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Develop Child and Orphan Device Evaluation support

Project Number: 101160939

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Task name: T2.1 Mapping of initiatives and gap analysis, T2.2 Identification and creation of network of key stakeholders and building of stakeholder platform

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Symbols, abbreviations and acronyms

CSV	Comma-Separated Values
D	Deliverable
DeCODe	Develop Child and Orphan Device Evaluation support project
EC	European Commission
ERN	European Reference Network
EU	European Union
IST	InSilicoTrials Technologies
M	Month
MS	Milestone
OPD	Orphan and Pediatric Device
Q	Question
RIA	Research and Innovation Action
SIT	Support, Initiative or Tool
UT	University of Twente
TCD	Trinity College Dublin
WP	Work Package

Executive Summary

This Deliverable D2.1 provides a detailed and structured analysis of the current landscape of supports, initiatives, and tools (SITs) available to foster the development of orphan and paediatric devices (OPD) across Europe. Developed under Work Package (WP) 2 of the Develop Child and Orphan Device Evaluation support (DeCODe) project, and gathering the results of Tasks T2.1 and T2.2, this report synthesizes data collected from four targeted surveys, extensive consortium input, and a multi-stakeholder workshop. The objective is to identify areas of strong support, expose gaps in the innovation ecosystem, and prepare the foundation for a stakeholder engagement platform.

A total of 81 SITs were identified and analysed, reflecting the collaborative efforts of the survey respondents and project partners. These SITs span the entire product development lifecycle—from concept to commercialisation—and are categorised by domain (e.g. clinical, regulatory, technology) and type (e.g. modelling tools, regulatory guidance, infrastructure). Notably, most of these tools cluster around the clinical (39 tools) and regulatory stages (multiple tools including 12 dedicated regulatory tools), while there appear to be deficits in the pre-clinical, commercial, and reimbursement phases. A total of 67 SITs (approximately 80%) specifically relate to use in OPD contexts.

Additional stakeholder surveys provided additional insight:

- European Reference Networks (ERNs) emphasised the need for improved device-specific data collection and infrastructure.
- Hospitals highlighted regulatory barriers, off-label use, in-house adaptations, and unmet device needs in rare disease settings.
- Patient representatives voiced concerns over affordability, usability, and availability of customised paediatric devices, and suggested decentralised innovation approaches (e.g., peer-led or family-driven device design).

The findings indicate that while a variety of SITs exists, more comprehensive support is needed across the innovation lifecycle. This includes a need for tools to support early development, facilitate commercial adoption, and promote meaningful engagement with underrepresented stakeholders like patient groups.

This deliverable is input for the critical path analysis of OPD development, currently developed within WP3 and to be publicly reported as D3.1 at month M10; and will directly inform the development of the DeCODe stakeholder platform in WP4, enabling the aggregation, visibility, and strategic use of SITs to better serve developers and patients. It also lays the groundwork for subsequent project activities including regulatory and development coaching in WP5.

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1. Introduction

The Develop Child and Orphan Device Evaluation support (DeCODe) project aims to catalyse innovation and address the unique healthcare needs of children and people living with a rare disease who rely on medical device technologies.[1]

Work Package (WP) 2 has undertaken a mapping of tools and stakeholders in orphan paediatric medical device (OPD) development. This work focussed on mapping Supports, Initiatives and Tools (SITs), to understand where there may be gaps in current support (Task T2.1); it also included the identification and creation of network of key stakeholders and dissemination of this information in a stakeholder platform (T2.2).

To complete this task and deliverable, four surveys were prepared to gather data:

- A survey to **identify SITs** for OPD development
- A survey of **European Reference Networks** (ERNs) on OPD
- A survey for **Hospitals** participating in ERNs on experience with OPD
- A survey for **European Patient Representatives** on challenges and needs relating to OPD

To supplement the data concerning SITs, a mapping of EU-funded research projects relevant to orphan and paediatric devices was also undertaken.

The preliminary data and findings were presented at an in-person "Workshop for critical path analysis of orphan medical device development" organized by the DeCODe consortium and held on 8 and 9 April 2025 in Brussels. This workshop was attended by all but one project partners, the external advisory board and a variety of external experts representing the European Commission (EC), notified bodies, ERNs, academia, industry, rare disease networks and funders. The mapping of SITs and stakeholders formed the basis for a discussion on the development of a framework for the development of orphan and paediatric devices. This framework was divided into four domains - technology, regulatory, business and clinical, and the consortium meeting discussion focussed on identifying the most critical needs in the current framework. The results of the workshop will be reported as Milestone (MS)4 at Month (M)10.

The mapping presented in this deliverable will support preparation of the critical path analysis of orphan medical device development within WP3; will be integrated in the DeCODe support platform built in WP4; and will be used during coaching activities in WP4 and the regulatory advice to be provided in WP5.

[1] https://decode-rd.com/index.php/about-decode/

2. Methodology

The four surveys were developed by WP2, and then subject to consultations with relevant stakeholders who are partners in the project (ERNs, hospitals, patient representatives). Survey questions are presented in Appendices 2-5. The finalised surveys were granted ethics approval at University of Twente (UT) (Application nr: 241095).

A web-based survey hosted on the Qualtrics platform[2] was selected as this is a secure platform, complying with applicable data privacy laws, and accessible to the DeCODe project coordinator UT. Anonymous links were provided to access the surveys, which included informed consent:

- Survey to identify **SITs**[3]
- Survey of **ERNs** (to be completed by ERN Full Members and Affiliated Partners)[4]
- Survey for **Hospitals connected to ERNs** (to be completed by ERN Full Member and Affiliated Partners)[5]
- Survey for **Patient organisations (to be completed by European Patient Advocacy Groups ePAG members)**[6]

The surveys were opened on 10 January 2025 and closed on 28 February 2025. The surveys were publicised via the project website, social media postings and direct invitations circulated by partners. The data gathered in the surveys was downloaded in Comma-Separated Values (CSV)) format, to allow for analysis. For the surveys, each response was screened to exclude empty responses.

For the survey to identify SITs, the screened results were then categorised by domain (Pre-clinical development, Clinical development, Business development, Technology development, Regulatory development, Other) and stage of development of the technology (Concept, Prototype, Pre-clinical, Clinical, Manufacturing, Marketing, Commercial Use, Reimbursement). The domains were adapted from a published framework for guidance and implementation tracking in medical product development; the categories pre-clinical and 'other' were added.[7] The lifecycle stages are adapted from the total product lifecycle framework.[8] These were completed by the survey respondents. The type of SITs was categorised as follows:

- Accelerator
- Dataset
- Development practice
- Development resource
- Funding
- Infrastructure
- Initiative
- Modelling and simulation tool
- Regulatory tool[9]
- Patient focus group

[2] https://www.qualtrics.com/
[3] https://utwentebs.eu.qualtrics.com/jfe/form/SV_0xPJljLnNfXepVA
[4] https://utwentebs.eu.qualtrics.com/jfe/form/SV_1UewzM8BVFnmpnw
[5] https://utwentebs.eu.qualtrics.com/jfe/form/SV_25o2jSI5CuGp6ya
[6] https://utwentebs.eu.qualtrics.com/jfe/form/SV_23PtRZ3C65WF2ho
[7] https://gaits.org/
[8] Public Health Effectiveness of the FDA 510(k) Clearance Process: Balancing Patient Safety and Innovation: Workshop Report (2010). Appendix D: Impact of the Regulatory Framework on Medical Device Development and Innovation - David W. Feigal, Jr. National Academies of Sciences, Engineering, and Medicine. 2010. Washington, DC: The National Academies Press. https://doi.org/10.17226/12960.
[9] Including relevant guidance or references that can support OPD development.

- Specific expert support or mentoring[10]
- Other

For the other three surveys, a narrative description of findings is presented.

A scouting of the past and current EU-funded Research and Innovation Actions (RIA) relevant to paediatric and orphan disease was performed as well, to identify relevant initiatives that the DeCODe consortium may reach out in the future.

This mapping provides a structured overview of the landscape of available supports and highlights key areas where potential gaps persist. These findings were then used to prepare the workshop to gather multi-stakeholder perspectives on these supports and gaps.

[10] Individual experts were included in the stakeholder mapping, organisations who provide specific expert support or mentoring were included in the SIT results.

3. Mapping of Supports, Initiatives and Tools

3.1. Overview of survey results

There were 213 responses to the survey, and following the exclusion of empty responses, this resulted in 179 responses. These responses were then reviewed to identify if a SIT was described or not. This resulted in 31 SITs.

A further 50 SITs were identified by the DeCODe consortium. Following removal of duplicates, this resulted in 81 SITs. These are presented in the adapted PRISMA flow diagram below (Figure 1).

