[xxiii].

The **European Commission** regulates the development of both **Medical Devices and *in vitro* diagnostic medical devices** through the following regulations:

- *Regulation (EU) 2017/745* of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.

- *Regulation (EU) 2017/746* of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU.

WORLD HEALTH ORGANIZATION (WHO)

WHO focuses on the global harmonization of paediatric drug regulations particularly in low- and middle-income countries. Their work includes providing guidelines and technical support to ensure that paediatric formulations are available and accessible globally.

EMERGING TRENDS

Globally, there is a growing trend towards harmonization of paediatric regulations, with agencies collaborating on international guidelines to reduce the burden on pharmaceutical companies and streamline the approval process. Additionally, there is increasing emphasis on the ethical considerations of paediatric trials, ensuring that children are protected while still benefiting from medical advancements.

In 2010, the World Health Organization (WHO), in partnership with EMA (EU), FDA (US) and the PMDA (Japan), created the *Paediatric Medicines Regulator's Network (PmRN),* a network to improve collaboration among regulators by encouraging discussion and sharing of information concerning the regulation of paediatric medicines.

CURRENT LEGISLATION IN THE EUROPEAN UNION IN PAEDIATRICS

The EU's current paediatric legislation, established under Regulations (EC) No 1901/2006[xxiv] and 1902/2006 in 2007, was introduced to improve the health of children, **increasing high quality research, promoting the development and authorization of medicines** and improving the information on medicines for use in children. This regulation also aims at encouraging manufacturers to research and develop medicines for children's specific therapeutic needs by using a system of rewards (in annex). It obliges industries to specifically plan the development of their medicine for children (e.g. by integrating it into the development for adults) and submit a corresponding PIP (Paediatric Innovation Plans). This financial incentive to stimulate industry has been widely used , although with limited proof of their effectiveness and safety[xxv]

Two main frameworks are organising paediatric regulations:

1. A Paediatric Committee (PDCO) meets regularly at the EMA and oversees the coordination of most aspects of the Regulation. The EMA's PDCO can grant deferrals or waivers under specific conditions.

2. A Paediatric Investigation Plan (PIP): Under Article 7 of the EU Regulation, a Paediatric Investigation Plan (PIP) is required for all new medicinal products intended for children. PIPs ensure that adequate R&D is dedicated to paediatric health by establishing plans for assessing a medicine's quality, safety, and efficacy in children.

- PIPs require pharmaceutical companies to collect data on the use of medicines in paediatric populations through clinical trials.
- Submission of a PIP is necessary when applying for marketing authorization of new medicines and for new indications of existing medicines, forms, or routes of administration.
- EMA offers scientific advice and protocol assistance to support PIP development.

Several rewards and incentives for the development of paediatric medicines for children are available in the European Union (EU)[xxvi]

- **Supplementary Protection Certificates (SPCs)** – Extends market exclusivity.
- **Orphan Drug Incentives** – Encourages the development of treatments for rare conditions.• Paediatric-Use Marketing Authorisation (PUMA) – Specifically for paediatric-use indications.
- **Paediatric-Use Marketing Authorisation (PUMA)** – Specifically for paediatric-use indications.• Joint EMA/FDA Guidance – Collaborative advice for streamlined transatlantic development.
- **Scientific Advice and Protocol Assistance** – Guidance from EMA for study planning.
- **Joint EMA/FDA Guidance** – Collaborative advice for streamlined transatlantic development.
- ***Innovation Task Force (ITF)*** – Briefing meetings as a support tool during the early phases of developing innovative medicine, methodology and technology. They are free of charge and involve experts from the EU Regulatory Network. Regulatory Support is also provided at national level through *National Innovation Office*, offering innovation meeting to harmonise support to innovation in Europe.

Regulators in the European Union (EU) have taken several initiatives since 2018 to increase the efficiency of paediatric regulatory processes and boost the development of medicines for children. These achievements are highlighted in the *Boosting the development of medicines for children: Closing report of the European Medicines Agency and European Commission* (DG Health and Food Safety) and include:

• Strengthened focus on unmet medical needs: EMA and key stakeholders have raised awareness and better identified areas where medicines for children are particularly needed (i.e. childhood cancer and inflammatory bowel disease) with a goal to shift the research agenda to these areas involving clinicians, patients, academia and developers. These insights are now considered in PIPs for new medicines.

• Adapting regulatory processes to better support innovation: to facilitate the establishment of PIPs, the EMA launched a pilot phase for a 'stepwise PIP' agreement[xxvii]: under this framework, it will be possible to agree on a partial development program, with a full PIP to submit once sufficient evidence is available. This approach permits agreements on PIPs despite initial data gaps with the flexibility to return to EMA's PDCO to address uncertainties as new data becomes available.

• Increased alignment of data requirements between decision-makers: EMA has enhanced international collaboration, particularly within the FDA pediatric cluster. The European network of paediatric research (Enpr-EMA) played a crucial role in aligning international requirements for pediatric clinical trial authorization and standards.

The existing legislation is currently undergoing reform to become a more comprehensive EU Medicine Regulation. This revision will update the EU Pharmaceutical Strategy 2020, *introducing a new regulation and directive,* with implementation expected by 2026. It will include a framework applicable for children's medicines, aiming at reducing off-label prescription and reduced time of PIPs [xxviii]

REGULATORY BARRIERS

Regulation is essential to ensure the safe adoption of paediatric healthcare innovations, especially as technology advances, enabling improvements like remote monitoring or advanced therapies to enhance care for children. However, market access for paediatric devices could be particularly challenging. Despite ongoing efforts by European agencies to accelerate paediatric and orphan disease solutions, market impact remains limited. The transition from the Medical Device Directive (MDD) to the Medical Device Regulation (MDR) in Europe has put many available paediatric solutions at risk. The new MDR/IDVR (In Vitro Diagnostic Medical Devices Regulation) has increased regulatory requirements. This regulation, which does not authorize off-label data, requires that solutions previously approved under the MDD undergo recertification with a new assessment, but many lack the required data. This process is often prohibitively expensive for manufacturers, which has led to the withdrawal of essential paediatric devices from the market. Indeed, once a device is rejected (if lacking the required data), it is flagged, and no alternative solutions are offered.

Tom Melvin
Expert Review of Medical Devices

"Clinicians have noted that certain essential devices, often the sole options for specific procedures, are becoming unavailable. The uncertainty of MDR assessments, combined with insufficient market incentives, puts the availability of orphan paediatric devices in Europe at risk."[xxix]

"NOT SMALL ADULTS"

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS
PAEDIATRIC RESEARCH IS STILL ADULT DRIVEN		
Most pediatric developments and products rely on adaptations of adult products, neglecting significant physiological differences and specific paediatric diseases. **Off-label use** is common due to the scarcity of child-specific designs. While incentives exist for new paediatric medicines, waivers enable the industry to bypass necessary developments, particularly problematic for unique conditions like those faced by neonates. **Developments and its validations and clinical trials not always take into account the children and young persons (CYP) context, burdens and needs.** This includes minimizing the number of hospital visits, adapating the informed consents to patient age reducing the amount of paperwork, and considering the time commitment required from the subjects or their parents/caregivers including family and impact in schooling.	**FDA:** Pediatric Research Equity Act (PREA) and the Best Pharmaceuticals for Children Act (BPCA). These laws incentivize paediatric research and require the inclusion of children in drug development processes. **EMA:** Paediatric Regulation and its incentives and waivers including the necessity of a Paediatric Investigation Plan (PIP) and the rewards and incentives established. **European YPAG Network (eYPAGnet):** eYPAGnet is a European network that promotes meaningful Patient and Public Involvement (PPI) with children, young people, and families. Through Young People's Advisory Groups (YPAGs), eYPAGnet collaborates with academies and industry to ensure that paediatric clinical research and innovation is patient-centered.	**Revision of the paediatric regulation waivers (under way):** Waivers have been overused to bypass paediatric trials. A review is underway. The impact in paediatric cancers is one of the triggers for revising the paediatric regulation. A fundamental change is that waivers will no longer be granted if a drug's mechanism indicates paediatric benefits, even if it targets adult cancer. This would encourage industry to expand development for paediatric needs, benefiting all patients. **Centering the Voice of Patients and Families:** Involve representatives from patient groups, rare disease associations, and families in decision-making bodies to ensure that priorities, availability, and off-label use of devices are guided by patient-centered values. Also to involve their voice in the design and approval process of clinical trials and informed consents to ensure paediatric health literacy adapted to age and patient group. **Generation of public grants to promote the creation of national or regional Young Persons Advisory Groups** that can be involved in study designs, product development and advisory boards of Ethical Committees to provide advice and solutions to ensure paediatric clinical research is patient centred.
FORMULATIONS AND DEVICES SHOULD BE ADAPTED TO THE DIFFERENT AGE RANGES		
The paediatric population's diversity—from newborns to adolescents—demands age-specific formulations, dosages, and devices. The FDA and EMA define paediatric age groups as: • Preterm newborn infants • Term newborn infants (0 to 27 days) • Infants and todders (28 days to 23 months) • Children (2 to 11 years) • Adolescents (12 to 18 years) Although it is necessary, this complexity can increase the costs of development and regulatory approval. For industry (large and small) it may represent additional financial and logistical hurdles during the clinical development phase.	**European Paediatric Formulation Initiative (EuPFI):** A consortium focusing on the development of better and more suitable paediatric formulations. **Best Pharmaceuticals for Children Act (BPCA) and Paediatric Research Equity Act (PREA):** US initiatives that incentivize the development of paediatric formulations and devices. **Innovative Medicines Initiative (IMI):** Supports projects like GRiP (Global Research in Paediatrics) to advance paediatric drug formulations. (EU)	• Providing **regulatory sandboxes and exemptions** for experimental development to facilitate and incentive the research and development of medical products (drugs, medical devices and digital therapeutics) focused on paediatric-specific indications. • **Programs to promote collaborations between SME and Large companies:** Larger companies may have more resources and expertise to navigate the regulatory hurdles. This presents an opportunity for innovation and collaboration, encouraging SMEs to develop unique solutions and look for industry partnerships to thrive in the market.

TIME, INCENTIVES AND RESOURCES NEEDED

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS

LACK OF INCENTIVES IN THE REGULATION FOR PAEDIATRIC INNOVATION DEVELOPMENTS

Although the EU paediatric regulation for medicines led to an increase in the number of medicines authorised for paediatric subjects, results suggest they had limited impact, mainly focused on drugs and pharmaceutical industry.

Low investments for R&D of medical products (including medicinal products, medical devices, and digital therapeutics) for orphan diseases and paediatrics often viewed by companies as having a low ROI, which discourages innovation in this area. However, the health of children has significant implications for society, both in the short and long term.

US: The **Humanitarian Device Exemption (HDE)** provides a pathway for devices intended for rare conditions, requiring only evidence of probable safety rather than proof of effectiveness.

EU: the **Orphan Medicinal Products Regulation** offers market exclusivity and financial incentives to developers of products targeting rare diseases.

• **Increase incentives for both drugs and devices:** increasing the time extension of the SPC[1] and market exclusivity for authorized medicinal products could benefit commercialization and investments It should be also applied similarly to medical devices, extending data protection timings.

• Reducing Costs for Paediatric and Orphan Drugs and Device Assessments: The high costs of regulatory evaluations for orphan drugs and devices, especially under the **Medicinal Products Directive** and **Regulation and the new MDR,** challenge small companies. A more affordable conformity assessment pathway, like those in the U.S. and Canada, could support new solutions.

1 An SPC (Supplementary Protection Certificate) is an intellectual property right that extends the protection of a patented product (usually a pharmaceutical or plant protection product) for up to five additional years beyond the standard patent expiration.

SMALL AND SCATTERED SAMPLE SIZES

Paediatric populations are smaller than adult populations, compounded by the dispersal of eligible participants in for clinical studies across multiple institutions, making it challenging to recruit a sufficient number of participants for clinical trials. This scarcity can lead to delays in the development and approval of paediatric drugs and medical devices.

FDA's Breakthrough Therapy/Device designation:
Designed to expedite the development and review of drugs and medical products that demonstrate substantial improvement over existing therapies for serious or life-threatening conditions. This pathway provides increased communication with the FDA, rolling reviews, and eligibility for priority review, helping to bring promising treatments to patients faster while maintaining rigorous safety and efficacy standards. The goal is to accelerate access to potentially transformative therapies for patients in critical need.

Paediatric Trials Network (PTN):
In the U.S., PTN works to conduct studies that provide data on dosing, safety, and efficacy specifically for children.

Global Paediatric Clinical Trials Network (GPCTN):
This international initiative facilitates multinational trials to gather comprehensive paediatric data.

EUDAMED:
The European Database on Medical Devices supports data sharing and harmonization of paediatric clinical trial information across the EU.

DARWIN:
Darwin initiative, led by the **Bid Data Steering Group**, represent an importance resource to collec paediatric data to drive regulatory decision

Adapt Breakthrough designation to EU for medicinal products and medical devices to accelerate time to market. This approach should include mandatory post-marketing follow-up and the involvement of an independent data safety monitoring board to ensure ongoing safety.

Promotion of Real World Data and Real World Evidence: Creating databases and legislation in Europe that accept real-world data (RWD) and real-world evidence (RWE) from existing clinical trials and research in paediatrics and disease-based registries on off-label use can significantly accelerate the development of paediatric and orphan medical products. By leveraging data from similar devices and medicinal products, manufacturers can justify the safety and efficacy of new products more efficiently. This approach aligns with initiatives like EUDAMED and the European Health Data Space. These registries should be publicly co-funded and independently managed by academic institutions.

DEVELOPMENT OF ORPHAN AND PEDIATRIC MEDICAL DEVICES LAGGING BEHIND

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS
LAG IN THE DEVELOPMENT OF ORPHAN AND PAEDIATRIC MEDICAL DEVICES AND DIGITAL THERAPEUTICS		
Although efforts have been put in EU and EMA regulations to accelerate the development of medicinal products for pediatrics there is a lag in the development, approval and labeling of paediatric and orphan medical devices and digital therapeutics as compared to orphan drugs, probably due to the lack of similar stablished resources. **New Regulatory Challenges:** The MDR's implementation has heightened regulatory requirements, resulting in increased costs and extended approval timelines. This poses significant challenges, especially for devices intended for smaller patient groups, including paediatric patients and rare diseases.	**FDA Paediatric Device Consortia Grants Program** (in funding section) **New orphan devices in paediatrics (EU)** The EMA has launched **a pilot program for expert panels to support the development and assessment of orphan medical devices.** The initiative offers free advice to selected manufacturers and notified bodies on the orphan device status and the data needed for their clinical evaluation. Although the pilot runs until the end of 2025, it aims to establish a long-term support process.	• **Adapting regulation for medical device and digital therapeutics:** Adapting the EU Paediatric Regulation and its incentives and waivers for Pharmaceutical Industry and medicinal products to Medical Device and Digital Therapeutics research and development. • **Stablishing a European Expert Panel and single point of contact:** Direct, no-binding advice service from the EMA and the European Commission to consult and assist in the research,development and validation requirements of new medical devices and digital therapeutics for paediatrics and orphan diseases. • Promote the generation of **EU publicly co-funded public-private partnerships**, including large and small companies, to accelerate the development of solutions for pediatrics and rare diseases. Similar to the FDA Pediatric Device Consortia. • **Harmonisation of EU Guidelines on paediatrics regarding medical products, specially devices:** The EU is developing **paediatric guidelines** (with addendums to adult guidelines when disease common to both groups) to harmonize procedures. While current guidelines on medicines, there is a need for unified guidance and robust frameworks for medical devices and digital therapeutics for children.

CLINICAL TRIALS CHALLENGES AND THE IMPORTANCE OF CHILDREN AND YOUNG PERSONS (CYP) AND FAMILY INVOLVEMENT IN STUDY DESIGN

LACK OF SPECIALIZED CLINICAL TRIALS CENTERS:		
Clinical trials require product validation at multiple centers. However, in paediatrics, population tends to be small and scattered, making it challenging to recruit a sufficient number of participants for clinical trials. Yet, there are relatively few paediatric centers in the EU specialized in paediatric and orphan clinical trials making clinical trials a considerable constraint to innovation. This challenge is specially impactful for start-ups in cost and time needed for the developments. Additionnaly, **paediatric trials often require long term follow-up** to assess safety and efficacy as children grow up and develop . With the post-market surveillance requested by the MDR, this follow-up becomes even more challenging.	**Connect4Children (c4c-s) (Europe):** Connect4Children-S is a start-up that emerges from a European Project. It is an innovative pan-European paediatric clinical trial network of high-quality, trial-ready sites, and multidisciplinary experts. The network aims to facilitate the development of new drugs and other therapies for children. **National Paediatric Clinical Trials Networks:** • **GermanNetPaeT:** The German Network for Paediatric Trials was founded in 2018. Its aim is to improve pharmacotherapy in paediatric patients regarding safety and efficacy by making clinical trials in children and adolescents more effective.	• **Promote a large pan-European network of publicly co-funded clinical trials centers focused** on pediatrics and rare diseases to ensure enough data and expertise to conduct clinical trials methodologies taking into account patient age and the needed involvement of their family or tutor. • **Create in-silico clinical trials initiative for children** to improve paediatric clinical trials in Europe, which uses existing data and computer simulations for paediatric clinical research (i.e to model drug effects), alongside traditional clinical trials with children. This approach could address the lack of specialized paediatric clinical trial centers and scarcity of data by enhancing trial efficiency and reducing the physical burden on child participants. Paediatrics could serve as a safe and high impact space to pioneer this novel approach, extending in the future to other populations, following the "paediatric-first" approaches.