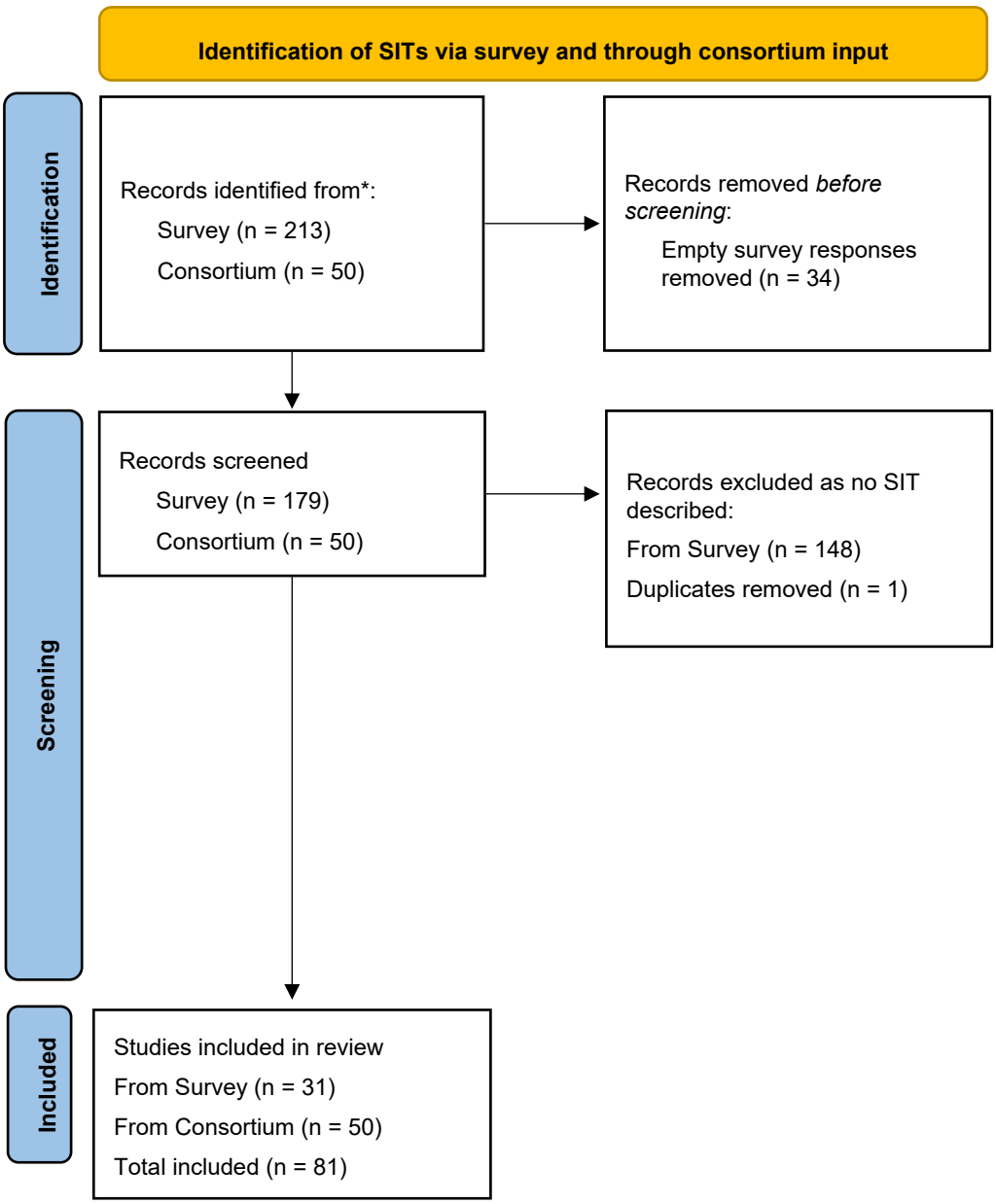

Figure 1 - Adapted PRISMA flow for inclusion of results

3.2. Categorisation by Domain

We categorised the responses based upon the following domains:

- Pre-clinical development
- Clinical development
- Business development
- Technology development
- Regulatory development
- Other

Each of the 81 SITs was classified according to the domain it supported. There was overlap in the identified SITs, with some of them supporting more than one domain, as shown in Table 1 and Figure 2.

Table 1 - Domain relevance of Supports, Initiatives and Tools Identified

Domain	Number of SITs
Pre-clinical development	42
Clinical development	59
Business development	20
Technology development	30
Regulatory development	39
Other	2
Uncategorized	9

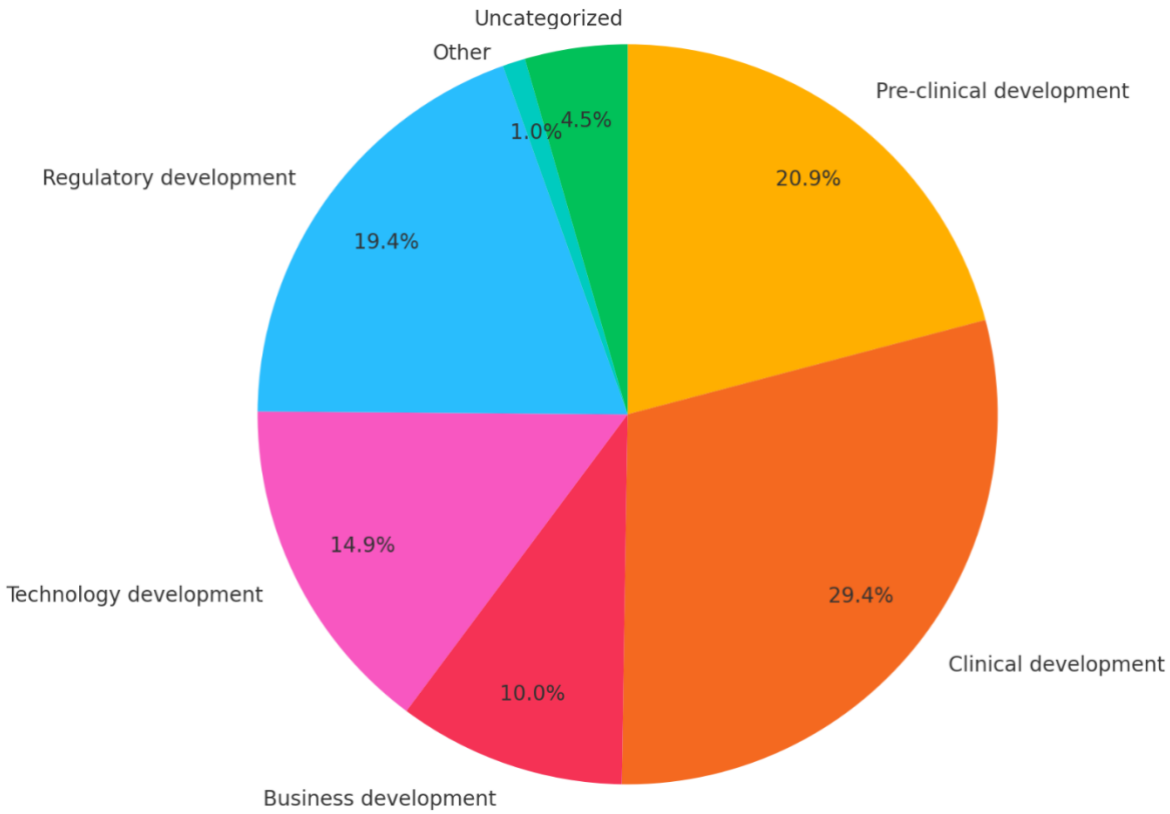

Figure 2 - Domain relevance of Supports, Initiatives and Tools Identified

3.3. Categorisation by Lifecycle Stage

Each of the 81 SITs identified was also classified according to the lifecycle stages it supports. Also in this case, there was overlap in the identified SITs, with some for example supporting more than one lifecycle stage, as shown in Table 3 and Figure 3.