2.3 COMMERCIAL, ADOPTION AND REIMBURSEMENT OF PAEDIATRIC INNOVATION

COMMERCIAL, REIMBURSEMENT & ADOPTION BARRIERS:

Start-ups, large companies, and investors perceive commercial and adoption barriers as a greater impediment than other stakeholders, being directly involved with the go-to-market and commercialisation process on a daily basis, either for their own products or as part of their investment portfolio. This is a multistakeholder activity where medical devices, medicines, products, and services navigate separate reimbursement and adoption frameworks. In addition to the common hurdles faced in healthcare commercialization, paediatric innovation encounters the following specific challenges:

Arnau Valls Esteve
Innovation Coordinator & Director of i4KIDS, Hospital ant Joan de Deu (Spain)

"A paediatric innovation that fails to reach the market loses its value, as it never fulfills its fundamental purpose of improving someone's life"

COMMERCIALISATION HURDLES FOR START-UPS & NEED FOR PUBLIC-PRIVATE COOPERATION IN PAEDIATRICS

BARRIERS	SUCCESS CASES	RECOMMENDATIONS
EXCESSIVE HURDLES IN MARKET ACCESS IN PAEDIATRICS REDUCE INNOVATION POTENTIAL		
For companies with a diverse product portfolio, the ROI for paediatric innovations is not profitable when competing for the same budget as adults, paediatric dealing with a smaller market and higher development costs. **Start-ups in the paediatrics sphere** face considerable challenges in growing and scaling up in Europe: market access is hindered by the long regulatory pathways and limited reimbursement opportunities. Innovators face that, once a grant ends, a project – whether successful or not – is unable to receive subsequent funding, hindering the scale-up of interesting paediatric innovations. In line with data from the **Europe´s Innovation Ecosystem Survey Report,** better leveraging of diverse funds is viewed as particularly important to support and accelerate scale-ups (52%).Healthcare institutions are complex for external stakeholders to navigate, making it difficult to enter the system and validate innovations. On the other hand, **hospitals often perceive start-ups as risky partners.** Meeting the same quality standards as multinationals is highly demanding for start-ups, which would benefit from a more flexible regulation for market entry. Indeed, start-ups often struggle to survive the commercialization phase: looking for industry partners is key, but distributors are scarce and limited in paediatrics.	**Key acceleration programs** to support solutions developement and operation expansion across market: • **KidsX accelerator (US):** Technical, business, and mentorship accelerator organised annually focused on making paediatric care more effective and safe for children and families. Through this accelerator, start-ups validate their product market fit by collaborating with decision-makers and piloting solutions with leading children's hospitals. Hospital San Juan de Déu (Spain) is the only European hospital participating in KidsX. • **I4KIDS Accelerator (Spain)** Yearly acceleration program selecting five fetal, paediatric and maternal health projects, designed to guide them toward market readiness. • **Mother and Child Start-up Challenge (Poland)** The initiative addressed to start-ups that create innovative solutions around healthcare for paediatrics, winning a pilot of an innovative product in a Polish hospital. • **I4KIDS 4RARE's (Europe)** Recognizing that approximately 75% of rare diseases manifest in childhood, this accelerator focused on developing orphan medical devices. Two specific programs exist: **1.** "Validation and Valorisation 4RARE Program" focusing on two paediatric use cases: congenital heart disease and rehabilitation of children with Spinal Muscular Atrophy (SMA). **2.** "Challenge-based 4RARE Programme" to identify and prioritize clinical needs in children with neuroepilepsy disorders, involving the industry in finding potential solutions. **188 start-ups** have been identified in Europe focusing on paediatrics (success cases in EU and beyond available in annex).	• **Creation of a label of "certified start-ups"** to compete against industry and have an easier access to healthcare providers/systems and not be only perceived as a risky company as start-up. • **Facilitate SMEs access to agreements,** in terms of covering intellectual property, data security etc, in relation to the process of transferring technologies from research institutions, as well as commercial development agreements with stakeholders (e.g., corporates, healthcare institutions). • **Introducing micro sampling and micro testing** would greatly facilitate the transition from adult-focused solutions to paediatric applications, eliminating the numerous restrictions associated with current tools.

BARRIERS	SUCCESS CASES	RECOMMENDATIONS
LIMITED COLLABORATION BETWEEN PUBLIC HEALTH AND COMMERCIAL SECTORS IN PEDIATRICS		
The lack of public-private cooperation results in an **insufficient number of successful visible initiatives that foster co-creation** among innovation of the value chain. This hampers the implementation of innovative solution. Future paediatric innovation should focus on enabling the formation of public-private partnerhsips to align unmet needs, speed up the commercialisation and facilitate the solution's adoption. In the development of medical devices it is often exceedingly challenging to transition an innovation from a hospital setting to a manufacturer. Unless the hospital assumes the role of the manufacturer, which is typically not feasible, this step becomes a significant hurdle. The process of securing an appropriate manufacturer is frequently overlooked, yet it is a crucial phase in the successful development and commercialization of medical devices.	**Industrial PhD programs** (EU) foster collaboration between academia and industry, allowing researchers to work on real-world challenges. They drive innovation and strengthen public-private partnerships to accelerate the development of practical solutions. **CleverHealth Network (Finland):** Platform that facilitates co-development opportunities with companies and clinicians to fast-track treatment solutions. **Paediatric Innovation Challenge (Spain):** Collaboration between a hospital and an industrial partner to co-define a shared challenge and find a solution to address this identified mutual unmet need. **Novonate (US):** Solution for neonatalogy that has been licenced directly by an hospital.	• **Support the continuity of the Paediatric Innovation Day,** a Pan-European Annual Conference that creates synergies, enhances innovation and share best practices with stakeholders from leaders and emerging innovation countries. • **Organise a European Open Innovation Challenge** to attract right people in innovation and promote paediatrics as an attractive area, gaining also public engagement. • **Promote more public-private** collaboration that connect different understandings and expertise e.g. clinicians and investors. Replicate initiatives such as Clever Health at European level. • **Build a European Biodesign innovation program** to train fellows and facilitate access to clinicians. • **Facilitate the relationship between hospitals and industry** by creating joint pilot projects with the intended objective of implementation and manufacturing, ultimately enhancing the innovation capacity on both sides.
INCENTIVES AND HARMONIZATION OF REIMBURSEMENT PATHWAYS		
NEED FOR A DEDICATED REIMBURSEMENT SCHEME		
Lack of harmonization and complex requirements hinder reimbursement effort: rules and levels of reimbursement vary widely by region, making it difficult to navigate reimbursement criteria and be aware of them. Apart from the significant time and financial resources to adapt to each case, it makes it also challenging to establish a strong foothold in an already smaller market and a considerable struggle to scale-up at EU level. **Digital Health opportunities are still fragmented:** These limited reimbursement opportunities have seen some improvements through digital health, which business cases are more attractive for investors and larger companies as it reduces the need for capital and smaller market impact. However, reimbursement frameworks that facilitate commercialization are only established in certain European countries (i.e. DIGA in Germany, PECAN in France): this existing fragmentation creates difficulty for market access. **Lack of paediatric-specific reimbursement codes:** Regulatory requirements for labelling (getting certain aspects in the label) to support reimbursement is more difficult in the paediatric population (e.g. scales no validated in children).	**Fund to reward innovativeness of drugs for reimbursement (Italy)** In 2017, Italy's Medicines Agency (AIFA) introduced an algorithm to assess drug innovativeness for reimbursement from the €1 billion innovative medicine fund, based on unmet therapeutic needs, therapeutic value and the quality of clinical trial evidence. Drugs are categorized as: Innovative (full access to the fund, immediate formulary inclusion, and pay-back exemption), Conditionally Innovative (Immediate formulary inclusion) and Not Innovative (No benefits). Five years later, studies show a strong correlation between therapeutic value and the innovative status awarded, prompting manufacturers to prioritize clinical evidence over budget impact for reimbursement in Italy.	• **Implementing a revised reimbursement framework in the field of paediatrics,** similar to Germany's DiGA program, to significantly advance and harmonize the reimbursement and adoption of paediatric innovations. • **Developing common coding** systems, billing practices, and documentation requirements specifically tailored to paediatric healthcare innovations. • **Early alignment between committees and expert groups** is key to reducing time to market and offering a more predictable pathway for companies to invest in pediatric studies. Currently, this involves the alignment of the PDCO and the CHMP (Committee for Medicinal Products for Human Use). However, with the introduction of the new EU pharmaceutical regulation, new frameworks will emerge, which will require a harmonized process to better focus on pediatric-specific needs."
REIMBURSEMENT RATES CAN BE LOWER IN PAEDIATRICS AND NEED INCENTIVES		
Commercialization in paediatrics is hindered by the overinvestment required: for instance, in Germany, adding the paediatric indication to a product reduce the price for the adult product during the renegotiation of the price. On top of that, high investment costs for paediatric studies are not reflected in the reimbursement. Reimbursement rates for paediatric may be lower than those for adult devices, disincentivizing manufactures to invest in this market. Without incentives, it is difficult to support the business and push innovation forward.	**The US Rare Pediatric Disease Priority Review Voucher (PRV)** program is an initiative established by the FDA to incentivize pharmaceutical companies to invest in R&D for rare paediatric diseases (prevalence of 200.000 individuals in the US). When a company develops a drug that receives FDA approval for a rare paediatric disease, the company is rewarded with a voucher that can be used to receive a priority review for another new drug application or be sold or transferred to provide a financial incentive beyond the direct revenue from the drug.	• **Reward companies and establish incentives for companies investing in paediatric innovation** by replicating the US Rare Pediatric Disease Priority Review Voucher (PRV) program at the European level. Incentives should be implemented at European level on Value based managed entry agreements, following the reimbursement model in Italy.[xxx] • **Introduce incentives at an earlier stage** to encourage companies in pediatric innovation prior to adoption, drawing on the successful Italian model of rewarding innovation through reimbursement.