Table 2 - Lifecycle stage of Supports, Initiatives and Tools Identified:

Lifecycle Stage	**Number of SITs**
Clinical	39
Prototype	28
Pre-clinical	26
Concept	20
Marketing	14
Commercial Use	13
Manufacturing	13
Reimbursement	7

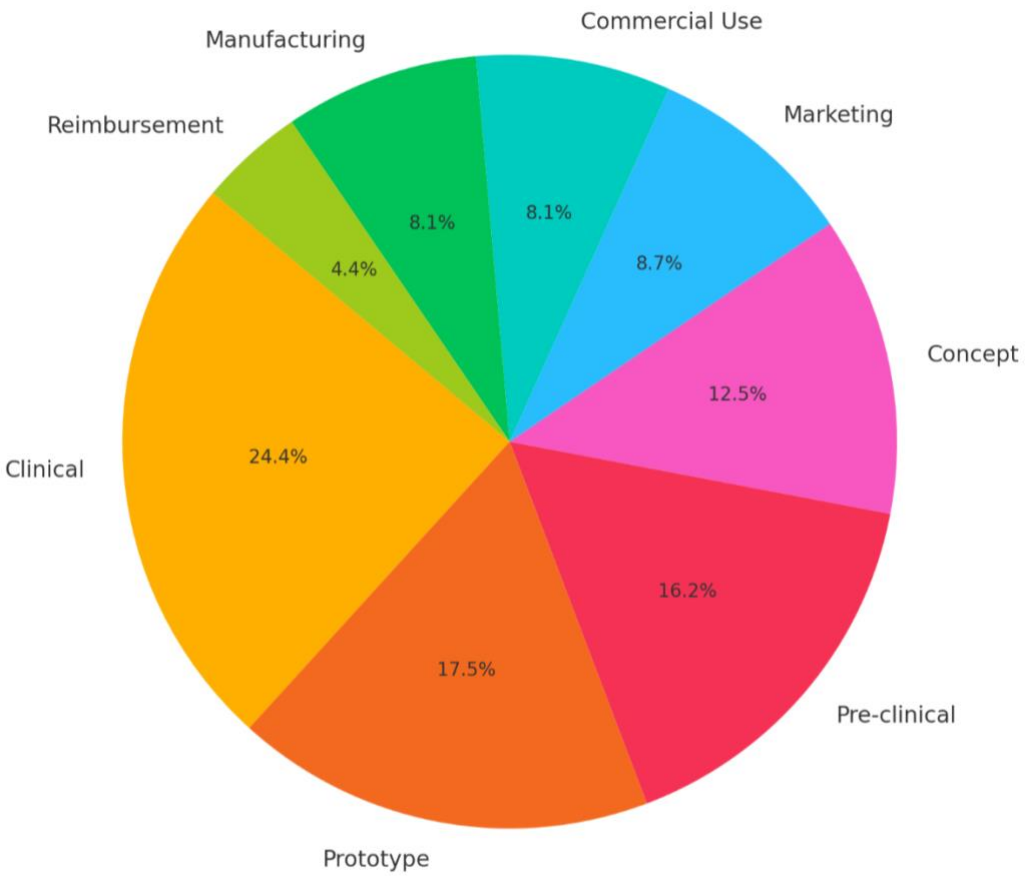

Figure 3 - Lifecycle stages of Supports, Initiatives and Tools Identified

3.4. Specificity to Orphan and/or Paediatric Devices

Each of the 81 SITs identified was also classified according to the medical technology it supports, as shown in Table 3 and Figure 4.

Table 3 – Medical Technology relevant to the Supports, Initiatives and Tools Identified:

Medical Technology relevance	Number of SITs
OPD	67
Generic Medical Device	7
General Health Product	1
Other	2
Uncategorized	4

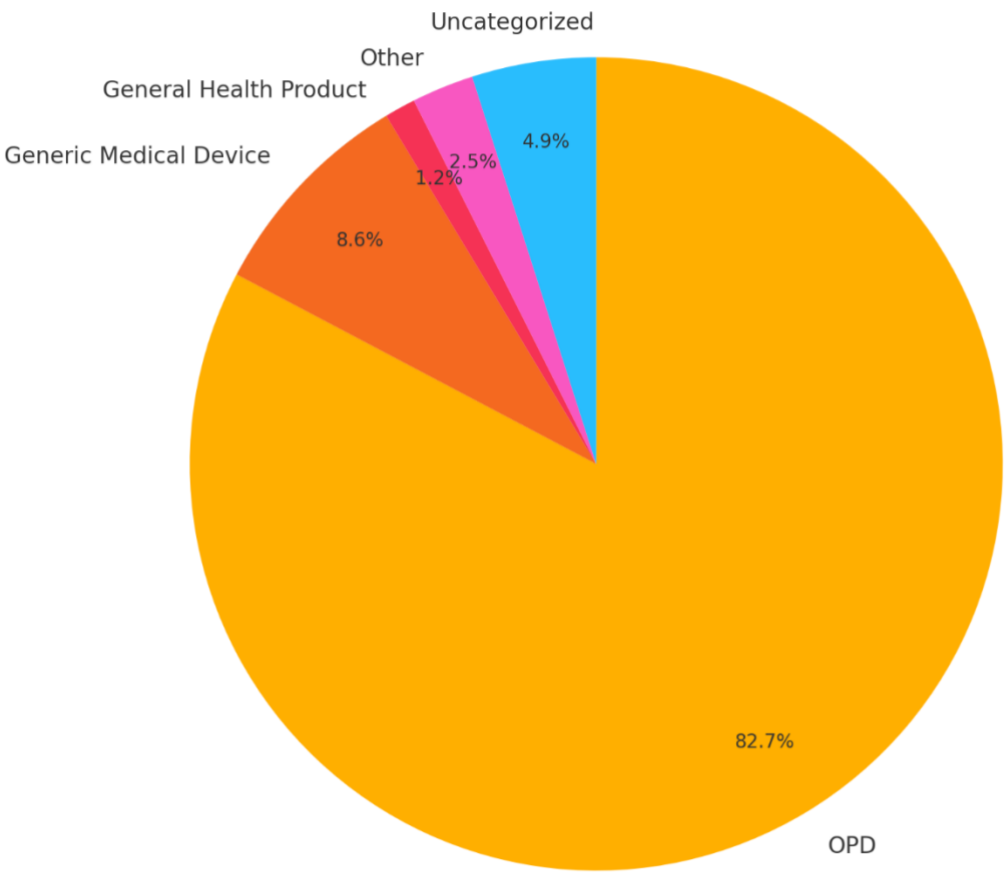

Figure 4 – Medical Technology relevance of Supports, Initiatives and Tools Identified

3.5 Summary of Supports, Initiatives and Tools identified

In this section, we provide an overview of the 81 SITs that have been identified. We take one example of each type of SIT and provide a brief description. The full table with all SITs, and links to external references is presented in Appendix 1.

- **Development Resources – 23 SITs identified**
  Example: Connect 4 Children (C4C) – A European-wide paediatric clinical trial network that facilitates multi-centre studies, enabling better and faster access to high-quality clinical trials.
- **Development Practices – 20 SITs identified**
  Example: IDEAL-D Framework – A structured evaluation model supporting innovation in surgical procedures and medical devices, tailored for stepwise development from concept to clinical use, which has been developed for medical technologies generally, but can be applied in rare and paediatric contexts.
- **Regulatory Tools – 14 SITs identified**
  Example: MDCG 2024-10 Guidance – EU regulatory guidance specifically addressing the clinical evaluation of orphan medical devices, designed to reduce regulatory uncertainty and streamline CE marking processes.
- **Modelling and Simulation Tools – 8 SITs identified**
  Example: Heart Models for Paediatrics – Age-specific cardiac simulation tools used to safely test paediatric devices *in silico* before human trials, reducing risk and development time.
- **Infrastructure – 4 SITs identified**
  Example: PEDSTART – A European clinical research infrastructure by Inserm that provides paediatric-focused trial sites, expert support, and coordination for device studies in rare populations.
- **Initiatives – 3 SITs identified**
  Example: Machine Learning Support – Uses AI to extract insights from limited datasets to support diagnostics, treatment planning, and design of paediatric and orphan medical devices.
- **Specific Expert Support / Mentoring – 2 SITs identified**
  Example: Trial Nation – A Danish platform connecting academic and clinical expertise to support the planning and conduct of paediatric device trials, including in rare conditions.
- **Patient Focus Group – 1 SIT identified**
  Example: Bioptic Driving Licence – A user-led initiative providing optical aids (e.g., bioptic lenses) tailored to individuals with rare visual impairments to support education and mobility.
- **Datasets – 1 SIT identified**
  Example: AI for Diagnosis and Synthetic Data – Provides synthetic datasets and AI models to support rare disease diagnostics where real-world data is scarce or unavailable.
- **Funding – 1 SITs identified**
  Example: Crowdfunding – An alternative financing strategy allowing early-stage developers of rare and paediatric devices to secure funding from patient communities and the public when traditional investors are absent.
- **Other types – 4 SITs identified**
  Example: Unique teeth – It is a search tool and directory of rare diagnoses with findings in the oral cavity.

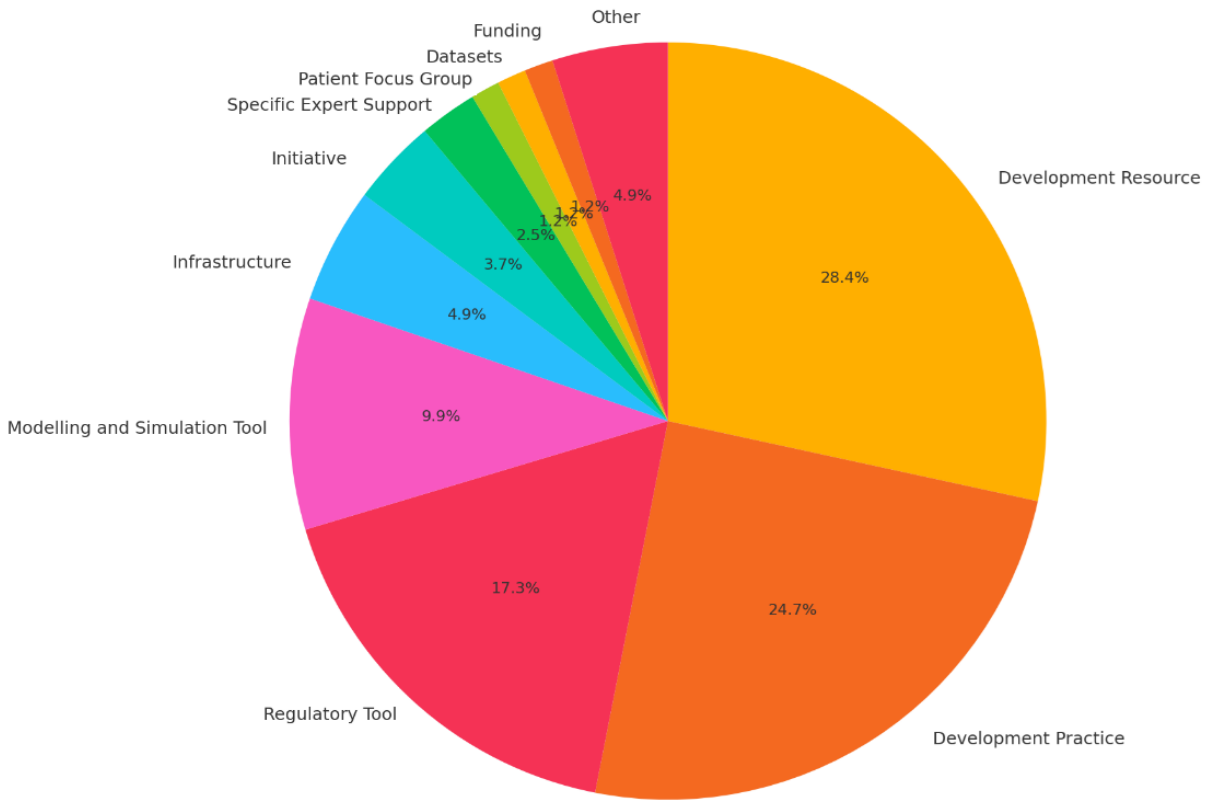

Figure 5 - Type of Supports, Initiatives and Tools Identified

4. Survey of European Reference Networks (ERNs) on Orphan and Paediatric devices

ERNs are cross-border networks that bring together European hospital centres of expertise and reference to tackle rare, low prevalence and complex diseases and conditions requiring highly specialised healthcare; there are currently 24 ERNs[77]. A survey was circulated to each ERN, with the support of ERN project members in DeCODe. This survey sought to explore the experiences and challenges relating to orphan and paediatric medical devices.

28 responses were provided, representing 10 unique ERNs who responded to the survey:

1. ERN BOND
2. ERN EpiCARE
3. ERN GENTURIS
4. ERN eUROGEN
5. ERN-RND
6. ERNICA
7. Endo-ERN
8. GUARD-Heart
9. MetabERN
10. TransplantChild

Presented here are the key findings based on ERN responses. These have been thematically arranged to cover the use of registries and support infrastructure; the importance of medical devices to the ERN; and the reliance of that ERN on medical devices.

4.1. Use of Registries and Support Infrastructure

The survey asked ERNs to indicate their use of registries related to orphan and paediatric medical devices. We found that 9 ERNs maintain or contribute to patient registries (Question Q6): ERN BOND, ERN EpiCARE, ERN GUARd-Heart, ERN eUROGEN, ERN-RND, ERNICA, Endo-ERN, MetabERN, TransplantChild. 7 out of 9 responses noted that the registry does not routinely collect data related to medical devices used. We did not identify any registry associated with an ERN that currently collects data on the medical devices used. ERN-RND reported indirect registry use for devices, as the focus of the registry is on the disease and outcomes, rather than on the technologies utilised.

In free-text responses, MetabERN proposed a "dedicated page" to consolidate device-related information, pointing to a gap in current data infrastructure. ERN eUROGEN stated that device-specific features are not yet included in their new registry, but this could be integrated in future.

6 ERNs reported outcomes from their registries (Q7): ERN GUARd-Heart, ERN eUROGEN, ERN-RND, Endo-ERN, MetabERN, TransplantChild and one does not (ERN GUARd-Heart).

4.2. Importance of Medical Devices from the ERN perspective

Responses to Q15 of the survey assessed the importance of medical devices on a scale from 0 to 10 (of increasing importance). The reported scores from the 7 ERNs that responded to this question are:

- Endo-ERN: 2
- TransplantChild: 5
- ERN GUARd-Heart: 8
- ERN-RND: 8
- MetabERN: 7
- ERN eUROGEN: 10

Out of 7 valid responses, 6 ERNs (86%) rated medical devices as “important”, “very important” to “extremely important” (scores 7–10). These scores reflect the importance of medical devices in the treatment of rare disease, with varying degrees of emphasis. Notably, ERN eUROGEN rated the importance at the maximum level, highlighting a critical reliance.

Free-text elaborations stressed the importance of diagnostic devices, long-term monitoring tools, and assistive technologies, especially for paediatric populations. One ERN noted that medical devices often complement pharmaceutical interventions in integrated care plans.

4.3. Reliance on Medical Devices

Q17 explored the reliance of ERNs on medical devices, with questions asked about high-risk devices (e.g., implantables), and low-risk devices (e.g. wound dressings, splints). Responses were received from 7 ERNs for this question.

High-Risk Devices (e.g., implantables)

Reliant:	ERN GUARd-Heart, ERN-RND
Somewhat reliant:	TransplantChild, MetabERN
Not reliant:	Endo-ERN, ERN eUROGEN

Low-Risk Devices (e.g., wound dressings, splints)

Reliant:	ERN GUARd-Heart, ERN-RND, ERN eUROGEN
Somewhat reliant:	TransplantChild, MetabERN
Not reliant:	Endo-ERN

The data suggests that while reliance on different risk categories of medical device varies across the ERNs, two ERNs (ERN GUARd-Heart, ERN-RND) are dependent on both high- and low-risk technologies.

5. Survey of hospitals participating in ERNs on experience with Orphan and Paediatric Devices

Presented here is a summary of responses from hospitals involved in ERNs regarding their experiences with OPD. The survey focused on challenges in development and access, and gathered feedback on practical experience with clinical studies, device adaptation, shortages, and in-house manufacturing.

This survey received a total of 70 responses from 43 unique respondents, which appear to represent hospitals (in some cases, e-mail contacts rather than hospital names were provided which limits the ability to calculate the number of unique hospitals).

5.1. Challenges in Development and Access

Hospitals reported several barriers to the development of medical devices for rare diseases. Common themes in Q4 included:

- Limited funding opportunities for device development tailored to rare conditions (3 hospitals)
- Lack of regulatory clarity or guidance for custom or niche device development (3 hospitals)

Regarding access to medical devices (Q5), hospitals cited:

- High costs and limited reimbursement pathways (5 and 2 hospitals, respectively)
- Lack of market incentives for producing devices targeting small patient populations (1 hospital)

5.2. Practical Experience with Medical Devices

14 hospitals reported experience in conducting clinical studies for medical devices (Q6). One respondent referenced participation in the Harmony2020 and MyPal projects. 15 hospitals confirmed experiencing unmet needs due to device shortages, affecting patient care (Q7). 20 hospitals acknowledged using devices off-label to meet specific rare disease requirements (Q8). 14 hospitals described adapting device technologies to suit rare disease treatment, including one case involving pyeloplasty stents for paediatric urological care (Q9). 18 hospitals reported preparing devices in-house, including the use of 3D printing for personalized solutions (Q10).

5.3. Additional Insights

Free-text comments indicated that regulatory restrictions and limited hospital-level autonomy often delay access to needed devices (Q11). One hospital proposed improved coordination between clinical and technical teams to accelerate paediatric device innovation (Q12).

6. Survey of European Patient Representatives on challenges and needs relating to Orphan and Paediatric Devices

This section summarizes survey responses from European Patient Representatives concerning challenges and needs related to OPD. The survey explored obstacles to development and access, device availability and suitability, and the role of patient communities in supporting device use. This survey received 37 responses. After removing empty and duplicate responses, 18 responses were included in the analysis.