BARRIERS	SUCCESS CASES	RECOMMENDATIONS

GAPS IN DATA ON UNMET NEEDS DISCOURAGE COMMERCIAL ENGAGEMENT

CLEAR LACK OF RELEVANT DATA SUPPORTING THE REAL UNMET NEEDS IN PAEDIATRICS

When a medicine or a device is used off-label, there is no evidence to validate its benefits or harm of this practice on children's health. This creates a lack of real data, as pharmacy hospital does not study the compassive use of these off-label applications, as such use is not ethically accepted.

Clinical studies serving as a viable source of information for use of medicines in children are scarce, which justify a lower investment by the pharmaceutical industry. Consequently, there is insufficient evidence to support the commercial need and paediatric population appears having lower clinical needs, and therefore, as a less attractive market.

MOCA (Mechanism of Coordinated Access) in Rare diseases is a framework that helps improve patient access to orphan drugs across European countries. It allows for joint price negotiations and streamlined reimbursement discussions among stakeholders, making it easier for rare disease treatments to reach patients more efficiently. By coordinating cross-border efforts, MOCA aims to reduce delays and disparities in access to vital therapies.

- **Set up an advisory service in early stage** to ensure the early engagement of companies – implementing a process similar to MoCa in Rare Diseases), creating a working group and early engagement

- **Change in process driven by HTAs to reward companies,** so they will promote early engagement

CLINICAL TRIALS ARE POORLY DESIGNED TO SUPPORT COMMERCIALIZATION

To be effective, clinical trials must be designed with an emphasis on demonstrating added value, beyond safety and efficacy. This includes providing evidence that meets market access requirements, such as improvement of quality of life for patients, families and clinicians, and to an extent, the successful adoption of the solution.

Clinical trials hence need to be co-designed with market access experts. Patient numbers are often too low to make certain claims on labels which in turn affect reimbursement.

INEFFICIENCIES IN ADOPTION PROCESSES

VERY SLOW SALES CYCLES AND INSUFFICIENT PUBLIC PROCUREMENT TOOLS

After successful achieving commercialization, adoption is considered a new difficulty to overcome for innovators: **inefficiencies in hospitals processes hinder market entry** due to varying adoption requirements on a case-by-case basis, exacerbated by the absence of a streamlined adoption framework and clear pathways for external parties. It requires a robust field sales force from the seller's side to introduce successfully a solution, yet start-ups often lack the resources for such a position.
On the other hand, **tenders are a vital element for adoption**, but children's hospitals are considered as customers with very slow sales cycles which enlarge commercialization timelines. Existing public procurement tools such as Pre-Commercial Procurement (PCP) and Public Procurement of Innovative Solutions (PPI) are underused in paediatrics, which hinders adoption of solutions.

LESSONS LEARNED FROM AN UNSUCCESSFUL PROJECT IN A HOSPITAL:
Context: A project involved developing an internal tool for a hospital to perform sentiment analysis on open feedback from patients and families. The tool used artificial intelligence to analyze positive and negative feedback, showing promising potential. However, in many countries, public hospitals must change partners every five years through a public tender. The initial partner for this project was not reselected, leading to its discontinuation.
Lessons learned:
- A project was overly reliant on the initial supplier and was developed around their processes. A more sustainable approach would have been to develop a modular system adaptable to various suppliers.
- It is crucial to consider the overall regulatory environment and anticipate potential compliance requirements to ensure the project's continuity and adaptability.

- **Provide demand-driven and simplified procurement pathways;** the ADD4KIDS European project on public procurement will publish an action plan intended to tackle this issue. Advocate demand-driven vehicles to align cross-border values at different levels to tackle bigger challenges.

- **Pooling together/ create agreement across hospital systems** for purchasing. Use common value analysis or IT approval especially for non- therapeutic innovations.

FRAMEWORK FOR SUCCESSFUL ADOPTION OF EXTERNAL SOLUTIONS ARE NOT IMPLEMENTED

While interesting research projects often are introduced to hospitals, it is unclear for employees of both start-ups and hospitals, on the next steps to take. **The system structure lacks proper framework on how to articulate this adoption with external parties.** For start-ups, it is often unclear (i) who the contact person should be; (ii) who is responsible for the final decisions; and (iii) who will be the main advocate. At the same time, it is difficult for hospitals to reach supporting actors in the value chain, that could guide the implementation into hospital effectively.

Furthermore, because they relate to higher risks, start-ups are frequently not regarded as a suitable partner by hospitals.

LESSONS LEARNED FROM AN UNSUCCESSFUL PROJECT IN A HOSPITAL:
Context: The hospital participated in a "Healthcare Program Providers" initiative, featuring a start-up challenge to develop a platform for patients and families to connect. Despite the effort, the winning solution was never adopted by the hospital: there was no practical process for integrating the solution into the hospital workflows, insufficient funds for procurement, and a rigid hospital system that lacked flexibility for integrating start-ups innovations. Additionally, there was an absence of legal support to navigate the adoption process.
Lessons learned: The adoption process for new solutions in a hospital environment needs to be planned: establishing clear guidelines beforehand is essential to ensure smooth integration. Strengthening legal support within hospitals is essential, with dedicated legal experts to facilitate the adoption of new technologies, ensure compliance and address any legal considerations that arise.

- **Market access and value-based contracting experts are needed** to support start-ups in the adoption process. In hospitals, legal teams and lawyers that have knowledge of compliance and adoption of new technologies are a must.

2.4 HUMAN & INFRASTRUCTURAL RESOURCES FOR DRIVING PAEDIATRIC INNOVATION

HUMAN & INFRASTRUCTURE BARRIERS:

Human barriers are more prevalent in emerging innovators' territories but are a common issue across the European Union, varying in degree depending on regional innovation development. Healthcare providers are often not directly engaged with innovation daily, yet they are responsible for delivering innovative solutions to patients. To bridge the gap between clinical practices and innovative technologies, there is room for improvement.