The participating organisations included:

- AFG (Association Francophone des Glycogenoses) French GSD PO
- Pitt Hopkins UK
- Association Phelan-McDermid Portugal - APMP
- ChILD Lung Foundation
- EAT Easophageal atresia global support groups
- AICI (Interstitial Cystitis Italian Association)
- Raramente, CRL
- PCD Sverige / PCD Sweden
- Cutis Laxa Internationale
- PEM Friends UK
- Foundation for Angelman Syndrome Therapeutics
- Fett-SOS e.V. (Support Group for inborn Fatty Acid Oxidation Disorders)
- Cyprus Association for patients with Inherited Metabolic Diseases Aspida Zois
- Asociación Española Déficit de Lipasa Acida Lisosomal (AELALD)
- Latvia Hemophilia Society
- Alpha-1 Europe Alliance asbl
- European Patients' Forum (EPF)
- Ziekte van Hirschsprung

All but two of these patient groups (EPF and the Latvia Hemophilia Society) are associated with an ERN.

6.1. Development and Access Challenges

Patient representatives highlighted a range of concerns with respect to development and access challenges.

With respect to development challenges (Q4, Q12), key barriers mentioned include:

- Funding constraints: 3 respondents (Pitt Hopkins UK, AFG, Phelan-McDermid Portugal)
- Market limitations and development costs: Reported by AFG and Phelan-McDermid Portugal
- Specific patient and design needs (e.g., miniaturized/custom devices): Pitt Hopkins UK, AFG
- Ethical or safety concerns and regulatory complexity: Pitt Hopkins UK, Phelan-McDermid Portugal

With respect to access challenges (Q5), issues raised include:

- Device availability: AFG, Phelan-McDermid Portugal
- HCP awareness: AFG, Pitt Hopkins UK
- Costs and reimbursement: AFG, Pitt Hopkins UK, Phelan-McDermid Portugal
- Adaptability and daily usability of devices: Pitt Hopkins UK, Phelan-McDermid Portugal

6.2. Device Gaps and Community Actions (Q6–Q8)

Respondents identified missing or inadequate devices, with examples provided such as nutrition pumps and paediatric-sized tools. Training for device use was identified by one group (EAT Federation) which called for parental and patient training for inhalers. 2 respondents noted the need for affordable access mechanisms for available technologies. 2 respondents described peer support networks or family initiatives (Pitt Hopkins UK, EAT Federation) which could support knowledge sharing. Phelan-McDermid Portugal emphasized a need for a central device portal, and described the importance of knowledge-sharing through family groups. One group (Pitt Hopkins UK) is developing a wearable wheelchair-monitoring suit.

7. Overview of EU-funded projects relevant to orphan and paediatric diseases

A mapping of the closed and ongoing Research and Innovation Actions (RIA) relevant to orphan and paediatric disease was performed on the EU Funding & Tenders Portal[11]. Five calls were identified, as indicated below.

7.1. Pilot programme on a Clinical Compound Bank for Repurposing: Rare/orphan diseases

Programme: Horizon 2020 Framework Programme (H2020 - 2014-2020)

Call: H2020-JTI-IMI2-2017-13-two-stage (H2020-JTI-IMI2-2017-13-two-stage)[12]

Type of action: IMI2-RIA Research and Innovation action

Scope: The overall objective of this pilot programme was to take one of the previously deprioritised clinical compounds and investigate their therapeutic potential in new clinical indications in the area of Rare/orphan diseases.

Projects funded under this topic: 1

7.1.1. STOPFOP

Project Title: Saracatinib Trial tO Prevent FOP

Project ID: 821600

Status: Ongoing

Start date: 01 May 2019

End date: 31 May 2025

Project website: www.stopfop.com

Coordinated by: STICHTING AMSTERDAM UMC

Objective: The aim of the STOPFOP trial is to see if the investigative drug AZD0530, also known as Saracatinib, could be used to treat fibrodysplasia ossificans progressiva (FOP). In people with FOP, a mutation occurs in the gene ACVR1 that encodes for the protein kinase ALK2. As a result, ALK2 becomes overactive causing muscles and connective tissues (e.g. tendons) to slowly turn into bone, which severely limits mobility and even breathing. Scientific research by the STOPFOP team has shown that AZD0530 blocks the activity of the pathogenic ALK2 kinase. The team has demonstrated in FOP-mice that the drug was effective in preventing ectopic bone formation which led to preserved mobility of joints.

Results: https://cordis.europa.eu/project/id/821600/results

[11] https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/calls-for-proposals
[12] https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/IMI2-2017-13-15

7.2. Establishing effectiveness of health care interventions in the paediatric population

Programme: Horizon 2020 Framework Programme (H2020 - 2014-2020)

Call: Personalising health and care (H2020-PHC-2014-2015)

Topic: PHC-18-2015[13]

Type of action: RIA Research and Innovation action

Scope: Proposals should focus on clinical research approaches providing a deeper understanding of effectiveness, efficacy and safety of healthcare interventions and the use of health technology assessment methods in the paediatric population.

Projects funded under this topic: 4

7.2.1. CRADL

Project Title: Continuous Regional Analysis Device for neonate Lung

Project ID: 668259

Status: Ended

Start date: 01 January 2016

End date: 30 June 2019

Coordinated by: MIDDLESEX UNIVERSITY HIGHER EDUCATION CORPORATION

Objective: 1) To deliver a tool that provides continuous, non-invasive, radiation free, bedside information on regional lung aeration and ventilation during daily clinical care of (preterm) infants and children with respiratory failure. 2) To assess the effectiveness, efficacy and safety of such a system in guiding respiratory management and supportive care of the most common causes of paediatric respiratory failure (respiratory distress syndrome, bronchiolitis and acute respiratory distress syndrome), with the final goal to reduce short- and long-term adverse effects of disease and its treatment in this population.

Results: https://cordis.europa.eu/project/id/668259/results

Conclusion: Clinicians expect Electrical Impedance Tomography monitoring to better inform decisions on ventilation management and - as a consequence - to reduce the number of patients requiring mechanical ventilation, overall complication rates and hospitalisation length. Electrical Impedance Tomography monitoring was estimated to be cost saving, mainly due to a shorter average hospitalisation length.

7.2.2. ALBINO

Project Title: Effect of ALlopurinol in addition to hypothermia for hypoxic-ischemic Brain Injury on Neurocognitive Outcome

Project ID: 667224

Status: Ongoing

Start date: 01 January 2016

End date: 30 June 2025

[13] https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/phc-18-2015

Project website: www.albino-study.eu

Coordinated by: EBERHARD KARLS UNIVERSITAET TUEBINGEN

Objective: This project aims to evaluate the efficacy and safety of allopurinol administered immediately after birth to near-term infants with HIE in addition to hypothermic treatment. Beyond this primary objective, the project will provide information on the effect of hypothermia on pharmacokinetics of drugs with a similar metabolism as allopurinol in neonates.

Results: https://cordis.europa.eu/project/id/667224/results

7.2.3. ChiLTERN

Project Title: Children's Liver Tumour European Research Network

Project ID: 668596

Status: Ended

Start date: 01 January 2016

End date: 31 December 2021

Coordinated by: THE UNIVERSITY OF BIRMINGHAM

Objective: The ChiLTERN project aimed to establish effective health care for children with liver cancer, of which there are two types: hepatoblastoma (HB) and hepatocellular carcinoma (HCC).

Results: https://cordis.europa.eu/project/id/668596/results

Conclusion: CHILTERN established the most complete worldwide biorepository of clinically and pathologically annotated biological samples from children with liver cancer. It includes 2076 high-quality samples (blood, plasma, tissue, urine) obtained at different time points from 277 (89%) of Paediatric Hepatic International Tumour Trial patients and has established the largest pre-clinical platform of childhood liver cancer with 24 hepatoblastoma patient-derived xenografts, 13 tumour organoids and 15 non-tumour organoids

7.2.4. PIBD-SETQuality

Project Title: Paediatric Inflammatory Bowel Diseases Network for Safety, Efficacy, Treatment and Quality improvement of care

Project ID: 668023

Status: Ended

Start date: 01 January 2016

End date: 30 June 2021

Coordinated by: UNIVERSITE PARIS CITE

Objective: 1) Development of an accessible and feasible risk-stratified treatment algorithm for new onset paediatric Inflammatory Bowel Diseases on an existing inception cohort and validation in an independent cohort; 2) Generation of a prospective large longterm real world inception cohort in a registry designed to analyze effectiveness and safety signals and correlate them to individual risk factors 3) Design and performance of a risk algorithm-based prospective large-scale multicenter randomized clinical trial (RCT) (stratification into high or low risk groups based on specific aim#1) in order to provide optimal personalized therapy : low risk azathioprine vx. methotrexate, high risk: methotrexate vx. adalimumab

Results: https://cordis.europa.eu/project/id/668023/results

7.3. European Partnership on Rare Diseases

Programme: Horizon Europe (HORIZON)

Call: Partnerships in Health (2023) (HORIZON-HLTH-2023-DISEASE-07)

Topic: HORIZON-HLTH-2023-DISEASE-07-01[14]

Type of action: HORIZON-COFUND HORIZON Programme Cofund Actions

Scope: The Partnership should contribute to priorities of the "Communication on effective, accessible and resilient health systems", the "Communication on enabling the digital transformation of health and care in the Digital Single Market; empowering citizens and building a healthier society" and support the objectives of the new EU4Health Programme.