INNOVATION CULTURE IN HOSPITALS

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS
HOSPITAL STRUCTURE OFTEN LACKS AN INNOVATION DEPARTMENT		
There are limited positions typically dedicated to innovation activities *per se in hospitals.* These independent departments work closely with clinicians and various hospital units to develop innovative ideas and practices, as well as actively seek external partnerships and stay in tune with emerging trends. Oftentimes, personnel responsibilities fall either under direct patient care which are overloaded, or under running hospital operations (e.g., IT departments), leaving it unclear as to which department should take up the responsibility and leadership of innovation activities.	**Hospital Sant Joan de Déu's Innovation Department** stands as a pioneer in paediatric healthcare by developing groundbreaking technologies, such as AI-driven diagnostics and wearable devices specifically designed for children. Their collaborative approach with top research institutions and tech partners accelerates real-world solutions, setting new standards in personalized and digital pediatric care across Europe. Reference paediatric hospitals with established innovation departments, such as GOSH (UK), HUS (Finland), Bambino Jessu (Italy), SJD Barcelona Children's Hospital (Spain) and other pediatric reference university hospitals stands as pioneers in pediatric healthcare helping translate research results and clinical unmet needs to groundbreaking technologies.	• **Support the set-up of innovation departments within hospitals,** creating a specific team with paediatric innovation know-how. Hospitals should create professional roles for physicians, other specialists, and nurses where some part of their work time is allocated for innovation activities; in addition, ECHO could explore and tap into the capabilities of its member hospitals and develop shared innovation training, mentoring, and professional recognition possibilities.
OVERLOAD OF STAFF LIMITS ABILITY TO ENGAGE IN INNOVATION		
For non-management personnel, innovation activities tend to fall outside of standard working hours, thus requiring high levels of motivation from individual healthcare professionals to ideate innovations and improve the quality of care. When specific innovation departments or positions do exist, these are typically limited, rendering them over-stretched and incapable of assessing all innovation opportunities adequately.	**European Children's Hospital Organisation - ECHO (EU)** represents many of the leading paediatric hospitals across Europe. Its mission is to advocate for children's health through the collaborative work of children's hospitals. Fosters networking and joint initiatives among children's hospitals and represents them in different European forums. Some European universities and hospitals have established internal grant programs to encourage clinicians and researchers to engage in innovation by providing intensification schemes such as: • **Great Ormond Street Hospital** (GOSH, UK) – GOSH Charity Programme Grants • **Aarhus University (Denmark)** - AU Distinguished Senior Innovators grant	• **Adopt digital solutions to free up expert's time** rather than create a burden • **Implement incentive systems that enable clinicians to spend time focusing on innovation** activities within their day-to-day: - Have dedicated hours for innovative activities that can be included in their clinical routine practice. It could be articulate as "research leaves" for enthusiastic innovators to dedicate time to innovation. - Reward innovation with funding for projects responding to clear unmet clinical needs identified in the hospital and participated by hospital staff. - Motivation system for Innovation Champions, recognizing their out-of-the-box thinking to innovation through financial support. Hospitals could create yearly internal prizes to amplify the voice of those who are transforming paediatrics innovation. • **Encourage the establishment of dedicated roles for administrative support** in grant applications or foster partnerships with consultants to streamline this process.

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS

LACK OF INNOVATION LEADERSHIP AND A COHERENT DEVELOPMENT STRATEGY

Opinion leaders are missing and are not always positively perceived in hospital culture. There is a perception that innovation may disrupt the "traditional" healthcare career path, where medical and scientific work is more value and prioritize success metrics such as publications, educational career and clinical practice.

As a result, **innovation skills are often undervalued,** leading to the absence of a coherent development strategy for innovation within hospitals.

Some European universities and hospitals have established internal grant programs to encourage clinicians and researchers to engage in innovation by providing intensification schemes such as: Great Ormond Street Hospital (GOSH, London, UK) **GOSH Charity Programme Grants**, Aarhus University (Aarus, Denmark) **AU Distinguished Senior Innovators grant.**

- **Integrate innovation into clinical practice** by offering every patient visiting a hospital the opportunity to participate in an innovation project as part of their care.
- **Enhance collaboration with universities** to promote staff exchanges and internships, fostering a culture of innovation through best practices and personal exchange programs within hospital innovation units.
- **Revise internal policies to incorporate success metrics,** such as the number of patents and products generated through innovation, and assign equal value to innovations, patents, and publications

BUILDING BRIDGES: INTEGRATING CLINICIANS INTO THE INNOVATION ECOSYSTEM

Integrating Clinicians into the Innovation Ecosystem

Within healthcare, the organizational culture is often closed and risk averse, engagement with external innovators is poor, and procurement and deployment practices do not allow innovative solutions to succeed. Collaboration between all entities of the value chain could be explored to share knowledge, costs and facilitate innovation.

Besides, current innovation networks do not sufficiently include the professional societies where healthcare professionals are active.

For instance, Israel has a strong medical device innovation culture and ecosystem which compensates for the lack of innovation education, which comes from a well-connected ecosystem.

Stanford Biodesign IMPACT 1 (US)

Impact1 applies Stanford's Biodesign methodology to paediatrics, accelerating the high-impact technologies. The program leverages Biodesign's need-driven innovation process, providing access to a renowned network of experts.

Stanford Biodesign's fellowship program brings clinicians, engineers, business experts, and designers together for an 10-month, hands-on experience in identifying and solving unmet clinical needs, fostering a multidisciplinary approach to healthcare innovation. This model empowers clinicians to lead innovation while enhancing collaboration across the healthcare value chain.

Outcomes: Technologies developed by Biodesign program trainees have benefited over 13 million people (not paediatric-specific). It has also inspired numerous programs to replicate the methodology:

- **d·HEALTH Barcelona,** an 8-month program for graduates, researchers, and professionals interested in healthcare innovation and entrepreneurship in Catalonia, Spain.
- **Biodesign Finland,** a 10-months full-time MedTech Entrepreneurship training program for professionals. The first successful project was in paediatrics (2016). It is considered as one of the best tools to create truly innovative solutions on needs, based on medical devices development.

- **Establish networks with pediatrician professional associations** and other relevant groups across Europe. Prioritize visibility by actively participating in their annual conferences and regional activities. With support from national and regional expert organizations, hospitals should enhance their innovative procurement practices and engage in ongoing dialogue with the market.

- **Build a Support programme where doctors are exposed to innovative ideas to co-create** with e.g. entrepreneurs – hackathon, reverse pitching, challenge competitions where they can reach out to lacking skills. Ensure that interested professionals working on innovation are well identified by their start-ups ecosystem to facilitate connections. ECHO could act as a facilitator.

- **Bringing innovation to "classical" paediatric conferences** could be a game changer to bridge education and inspire HCPs.

INFRASTRUCTURE TO SUPPORT INNOVATION ARE INSUFFICIENTLY RESOURCED

IT INFRASTRUCTURE IS REGARDED AS OUTDATED AND NOT BENEFITING FROM LATEST TECHNOLOGIES

Hospitals often **struggle to attract young talent due to perceptions of outdated IT infrastructure** and a lack of cutting-edge technologies, which do not prioritize cloud-based solutions. This challenge extends to attracting top professionals in technology (data scientists, AI) and commercial-oriented positions.

In emerging and moderate innovation countries, efforts to shift to data-driven integrated care pathways are not necessarily in place are limited by insufficient physical infrastructure (i.e., IT systems), necessary for effective coordination.

Moreover, **inadequate IT infrastructure hampers the adoption of digital solutions** developed by start-ups and complicates successful collaborations with the private sector, which can be challenged by data privacy issues and improper data transfer systems.

The **PHEMS** european project aims to revolutionize the way health data is managed and utilized across Europe, particularly adressing the challenges posed by privacy concerns and the complexity of data sharing. By developing a decentralized and open health data ecosystem, PHEMS strives to facilitate easier access to health data, thereby advancing federated health data analysis and creating services for generating shareable synthetic datasets.

- **Create testing environment for digital solutions to test interoperability.**

- **Expand access to telemedicine in the field of paediatrics,** ensuring that patients and their families in remote or underserved areas can connect with paediatric experts for consultations and care.

- **Support to initiatives such as PHEMS which aims at creating European paediatric measures** to harmonize and unleash the potential of health data especiallyfor innovative purposes, such as research.