Projects funded under this topic: 1

7.3.1. ERDERA

Project Title: EUROPEAN RARE DISEASES RESEARCH ALLIANCE

Project ID: 101156595

Status: Ongoing

Start date: 01 September 2024

End date: 31 August 2031

Coordinated by: INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE

Objective: The European Rare Diseases Research Alliance (ERDERA) aims to improve the health and well-being of the 30 million people living with a rare disease in Europe, by making Europe a world leader in Rare Disease (RD) research and innovation, to support concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment. This Partnership will deliver a RD ecosystem that builds on the successes of previous programmes by supporting robust patient need-led research, developing new diagnostic methods and pathways, spearheading the digital transformational change connecting the dots between care, patient data and research, while ensuring strong alignment of strategies in RD research across countries and regions.

Results: https://cordis.europa.eu/project/id/101156595

[14] https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/HORIZON-HLTH-2023-DISEASE-07-01

7.4. Modelling and simulation to address regulatory needs in the development of orphan and paediatric medicines

Programme: Horizon Europe (HORIZON)

Call: A competitive health-related industry (Single stage - 2023) (HORIZON-HLTH-2023-IND-06)

Topic: HORIZON-HLTH-2023-IND-06-04[15]

Type of action: HORIZON-RIA HORIZON Research and Innovation Actions

Scope: Clinical trials for orphan and/or paediatric medicines are often smaller than traditional large-scale randomised ones and they require the development of efficient trial designs relevant to small. Model-based approaches are significantly advantageous in small populations.

Projects funded under this topic: 2

7.4.1. ERAMET

Project Title: Ecosystem for rapid adoption of modelling and simulation METhods to address regulatory needs in the development of orphan and paediatric medicines

Project ID: 101137141

Status: Ongoing

Start date: 01 January 2024

End date: 31 December 2027

Coordinated by: UNIVERSITE DE NAMUR

Objective: ERAMET will provide an integrated approach for developers and regulators' decision-making for paediatric and orphan drugs, centred on the drug development questions. This will constitute a transparent ecosystem for drug development and assessment, which will facilitate the adoption of modelling and simulation (M&S) methods and related data.

Results: https://cordis.europa.eu/project/id/101137141

7.4.2. INVENTS

Project Title: Innovative designs, extrapolation, simulation methods and evidence-tools for rare diseases addressing regulatory needs

Project ID: 101136365

Status: Ongoing

Start date: 01 January 2024

End date: 31 December 2028

Coordinated by: INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE

Objective: INVENTS project seeks to refine longitudinal model-based disease trajectories, improve extrapolation models, and implement in silico trials, considering patient's needs, to enhance regulatory decision-making. The project's outcomes are expected to enable researchers, regulators and the European pharmaceutical industry to leverage innovative in silico trials, and real-world data analysis.

Results: https://cordis.europa.eu/project/id/101136365

[15] https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/horizon-hlth-2023-ind-06-04

7.5. Call for proposals for a program on orphan medical devices, in particular targeting paediatric patients (HS-g-23-65)

Programme: EU4Health Programme (EU4H)

Call: EU4H Action Grants 2023 (EU4H-2023-PJ)

Topic: EU4H-2023-PJ-11[16]

Type of action: EU4H-PJG EU4H Project Grants

Projects funded under this topic: 3

7.5.1. OrphaDev4kids

Project Title: Orphan Device for paediatric patients: a unique platform providing innovative services

Project ID: 101161377

Status: Ongoing

Start date: 01 July 2024

End date: 30 June 2027

Coordinated by: CONSORZIO PER VALUTAZIONI BIOLOGICHE E FARMACOLOGICHE

Objective: The OrphaDev4kids proposal aims to address the issue of Orphan Medical Devices to be used in the paediatric population. Paediatric Medical Devices development faces unique challenges as children often differ from adults in size, growth, development, body composition, and disease features. Due in part to these aspects, paediatric Medical Devices development is more complex and riskier for developers and only a small number of approved Medical Devices are available, few designed specifically for children and others readapted from adult applications.

7.5.2. DeCODe

Project Title: Develop Child and Orphan Device Evaluation support

Project ID: 101160939

Status: Ongoing

Start date: 01 September 2024

End date: 31 August 2026

Coordinated by: UNIVERSITEIT TWENTE

Objective: The DeCODe consortium represents a ground-breaking initiative aimed at catalysing innovation and addressing the unique healthcare needs of people living with a rare disease, specifically children. This collaborative group, comprising clinicians, researchers, industry experts, and regulatory authorities, will develop a pivotal platform for developing safe and effective paediatric and orphan medical devices. It will do so to accelerate the development of novel, innovative paediatric and orphan medical device solutions at all stages of the product lifecycle towards implementation.

[16] https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/eu4h-2023-pj-11

7.5.3. i4KIDS 4RARE

Project Title: From challenge to adoption: acceleration of paediatric orphan medical devices

Project ID: 101161079

Status: Ongoing

Start date: 01 June 2024

End date: 31 May 2026

Coordinated by: FUNDACIO PRIVADA PER A LA RECERCA I LA DOCENCIA SANT JOAN DE DEU

Objective: To improve disparities in paediatric innovation, the Sant Joan de Déu Barcelona Children's Hospital created, in 2020, i4KIDS: the paediatric innovation hub. Over the last 3 years, i4KIDS has gained in-depth experience and knowledge in the acceleration of medical devices for the paediatric population, becoming a reference at regional level, from the identification of unmet needs to clinical validation for certification. With around 75% of rare diseases occurring in childhood, i4KIDS aims to create i4KIDS 4RARE: an accelerator to support the development of orphan medical devices for paediatric patients. Through the implementation of i4KIDS 4RARE, we will support pioneering solutions to improve the quality of life of children and families affected by rare diseases, raise awareness of the challenges and share the many opportunities and high-impact innovations.

Conclusion

This report presents findings from an analysis of the landscape for orphan and paediatric medical device development in Europe. Through structured mapping and multi-stakeholder engagement, it identifies a complex and fragmented ecosystem for orphan and paediatric medical device development.

While advances have been made in regulatory guidance and clinical trial facilitation, a disproportionate amount of innovation support remains concentrated at mid-development stages. Future priorities for enhancing support should include:

- Enhanced early-stage translational tools (e.g. design support, funding schemes);
- Strategic alignment between ERNs, hospitals, patient groups and regulators;
- Inclusion of end-user voices in regulatory and reimbursement frameworks.

This deliverable is input for the critical path analysys of orphan medical device development, currently developed within WP3 and to be publicly reported as D3.1 at month M10; and will directly inform the development of the DeCODe stakeholder platform in WP4, enabling the aggregation, visibility, and strategic use of SITs to better serve developers and patients. It also lays the groundwork for subsequent project activities including regulatory and development coaching in WP5.

The insights from this deliverable will inform the DeCODe stakeholder platform and regulatory coaching activities, and provide evidence to guide policymakers, funders, and innovators toward a more integrated and responsive ecosystem for orphan and paediatric medical technologies.

Appendix 1 – Supports, Initiatives and Tools identified

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
INSTITUTO PEDRO NUNES	ANIA	Development practice	Generic Medical Device, General Health Product, Other	Technology and Regulatory	2,3,4,7	1, 2, 3
MARIOLINO DE CECCO, UNIVERSITY OF TRENTO	Collaborative Robotic Walker - NovaWalk	Development practice	Orphan Paediatric Device	1,3,4	3	4
ROQUE CARDONA-HERNANDEZ - HOSPITAL SANT JOAN DE DÉU	Continuous glucose monitoring - Automated insulin infusion	Development practice				5
SANTIAGO MENCÍA - PEDIATRIC INTENSIVIST - HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑÓN	Specific material for advanced medical simulation	Development practice	Paediatric Device	4		6
MARC DOOMS, UNIVERSITY HOSPITALS LEUVEN, BELGIUM	Orphan and paediatric medical devices in Europe: recommendations to support their availability for on-label and off-label clinical indications	Development practice	Orphan and Pediatric Device	2	4	7
PROF. PETER MCCULLOCH HTTPS://WWW.IDEAL-	The IDEAL Framework, in particular IDEAL-D.	Development resource	Generic Medical Device	1,2,3,4,5	1,2,3,4,5,7	8 9

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SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
COLLABORATION.NET/PEOPLE/PETER-MCCULLOCH/						
BELGIAN PEDIATRIC CLINICAL RESEARCH NETWORK	Clinical research network, access to CTUs, clinical experts and patients	Infrastructure	Paediatric Device, Orphan Paediatric Device	2,5	4,7,8	10
SAINT-LUC UNIVERSITY CLINICS, INSTITUT DES MALADIES RARES	Institut des maladies rares PCIC	Infrastructure				11
PEDSTART	PEDSTART is one of the FCRIN Clinical research infrastructure for the Inserm. We take benefit of another FCRIN component that specifically target devices (Tech 4 Health) and may benefit from their expertise	Infrastructure	Other	1,2	3,4	12, 13
PETER MERKUS, RADBOUD UNIVERSITY MEDICAL CENTRE	www.luchtbrug.nl Software: online platform for management and monitoring of patients with chronic respiratory conditions.	Infrastructure	Paediatric Device, Orphan Paediatric Device, General Health Product	2,3,5	4,5,6,7,8	14, 15, 16, 17, 18, 19, 20, 21

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
ROBERT ZIMMER	Machine Learning Support Initiative	Initiative	Orphan Device, Paediatric Device, Generic Medical Device	1,2,4	2,4,5	
HPRA	MDCG guidance on clinical evaluation of orphan devices (to improve predictability of CE marking process) Pre-submission meetings to provide (academic and commercial) trial sponsors with advice for conducting pre-market clinical investigations	Initiative	Orphan Device	1,2,5	3,4	22
ANNALISA SECHI	Rehability neuro	Initiative	Generic Medical Device	2	4	23
YVES COUDIÉRE, UNIVERSITÉ DE BORDEAUX AND IHU LIRYC	CEPS, OpenCARP, Propag	Modelling and simulation tool	Generic Medical Device	Pre-clinical		24
OSCAR CAMARA, UPF BARCELONA	Computational tools to predict stroke or abnormal events, planning device interventions	Modelling and simulation tool	Generic Medical Device	1,2,4	2,3,4	25

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
CI2B- UNIVERSITAT POLITECNICA DE VALENCIA	Computer models of heart for paediatrics population at different ages	Modelling and simulation tool	Paediatric Device, Orphan Paediatric Device	1,2,3,4,5	2,3,4	
GIULIA RUSSO - UNICT - MIMESIS	ERAMET	Modelling and simulation tool	General Health Product, Other	1,2,3,4,5		26
XINSHAN LI, UNIVERSITY OF SHEFFIELD	PyPeCT2S pipeline - Pythonic Paediatric Computed Tomography to Strength	Modelling and simulation tool	Paediatric Device	4	2	27, 28, 29, 30
TARTU UNIVERSITY CHILDREN'S CLINIC	simulation tool	Modelling and simulation tool	Paediatric Device	1,2	3,4	
US FDA	Workflow for Assessing the Credibility of Patient-Specific Modeling in Medical Device Software	Modelling and simulation tool	Paediatric Device, Generic Medical Device	1,2,5	1,2,3,4	31
US FDA	The Virtual Family: A set of anatomically correct whole-body computational models	Modelling and simulation tool	Paediatric Device, Generic Medical Device	1,2,5	1,2,3,4	32
EUROPEAN PATIENTS' FORUM (EPF)	PARADIGM Patient Engagement Toolbox: https://imi-paradigm.eu/petoolbox/	Other	Generic Medical Device, General Health Product	1,2,4,5	1,3,6,7	33, 34
AXEL FRANZ, CENTER FOR PEDIATRIC CLINICAL STUDIES AT THE	The Center for Pediatric Clinical Studies is a full service academic CRO	Other	Orphan Device, Paediatric Device,	2	4	76

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
UNIVERSITY HOSPITAL TUBINGEN	specialized in neonatal and pediatric clinical trials with pharmaceuticals and medical devices and provides infrastructure for all phases of clinical trials to Sponsors who want to conduct such clinical trials		Orphan Paediatric Device			
OLE RASMUS THEISEN. TAKO-CENTRE: NATIONAL RESOURCE CENTRE FOR ORAL HEALTH IN RARE DIAGNOSES. OSLO, NORWAY	uniqueteeth.net	Other	Other	2,4	2	35
RENATA SARNO	Bioptic Driving Licence Tinted contact lenses for achromats and BCM, and bioptic telescope for driving licence, plus magnifiers for school usage to see to see the blackboard from the desk	Patient Focus Group	Orphan Device, Paediatric Device	Technology and Regulatory	7,8	

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
DEBORAH EASTWOOD, BOA	NICE Guidance	Regulatory tool	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	6	4,6,7	
CHRU LILLE FRANCE, PEDIATRIC SURGERY DEPARTMENT	Small endoscopic stapler (3 mm), small electrocautery (Ligasure, Harmonic)	Regulatory tool	Paediatric Device	2	4	36
MARIANA ISKIV, INSTITUTE OF HEREDITARY PATHOLOGY OF NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE	Education platform	Specific Expert Support or mentoring				
DANPEDMED	Trial Nation: https://trialnation.dk/professional/resources-2-2-4/	Specific Expert Support or mentoring		1,2	1,4	37
DR. ALEXANDER REIPRICH, KARL STORZ SE & CO. KG	Development resource, Development practice, Regulatory tool,		Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,3,4,5	1,2,3,4,5,6,7,8	38
DRA. MARÍA DEL MAR MAÑÚ PEREIRA	AI based models for diagnosis, prognosis and personalized medicine AI based models for	Datasets	Generic Medical Device	From pre-clinical to regulatory		

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
	synthetic data generation					
DECODE	Alternative designs for Small Population Clinical Trials	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2	4	39
DECODE	Connect 4 Children (C4C) – Pediatric Clinical Research Networks	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric Device	1,2	3,4	40
DECODE	Crowd funding	HTA and reimbursement	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,3,4,5	1,2,3,4,5	
DECODE	Development and use of Patient-Centered Outcome Measures	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2,5	3,4	41
DECODE	EMA pilot to support orphan devices	Regulatory	Orphan Device	2,5	3,4	42
DECODE	ERDERA	Development resources	Orphan Device	1,2,3	1,2,3,4,5	43
DECODE	EU Expert Panels	Development resources	Orphan Device, Paediatric Device,	2,5	3,4	44

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
			Orphan Paediatric Device			
DECODE	EU Medical Device Regulation	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	5	3,4,5,6	45
DECODE	European Commission funded programs and resources	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,3,4	1,2,3,4,5	46
DECODE	European Patients' Academy (EUPATI) toolbox	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2	3,4	47
DECODE	European Reference Networks	Development resources	Orphan Device	1,2	3,4	48
DECODE	European Strategy Forum on Research Infrastructures	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	4	2	49
DECODE	Extrapolation of efficacy and safety in device development	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric	1,2,5	3,4	

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT		REFERENCE
			Device, Generic Medical Device				
DECODE	FAIR principle for data use	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,3,4,5	2,3,4,5,6,7,8		50
DECODE	Patient engagement in device trial design and feasibility	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2	1,2,3,4		
DECODE	Guidance on the clinical evaluation of orphan medical devices	Regulatory	Orphan Device	2,5		4	22
DECODE	Horizon Scanning: Landscape analysis/ Stakeholder identification and engagement	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,3,4	1,2,6,7		
DECODE	InSilicoTesting	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,4	2,3		
DECODE	LeanEntries	Development resources	Orphan Device, Paediatric Device,	1,2,5	4		51

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
			Orphan Paediatric Device, Generic Medical Device			
DECODE	Natural History Studies (NHS)	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device	1,2,5	3,4	
DECODE	Orphanet database	Development resources	Orphan Device	1,2,5	3,4	52
DECODE	Patent framework	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	3,4	1,2,6,7	
DECODE	Patient organisations	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2	3,4	
DECODE	Patient surveys / Patient Preferences studies / Ethnographic research	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2	3,4	53
DECODE	Private funding	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric	2,3,4,5	1,2,3,4,5,6,7,8	

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
			Device, Generic Medical Device			
DECODE	Registries for Rare Diseases	Development practices	Orphan Device	1,2,4,5	3,4,7,8	54
DECODE	Target Patient Value Profile	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,5	1,2,3	55
DECODE	Technology transfer offices	Development resources	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	3,4	2,3,6	56
DECODE	Rare diseases clinical outcome assessment	Development resources	Orphan Device	1,2	4	57
DECODE	Adaptive designs medical device clinical trials	Development Practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,5	3,4	58
DECODE	IT support	Development resource	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,4	1,2,3,4,5,6	