BARRIERS	SUCCESS SYSTEMS	RECOMMENDATIONS
LACK OF DEDICATE SPACE FOR INNOVATION		
Hospitals lack dedicated spaces for healthcare professionals and external innovators to test ideas, develop prototypes, define value propositions and meet with external innovators. Without the proper infrastructure in-house nearby clinicians, innovation opportunities are limited, and progress is slowed.	**Innovation Lab – The "Batcave" (UK)** Alder Hey Children's Hospital's Innovation Lab, known as the "Batcave," is a dedicated space within the hospital, where ideas from all staff levels are encouraged to improve pediatric care, building a culture of innovation. This best-in-class model integrates creativity and problem-solving, using technology to turn ideas into impactful solutions for children's health.	• **Forge long-term collaborations between i4KIDS-EUROPE and venture capital firms or major industry players,** supported by targeted grants, to ensure that pressing unmet pediatric needs are effectively addressed by partners with the resources to bring innovations to patients. This initiative would include the establishment of innovation labs, strategically located within hospitals or designed to be accessible and highly visible to clinicians, to facilitate the seamless integration of new solutions into patient care. • **Establish mechanisms to foster collaboration between start-ups and schools/colleges,** creating opportunities for non-invasive clinical studies involving children. This initiative could also serve as an opportunity for launching health awareness campaigns to educate young individuals about their well-being.
HOSPITAL STAFF TRAINING & COMPETENCIES		
LACK OF INNOVATION TRAINING AND MINDSET FOR HCPS		
Besides this lack of structure to dedicate to innovation, future doctors and nurses are usually **not trained to think out of the box.** Even if they do, they might lack the commercial-oriented skills that could help them to push paediatric innovation. Many interviewees mentioned the need for medicine schools to integrate innovation classes to their career path to have higher qualified staff which could bridge the gap between innovation and care. **HCPs lacks adequate training to adopt new technologies,** resulting in slower adoption times. Organizational issues within healthcare structures are often identified lately, leading to resistance and demotivation among teams when integrating new solutions that do not align with their current work environment: providing new skills training in their worktime is necessary for better innovation adoption. Besides, **successful innovations require multi-disciplinary teams with professionals** such as designers, anthropologists, and patient organisations which can add interesting perspectives to identify problems and ideate solutions. It should not rely simply on researchers nor HCPs.	**TRAINING CAPSULE i4KIDS & i4KIDS-EUROPE (EU)** To tackle the identified gaps within the European pediatric ecosystem, 12 modules focusing on a specific challenge provides tools and first-hand experiences from key actors to take advantage of innovation opportunities in the pediatric field. ***EIT Health Education Programmes: (EU)*** • **Certified Innovation Path:** Personalized training combining innovation, entrepreneurship, leadership and latest industry and healthcare insights in Digital Medical Devices or Health Data. • **Health entrepreneurship 101:** Online course tailored for young innovators., empowering learners to spot commercial opportunities, drive product innovation, and launch new ventures. • **Healthcare Transformation Academy:** Program to equip HCPs with new competencies such as in innovation management, high-value care, digital health transformation, or leadership. **iRAISE (EU)** iRAISE is the first demand-driven education program in Europe focused on upskilling healthcare professionals to enhance the adoption of innovation within healthcare settings. It plays a key role in public procurement by offering educational programs that empower healthcare teams to recognize and implement innovative solutions. **Outcomes:** iRaise has successfully deployed 5 editions.	• **Create an innovation culture with engaging masterclasses for HCPs** (doctor, nurses) to improve soft skills, upskilling and innovation culture within paid working hours. • **Include innovation subjects to medical university as part of the curriculum.** It will support future healthcare providers to change the mindset towards innovation and implement in the daily practice. Medical faculties should make it mandatory and get new structural fundings and prepare motivational certificate programs. • **Raise awareness on existing pan-European programs, such as EIT Health Education Program** which help clinicians becoming familiar with innovation and develop commercial oriented skills (e.g., market research, pitching ideas, raising funds). This program could be offered to HCPs as a part-time initiative conducted during working hours in hospitals, supplemented with specialized pediatric workshops supported by ECHO hospitals and technical universities to further nurture these innovation champions. • **Implement an education program such as iRaise in paediatrics**, pioritizing the critical needs identification over focusing solely on technology to better leverage the HCPs involvement in the solution adoption. • **Develop a comprehensive publication plan to provide clinical teams with relevant publications** beyond just trial results, helping to convince clinicians that technology aligns with their workflows and needs. A well-defined communication strategy can build trust and address the resistance to change that often slows adoption.

CHAPTER 3

CALL FOR ACTION

Real actions at European level are required to push forward paediatric innovation and support start-ups and industry in Europe, with investment and powerful solutions that can prevent, improve and save children's lives.

ACTIONS

The European Union is playing a key role in pushing innovation and can speed up solutions to the market. The recent re-election of the president of the European Commission in July 2024 has disclosed exciting developments underway for start-ups and innovation in Europe with the 28th regime introduction.
This initiative aims to create a harmonized legal framework across Europe, a so-called 28th nation less regulated, to facilitate collaboration between EU members states, offering a new EU-wide legal status for innovative companies.

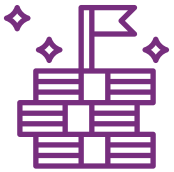
For start-ups, navigating the complex regulatory landscape of 27 different systems can be daunting; this initiative promises to simplify the process by:

ENHANCING ROBUST R&D FACILITIES

Providing the infrastructure and innovative laboratories researchers need to test and develop ideas through new public-private partnerships.

STREAMLINED COMPLIANCE AND MARKET ACCESS

A single set of harmonized rules will reduce the time and resources spent on administrative tasks, enabling start-ups to efficiently expand across borders and focus on innovation and growth.



ENCOURAGING INVESTMENT

A predictable regulatory environment that attracts investors, such as risk-absorbing measures to make it easier for investors to finance fast-growing companies is planned. Additionally, a European Savings and Investments Union that could leverage private savings to support innovation and transitions to clean and digital technologies is understudied, as well as a review of the European capital available to finance innovation that can be restrictive.

WHY PAEDIATRIC INNOVATION REQUIRES CONCRETE AND IMMEDIATE ACTIONS?

To capitalize on the current momentum and advance the field, paediatrics needs unique measures. Our actionable roadmap aligns with new European policies to empower start-ups, such as the 28th regime, and paediatric framework such as the new Orphan Devices Regulation. The proposed approach will yield considerable benefits for innovative children's solutions and create a landmark in social impact in the EU. We will outline specific actions that must be implemented to achieve a European boost in paediatric innovation:

3.1 ROADMAP ON ACTIONABLE KEY ACTIONS

	SHORT-TERM (2025) QUICK WINS & URGENT ACTIONS	MID-TERM (2026-2027) NECESSARY MEASURES	LONG-TERM (2028-2030) PROFOUND TRANSFORMATION
FINANCIAL	**A UNIFIED PLATFORM FOR PATIENT-CENTERED SOLUTIONS** Create a unified platform that connects the needs of patients, families and healthcare professionals with innovators, investors and industry partners. By consolidating these currently dispersed elements into a centralized space, we can increase both the quantity and quality of pediatric-focused solutions and applications and showcase success stories and opportunities.	**A PUBLIC INITIATIVE FOR TRANSFORMATIVE PAEDIATRIC HEALTH INNOVATION** Develop public programme dedicated to paediatrics, including fetal and maternal health, similar to the FDA's Pediatric Device Consortium in the US. This initiative should foster innovation through paediatric-focused public grants and impact investments, with an emphasis on long-term societal impact. To elevate paediatrics as a priority, a pilot social impact bond at the European level should be launched, positioning paediatric healthcare as a critical investment for society.	**NEW MECHANISMS TO INVEST SPECIFICALLY IN PAEDIATRICS** Generate new publicly co-funded investment in collaboration with Impact Funds, aimed at supported the development of orphan devices, medicines and paediatric innovation at EU level.
REGULATION	**ENHANCING EUDAMED FOR PAEDIATRIC INNOVATION TRACKING** Add a specific tag in EUDAMED and other public databases to facilitate the search and tracking of solutions with a pediatric indication, including specific age group categorizations.	**TAILORED EU GUIDELINES AND SUPPORT FOR PAEDIATRIC-FOCUSED MEDICAL DEVICES** Create tailored guidelines for the development of medical devices aimed at paediatric populations. This should be supported by establishing a dedicated point of contact for Medical Devices and Digital Solutions within the European Commission, similar to the Paediatric Committee (PDCO) of the European Medicines Agency (EMA).	**VALIDATING OFF-LABEL USE FOR PAEDIATRIC MEDICAL DEVICES** Generate a pan-European registry to systematically collect real-world data from off-label device uses in pediatric settings. This data would be evaluated by a dedicated Peadiatric Expert Panel, which would assess its quality and offer validation recommendations. Additionally, a conditional approval pathway for devices with strong off-label evidence would be established, allowing provisional market access while further data is gathered.
MARKET	**A EUROPEAN OPEN INNOVATION CHALLENGE IN PEADIATRIC HEALTHCARE** Strengthen public-private collaboration by launching a European Open Innovation Challenge focused on advancing pediatric healthcare solutions.	**CERTIFIED FOR CARE: TRUSTED START-UP SOLUTIONS FOR CHILDREN'S HOSPITALS** Establish a "Certified Start-Up" label to build trust and facilitate the adoption of start-up solutions within hospitals. A pilot program can be launched in regions with emerging and moderate innovation ecosystems, addressing the unique challenges of integrating innovative solutions into hospital settings in these areas.	**THE PEDIATRIC PRIORITY REVIEW VOUCHER PROGRAM FOR EUROPE** Establish a European Paediatric Priority Review Voucher (PPRV) program, similar to the FDA's PRV, to incentivize the development of treatments for pediatric diseases by providing vouchers that accelerate the regulatory review of other products, which can be used by the developer or sold to other companies. This would encourage early-stage investment in paediatric innovation by providing a tangible, tradable reward for companies addressing critical paediatric needs.
HUMAN	**INNOVATE WITH PURPOSE: BIODESIGN PROGRAM FOR COLLABORATIVE PEDIATRIC SOLUTIONS** Establish a European Biodesign Innovation Program to enhance clinician collaboration and develop impactful paediatric healthcare solutions. This program will support the creation of dedicated innovation departments within hospitals, staffed with specialized paediatric innovation teams, to drive targeted advancements in paediatric care.	**INDUSTRY PARTNERSHIPS FOR PAEDIATRIC CARE SOLUTIONS** Forge long-term collaborations between i4KIDS-EUROPE and venture capital firms or major industry players, supported by targeted grants, to ensure that pressing unmet pediatric needs are effectively addressed by partners with the resources to bring innovations to patients. This initiative would include the establishment of innovation labs, strategically located within hospitals or designed to be accessible and highly visible to clinicians, to facilitate the seamless integration of new solutions into patient care.	**INNOVATION TRAINING FOR TOMORROW'S HEALTHCARE LEADERS** Integrate innovation-focused subjects into the medical university curriculum to bridge innovation and healthcare, fostering an innovative mindset among future healthcare professionals. This will equip students with the skills needed to drive and adopt innovative solutions in clinical practice.

3.2 CONCLUSIONS AND TAKE-AWAYS

This actionable roadmap, developed in collaboration with innovators from emerging and leading regions, ensures the involvement of all European stakeholders **in shaping the future European Paediatric Innovation Ecosystem.**
Its goal is to guide decision-makers in activating this strategic roadmap to overcome key challenges, across financial, regulatory, commercial, and human capital dimensions.
All the best practices and recommendations provided should serve as **a foundation for drawing parallels with successful models, leading us towards the implementation of a more connected and competitive European paediatric innovation ecosystem.**

SO… WHY IS INVESTING IN PAEDIATRICS NECESSARY TO BUILD A HEALTHIER SOCIETY TOMORROW?

PERCEPTION	REALITY OF PAEDIATRIC IMPACT
1 The market is too small	**Growing Market Demand** Children represent over 25% of the global population. With advancements in healthcare and increasing awareness, there is a rising demand for specialized paediatric treatments and medical devices tailored to children.
2 Children are not sick	**Unmet Needs** Many diseases and conditions in children still lack effective treatments (over 6.000 rare diseases, 15 million preterm birth, 7,4 million autism spectrum disorder, etc.) representing a burden for healthcare systems as children grow into adults with unresolved health problems. The market presents significant opportunities for breakthroughs and market leadership.
3 The regulatory path is too long and risky	**Regulatory Incentives** Paediatric innovation has received increased attention in Europe recently, with new regulations that have shortened approval time and provided some incentives, such as the extended market exclusivity, encouraging innovation.
4 Paediatric projects will not translate to adult solutions	**Long-Term Impact** It is often easier to adapt development and regulatory framework from kids to adult application, than the other way around. Successful paediatric products can lead to lifelong brand loyalty and establish early market dominance.
5 There is no good project or success case in paediatrics	**Involvement of users and stronger ecosystem** 188 start-ups in Europe are focusing on paediatrics. On top of that, final users and institutions are particularly involved, helping with the development and facilitating its potential adoption.

ABBREVIATIONS

DG: Directorate General
EC: European Commission
ECHO: European Children's Hospital Organisation
EIT: European Institute of Technology
EUDAMED: European Database for Medical Devices
EMA: European Medical Agency
EU: European Union
FDA: Food and Drug Administration
HCPs: Healthcare Professionals
HR: Human Resources
HTA: Health Technology Assesment
ICF: International Classification of Functioning
ICU: Intensive Care Unit
IP: Intellectual Property
IT: Information Technology
MDR: Medical Device Regulation
NIH : National Institutes of Health
PCP: Pre-Commercial Procurement
PDC: Paediatric Device Consortia
PDCO: Paediatric Committee
PMA: Pre-Market Approval
PMDA: Pharmaceutical and Medical Devices Agency
PPI: Public Procurement of Innovation
PUMA: Paediatric Use Marketing Authorisation
R&I: Research and Innovation
R&D: Research and Development
ROI: Return On Investment
SMEs: Small and Medium Enterprises
TRL: Technology Readiness Level
TTOs: Technology Transfer Offices
VC: Venture Capital
UK: United Kingdom
US: United States
WHO: World Health Organisation

ANNEXES

List of some successful start-ups focused on paediatrics out of the 188 identified in Europe:

Generating sales:

- **Ephion (Spain):** Digital Health company revolutionising the monitoring of chronic patients.
- **Xploro (UK):** Empowering young patients with information.
- **Nixi for Children (Spain):** Virtual Reality that empowers patients.

In progress – pre-clinic or clinical stage:

- **Innocens (Belgium):** AI-empowered neonatal ICU support system for early detection of sepsis in newborns.
- **Gate2Brain (Spain):** Biotechnology company developing novel drug delivery systems that enable therapeutic agents to cross the blood-brain barrier effectively.
- **Lifeward (Germany):** Medical device company that designs and develops solutions that provide gait training and mobility for lower limb disabilities.

Six successful paediatric start-ups acquired or IPO'd out of Europe:

Emendo Biotherapeutics (Israel): They develop next-generation gene-editing tools for genetic disorders.
- **Founded:** 2015.
- **Exit Success:** Acquired by AnGes, a Japanese biopharma company, in 2020.

Orphan Technologies (Switzerland): A clinical-stage biopharmaceutical company focused on the development of orphan drugs for rare diseases, starting with the development of OT-58 to treat homocystinuria.
- **Founded:** 2015.
- **Exit Success:** Acquired by Travere Therapeutics in 2020.

Owlet Baby Care (US): A company providing wearable baby monitors that track vital signs.
- **Founded:** 2013.
- **Exit Success:** IPO in 2021.

Myomo (US): Produces wearable devices that help children with neuromuscular disorders regain movement with prosthetic sensorized limbs.
- **Founded:** 2004
- **Exit Success:** IPO in 2017.

Healthymize (Israel): Developing personalized, artificial intelligence (AI) based, voice monitoring that turns smart devices into remote patient monitoring devices for voice-affecting diseases such as asthma, pneumonia and COPD.
- **Founded:** 2016.
- **Exit Success:** Acquired by Beyond Verbal in 2018.

Novonate LifeBubble (US): Medical Device system for securing and protecting central lines umbilical catheter protection in neonates in the NICU. Born from the Stanford Biodesign Program.
- **Funded:** 2018.
- **Exit Succes:** License to Laborie Medical Technologies Corp. in 2023.

ANNEXES

CURRENT LEGAL FRAMEWORK OF OBLIGATIONS AND INCENTIVES IN PAEDIATRIC DRUG DEVELOPMENT AND MEDICALS DEVICES IN EU

	LAW	OBLIGATIONS	WAIVER	INCENTIVES	CONDITIONS
DRUGS[xxxi]	Paediatric Medicines Regulation (EC No 1901/2006)	When developing a drug for MA, (Marketing Authorisation) submit a PIP, including: • Studies in applicable age groups (0-17 years) • Drug formulation adaptations	Medicine · Is likely to either ineffective or unsafe ·Does not have substantial therapeutic benefit over existing treatments ·Is intended to treat a condition that only occurs in adults	6-month market exclusivity extension if the PIP is completed as agreed For drugs with orphan drug designation: additional 2-year extension (i.e. total orphan market exclusivity increases to 12 years)	PIP must be submitted after completion of adult PK (Pharmacokinetics) studies (i.e. end of phase 1 trials)
	Medicines for Rare Diseases Regulation	N/A	N/A	Reduction in fees for MA applications 10-year orphan market exclusivity	• Drugs must be intended to treat, prevent or diagnose a disease that is life threatening or chronically debilitating • Disease prevalence <5 in 10.000 or the product's market unlikely to generate sufficient returns to justify the investment • Significant benefit to patient from the new treatment or no satisfactory method of treatment in the EU
MEDICAL DEVICES	MDR: Medical Devices Regulation (EC No 2017/745)	Devices must bear the CE marking before being placed on the market	N/A	N/A	Devices must: • Be supported by clinical evidence demonstrating their safety and performance. • They must be appropriately labeled and accompanied by sufficient information for their safe use. • Devices must be marked with a UDI (Unique Device Identification): to improve traceability and ensure proper monitoring.