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
DECODE	Interest group HTA rare diseases	Development practice	Orphan Device, Orphan Paediatric Device	3,5,6	6,7,8	59
DECODE	i4KIDS platform	Development resource	Orphan Device, Orphan Paediatric Device	1,2	1,2,3,4	60
DECODE	Paediatric national networks	Development resource	Orphan Device, Orphan Paediatric Device, Paediatric Device	1,2	1,2,3,4	
DECODE	Assessment framework for digital health frameworks - EDIHTA	Regulatory tool	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	4,5	4	61
DECODE	FDA Catalogue: medical device development tools	Development resource	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,3,4	1,2,3,4	62
DECODE	SPARK	Development resource	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2,3,4	1,2,3,4,6	63
DECODE	Guidance of classification of device types	Regulatory	Orphan Device, Paediatric Device,	5	3,5	64

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
			Orphan Paediatric Device, Generic Medical Device			
DECODE	Post-registry networks	Development resource	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2,5	4,7	
DECODE	post-market surveillance studies	Development practices	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2,5	4,7	65
DECODE	Template EUDAMED submission	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	5	5	66
DECODE	Guidance document for summary of safety and performance	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2,5	4	67
DECODE	Joint HTA+SA advice for devices	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric	2,3,5	6,8	68

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
			Device, Generic Medical Device			
DECODE	Guidance of early feasibility studies	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	1,2	3,4	69
DECODE	IMDRF Guidance personalized devices	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	4,5	1,2,3,4	70
DECODE	Custom-made device guidance	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	4,5	1,2,3,4	71
DECODE	Guidance Legacy to MDR transition	Regulatory	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	3,5	4,5,6	72
DECODE	Registries of the registries	Development resource	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2	4	73

SOURCE NAME/INSTITUTION	TOOL	TYPE OF TOOL	TECHNOLOGY RELEVANCE	DEVELOPMENT ACTIVITY 1. PRE-CLINICAL DEVELOPMENT 2. CLINICAL DEVELOPMENT 3. BUSINESS DEVELOPMENT 4. TECHNOLOGY DEVELOPMENT 5. REGULATORY DEVELOPMENT 6. OTHER	MEDICAL DEVICE LIFECYCLE STAGE 1. CONCEPT 2. PROTOTYPE 3. PRE-CLINICAL 4. CLINICAL 5. MANUFACTURING 6. MARKETING 7. COMMERCIAL USE 8. REIMBURSEMENT	REFERENCE
DECODE	EPTRI	Development resource	Paediatric Device, Orphan Paediatric Device	2	4	74
DECODE	Guidance on developing interventions to improve health and health care	Development resource	Orphan Device, Paediatric Device, Orphan Paediatric Device, Generic Medical Device	2	1,4	75

Appendix 2: Survey questions to identify Supports, Initiatives and Tools

This survey was open to all relevant stakeholders involved in OPD development.

List of questions:

Q1 Your name, or the name of the organisation you represent

Q2 Contact email.

Q3 Which of the following best describe your organization?

1. Hospital
2. Patient Organization
3. Regulatory Agency
4. Healthcare Practitioner
5. Funder
6. Clinical or Regulatory Support Organization
7. Other

Q4 If other, please specify

Q5 How did you find out about this survey?

1. Internet Search
2. Open Call
3. Direct Invitation

Q6 What is your location?

1. Outside EU
2. Austria
3. Belgium
4. Bulgaria
5. Croatia
6. Cyprus
7. Czech Republic
8. Denmark
9. Estonia
10. Finland
11. France
12. Germany

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13. Greece
14. Hungary
15. Ireland
16. Italy
17. Latvia
18. Lithuania
19. Luxembourg
20. Malta
21. Netherlands
22. Poland
23. Portugal
24. Romania
25. Slovakia
26. Slovenia
27. Spain
28. Sweden

Q7 If outside the EU, please specify

Q8 What type of medical device technologies are you interested in? Please select all that apply

1. Orphan Device (this is a device rarely used, where there are insufficient alternatives and / or potential for significant clinical benefit)
2. Paediatric Device (a device used for interventions before birth, or for patients up to 18 years of age)
3. Orphan Paediatric Device
4. Generic Medical Device
5. General Health Product

Q9 Are you interested in any specific rare disease areas?

Q10 If yes, please specify

Q11 Name of support, initiative, or tool

Q12 Which of the following best describe the tools, initiatives or supports from your organization?

1. Initiative
2. Regulatory tool
3. Development resource
4. Development practice
5. Infrastructure
6. Datasets
7. Modelling and simulation tool

8. Accelerator
9. Funding
10. Specific Expert Support or mentoring
11. Patient Focus Group
12. Other

Q13 If other, please specify

Q14 Is there a publicly available source describing your tool, initiative or support?

1. Published literature
2. Web resource
3. EU project
4. US project
5. International project
6. National Competent Authority
7. US FDA
8. EMA
9. Notified Body
10. Research ethics committee
11. HTA / reimbursement body
12. Manufacturer
13. Other

Q15 If other, please specify

Q16 Can you provide a link to further information, for example a web-link or literature reference?

Q17 For the tool identified Q11, please describe the technology relevance of the tool

1. Orphan Device
2. Paediatric Device
3. Orphan Paediatric Device
4. Generic Medical Device
5. General Health Product
6. Other

Q18 If other, please specify

Q19 Is your tool, initiative or support relevant to the following activities? Please select all that apply

1. Pre-clinical development
2. Clinical development
3. Business development

4. Technology development
5. Regulatory development
6. Other

Q20 If other, please specify

Q21 Which of the following development stages is your support, initiative or tool relevant to? Please select all that apply

1. Concept
2. Prototype
3. Pre-clinical
4. Clinical
5. Manufacturing
6. Marketing
7. Commercial use
8. Reimbursement

Q22 Are there any aspects of the support, initiative or tool that are particularly relevant to Orphan and Paediatric Device development?

Q23 Are there costs or contractual requirements associated with the tool, initiative or support? For example, royalties, success fees, equity etc.

Q24 Please provide a general description

Q25 If possible, please provide a general cost estimate

Appendix 3: Survey questions for ERNs

This survey was aimed at ERN Full Members and Affiliated Partners

List of questions:

Q1 Name of the ERN

Q2: Contact in ERN

Q3 Disease/condition addressed

Q4 From your perspective, what are the key challenges for the development of medical devices for rare disease?

Q5 What are the key challenges for the access to, or use of medical devices for rare diseases?

Q6 Does your ERN have an active registry?

Q7 Please provide any links to publications or websites that provide this information

Q8 How important are medical devices in the treatment of rare diseases relevant to your ERN? (scale 1-10, 1 = not important, 10 = extremely important)

Q9 Please provide further information

Q10 Are you more reliant on high-risk medical device technologies (for example implantable devices) or low-risk devices (for example wound dressings, supportive devices such as splints etc.)

Q11 If you would like to add any further information regarding Orphan or Paediatric Medical devices that you are reliant on, please provide detail here

Q12 Please provide any other comments related to the development of Orphan and Paediatric Medical devices that were not captured above

Appendix 4: Survey questions for Hospitals participating in ERNs on experience with Orphan and Paediatric Devices

This survey was aimed at ERN Full Member and Affiliated Partners.

List of questions:

Q1 Name of the hospital

Q2 Contact in the hospital

Q3 Name of the ERN(s) that you participate in

Q4 From your perspective, what are the key challenges for the development of medical devices for rare disease?

Q5 What are the key challenges for the access to, or use of medical devices for rare diseases?

Q6 Does your hospital have experience in conducting clinical studies for new medical devices?

Q7 Please provide more information

Q8 Have you encountered unmet medical needs as a result of product shortages with medical devices?

Q9 Please provide more information

Q10 Have you used medical devices 'off-label' (i.e. a device marketed for one use which is used for another)

Q11 Have you adapted medical device technologies to suit the treatment of a rare disease

Q12 Does your hospital prepare medical devices for the treatment of rare diseases (known as 'in-house' manufacturing of medical devices), for example using a 3D-printer to make a splint matched to the patient's anatomy

Appendix 5: Survey questions for European Patient Representatives for Orphan and Paediatric Devices

This survey was aimed at ePAG members.

List of questions:

Q1 What is the name of your patient organisation?

Q2 Please provide the contact details for the patient organisation

Q3 Is your patient organisation associated with a European Reference Network?

Q4 Please describe the paediatric or rare disease focus of your patient organisation

Q5 From your perspective, what are the key challenges for the development of medical devices for rare disease and/or children?

Q6 What are the key challenges for the access to, or use of medical devices for rare diseases and/or children?

Q7 As patient representatives, have you experienced any of the following:

- Needs that are not currently addressed by available technologies
- Unavailability of medical devices that were previously available
- Difficulties in accessing available medical technologies
- Other

Q8 Do you share knowledge or experience on how to use medical device equipment which is provided to patients?

- Yes
- No

Q9 Are there other activities or supports that would be valuable to support the access and use of medical devices for children and patients with rare diseases? Please describe below:

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