TOTAL PMA AND HDE* APPLICATION APPROVALS FOR DEVICES WITH A PEDIATRIC INDICATION FROM FY 2008 TO FY 2021 IN THE US (PER CENTER)

FISCAL YEAR	APPROVED PMA AND DEVICES BY CENTER		TOTAL APPROVED PMA AND HDE DEVICES	APPROVED PEDIATRIC PMA AND HDE DEVICES BY CENTER		TOTAL APPROVED PEDIATRIC PMA AND HDE DEVIECES
	CDRH	CDER		CDRH	CDER	
2008	29	1	30	4	0	4 (13%)
2009	31	1	32	7	0	7 (22%)
2010	20	1	21	7	1	8 (38%)
2011	41	2	43	17	1	18 (42%)
2012	52	1	53	11	0	11 (22%)
2013	39	2	41	8	1	9 (22%)
2014	37	2	39	8	0	8 (21%)
2015	61	5	66	11	3	14 (21%)
2016	71	2	73	13	1	14 (19%)
2017	66	2	68	18	1	19 (28%)
2018	57	2	59	20	2	22 (37%)
2019	55	1	56	10	0	10 (18%)
2020	60	3	63	24	2	26 (41%)
2021	53	6	59	11	4	15 (25%)

PMA AND HDE APPLICATION APPROVALS INDICATED FOR PEDIATRIC SUBPOPULATIONS BY AGE FROM FY 2013 TO FY 2021 IN THE US

PEDIATRIC SUBPOPULATION	PMA	HDE	TOTAL
	FY 2021		
Neonates (birth - 28 days)	2	0	2
Infants (29 days to <2 years)	2	1	3
Children (2 - 12 years)	5	0	5
Adolescents (12 - 21 years)	5	0	5

**PMA and HDE:*

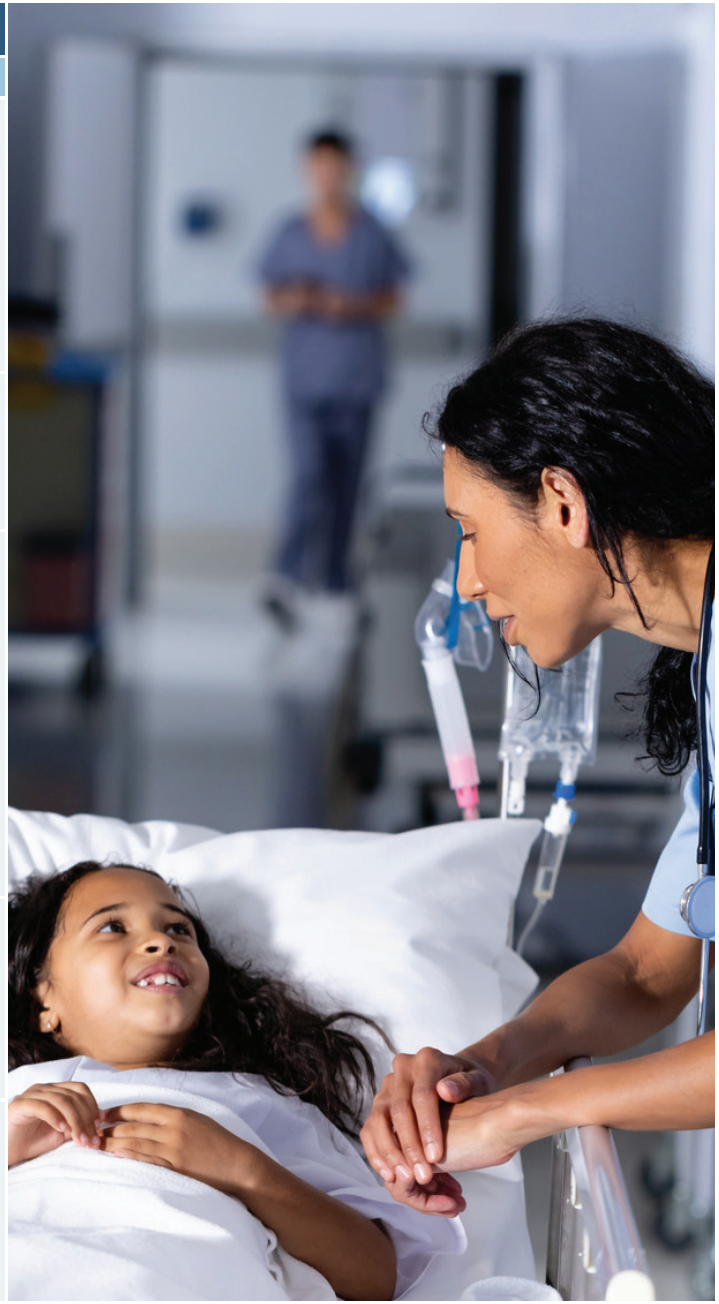
·PMA stands for Premarket Approval. It is the FDA's pathway for high-risk medical devices (Class III), which includes many pediatric devices. PMA requires evidence of safety and efficacy through rigorous clinical trials, making it the most stringent FDA review process.

·HDE stands for Humanitarian Device Exemption. This pathway is designed for devices intended to treat or diagnose rare conditions affecting fewer than 8,000 individuals per year in the U.S. It allows for a less extensive approval process compared to PMA and is commonly used for pediatric devices treating rare diseases. HDE does not require proof of effectiveness, only that the device does not pose unreasonable or significant risk.

ANNEXES

MAIN INCENTIVES FOR PAEDIATRIC MEDICINES IN THE EU

INCENTIVE	BENEFIT	EXPLANATION
Supplementary protection certificate (SPC)	+ 5 years extension to a patent right + 0.5 years if the SPC relates to a Paediatric Investigation Plan (PIP)	SPCs are intellectual property rights that extend patent protection for specific pharmaceutical and plant protection products, **addressing the loss of patent protection caused by the time-consuming mandatory testing and clinical trials required for regulatory approval.** They can extend a patent right by up to five years. For pediatric medicines, an additional six-month extension is available if the SPC is linked to a product for which data has been submitted according to a PIP.
Orphan medicines	+ 10 years of market exclusivity + 2 years if complied with an agreed PIP	Authorised orphan medicines benefit from 10 years of **protection from market competition with similar medicines with similar indications once they are approved.** This period of protection is extended by 2 years for medicines that also have complied with an agreed PIP granted at the time of review of the orphan medicine designation.
Paediatric-use Marketing Authorisation (PUMA)	8 + 2 years of data and market protection Centralised procedure Authorisation under the same name and branding	PUMA is a dedicated marketing authorisation covering the indication(s) and appropriate formulation(s) for medicines developed exclusively for use in the paediatric population. For medicines that are: • already authorised; • no longer covered by a SPC or a patent that qualifies as a SPC; • to be exclusively developed for use in children. • PUMA is particularly beneficial for companies that want to adapt existing medicines, which are already authorized for adults, for use in children. This might involve changes in formulation, dosing, or administration. The development of a PUMA must follow a PIP.
Scientific advice and protocol assistance	Free of charge advice from EMA in preparation of a PIP. Overall development strategy for paediatric developments	Applicants can request **scientific advice** from EMA in preparation of a PIP, which is free of charge for questions relating to the development of paediatric medicines.
Joint EMA / FDA guidance	Simultaneous submission of PIPs to the EMA and iPSPs to the FDA.	Joint procedural information is available from EMA and the **FDA** for medicine developers submitting a PIP to EMA and an **initial pediatric study plan (iPSP)** to the FDA. The joint guidance allows for the simultaneous submission of PIPs to the EMA and iPSPs to the FDA. This coordinated approach is aimed at reducing delays and facilitating more efficient development and authorisation processes for paediatric medicines.



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ACKNOWLEDGEMENTS

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Co-funded by the European Union

REGION Rigshospitalet

HUS Helsinki University Hospital

Bērnu klīniskā universitātes slimnīca

inveniam

KIDS KLUB INNOWATORÓW DZIECIĘCYCH SZPITALI

Design: ártico creative design s.l.
January 2025

Funded by the European Union

Funded by the European Union. Views and opinions expressed are, however those of the author(s) only and do not necessarily reflect those of the European Union or the European Innovation Council and SMEs Executive Agency. Neither the European Union nor the European Innovation Council and SMEs Executive Agency can be held responsible for them.