Children often do not have equitable access to safe, effective, and high-quality medicines adapted to their needs

Children frequently struggle to access the best medicines and health products tailored to their needs. This problem arises because the development and availability of high-quality, lifesaving commodities designed for infants, children and pregnant women are often lacking, inadequate or simply unavailable, particularly in low-resource areas (1).

Despite huge progress towards reducing child mortality, major disparities persist between countries and millions of children are needlessly suffering. Almost 5 million children under five still die every year in low- and middle-income countries (LMICs), mostly from preventable and treatable diseases (2). Despite the clear need to improve access to medicine for these children, the stark reality is that they are often left waiting last in line for new medicines matched to their specific needs. Complexities around clinical trial enrolment, regulatory requirements, formulations and dosage guidelines, combined with challenging market economics, all constrain availability of child-friendly treatments (3).

Appropriate medicines to save and improve the lives of infants and children, and to address their most pressing health priorities, often do not exist, are unavailable, or are not quality assured (1,4). A child born today could wait up to 10 years before a newly available medicine for adults is eventually tailored to their needs (4,5). This puts children’s lives at risk, hindering the achievement of the Sustainable Development Goals (SDGs) and universal health coverage (UHC) targets (6).

Ensuring access to essential medicines is an explicit component of the broad right to health, as enshrined in international human rights conventions. For example, article 24 of the Convention of the Rights of the Child states that:

“Parties recognize the right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health” (7).
The World Health Assembly has taken important steps to improve access to better medicines for children through the adoption of resolutions with a focus on access to medicines for children, such as:

- **Better medicines for children** (WHA60.20; 2007) (8).
- **Regulatory system strengthening for medical products** (WHA67.20; 2014) (9).
- **Promoting innovation and access to quality, safe, efficacious and affordable medicines for children** (WHA69.20; 2016) (10).
- **Addressing the global shortage of medicines and vaccines, and the safety and accessibility of children’s medication** (WHA69.25; 2016) (11).
- **Strengthening clinical trials to provide high-quality evidence on health interventions and to improve research quality and coordination** (WHA75.8; 2022) (12).

The latest World Health Assembly resolution, entitled *Accelerate progress towards reducing maternal, newborn and child mortality in order to achieve SDG targets 3.1 and 3.2* (6), calls on Member States, stakeholders and the WHO secretariat to enable access to essential safe high-quality and age-appropriate medicines for children through accelerating implementation of the actions laid out in resolutions WHA69.20 (8) and WHA75.8 (12), and by promoting, supporting and financing accelerated investigation, development, manufacturing, registration and supply of age-appropriate, quality-controlled formulations of medicines for diseases that affect children.

Objective of this advocacy brief

The objective of this brief is to mobilize global advocacy efforts on access to better – safer, more effective and quality-assured – medicines in optimal formulations suitable for children (14). It outlines some of the main challenges in accelerating the development of and access to #BetterMeds4Kids, and presents possible solutions to address those challenges. The brief can be used to support the alignment, messaging, mobilization and advocacy of stakeholders at global, regional and national levels.

The problem

Limited access to properly formulated medicines for children affects multiple diseases and has severe consequences for the well-being and lives of millions (Fig. 1).
Numerous factors contribute to this challenge, hindering access to the best possible treatments for children:

- Medicines are usually first developed for adults; it is only when that process nears or achieves completion that the paediatric adaptation process typically begins. For example, bedaquiline and delamanid were the first new tuberculosis (TB) treatments to be developed for over 40 years, yet child-friendly formulations were not available until about seven years after the adult versions (15).

- In many cases, suitable formulations and doses are never attempted or made available. An analysis by the Access to Medicines Foundation in 2021 showed that less than 7% of all product development and deployment projects assessed target children under the age of 12, revealing major gaps in the paediatric medicines development pipeline (3).

- There is a fragmented landscape of paediatric drug innovation and access, exacerbated by the lack of a unified global priority-setting mechanism across the many areas of paediatric health product development. The current approach is siloed, with stakeholders’ efforts often focusing on tackling just one part of the product life cycle, and insufficient upstream or downstream attention.

- Clinical research in paediatric populations (especially neonates) is particularly challenging, requiring specific capacities, as well as enabling norms and standards. Medicines administered in paediatric populations are often used off-label and in unlicensed ways. Even when new and innovative medicines are available with a paediatric indication, there is often limited evidence of long-term effects or risks. For example, a 2017 study revealed that only 11% of pharmacokinetic (PK) studies on medicines for neglected tropical diseases (NTDs) included children, and for most medicines paediatric PK data were not available (16,17).

- The lack of harmonized regulatory guidance for the development and introduction of paediatric medicines also disincentivizes innovation. Availability of treatments for NTDs are often delayed at the approval stage, for example, and recent analyses showed that less than half of WHO-recommended medicines for NTDs that are effective in children are approved for paediatric use. (18). There is a reported average delay of between four and over eight years from approval of cancer medicines for adults and
their approval for children; the approval process for some medicines for children has been delayed more than 20 years longer than their approval for adults (19,20).

- **There are logistical barriers in developing child-friendly formulations.** Bacterial infections, especially pneumonia, neonatal sepsis and gastrointestinal infections, are the leading cause of infectious mortality among children younger than five years worldwide (19). Yet, the number of product development and deployment projects for neonatal conditions such as sepsis is alarmingly low, with only five projects in development in 2021 (3). Although existing antibiotics, demonstrate a favourable benefit–risk ratio, many antibiotics are not indicated for use in children and do not exist in optimal formulations for children (20). When suitable formulations for children are designed, several factors should be considered, including patient tolerability, ease of administration by caregivers/health care providers, frequency of dosing, the need for special conditions during the compounding process, and the need for time-sensitive preparatory steps at the time of administration. Certain formulations can face logistical barriers to use. For example, the need for reconstitution or refrigeration may be a significant barrier to widespread use in LMICs. Parenteral medications require intravenous access and health care worker expertise in administration. Excipients used for oral liquid or syrup formulation stability may be unsuitable for children.

- **Country systems** are not always ready for the introduction of new medicines (21,22). This includes health technology assessment, prioritization and policy development, investments, quantification, planning and budgeting, among others. For instance, treatment with highly effective direct-acting antiviral drug regimens can cure hepatitis C infection and is recommended by WHO. But most countries, including LMICs with some of the highest disease burdens, do not have policies in place for the treatment of children (23).

- **Paediatric medicines represent a low volume market** and there may be limited epidemiological data for children, which disincentivizes pharmaceutical companies to invest (4,24,25). difficulties in forecasting demand and pooling procurement mean that supply often cannot meet demand, and traditional incentives for innovation and manufacturing are insufficient on their own (24,26).

- **There are limited investments in community mobilization and advocacy** to accelerate access to better medicines for children (27). Access to child-appropriate medicines is limited, even in countries with well-structured universal public health systems. Limited budgets, the lack of clinical practice standards, inadequately trained personnel, the absence of supporting policies and structures, and limited awareness of (and therefore demand for) improved products, are intertwined barriers (24,27). To improve access, global, national and local (subnational) support systems are needed.

- **A lack of access to testing and no active case-finding strategies** are also barriers, hampering not only treatment delivery but also restricting essential market intelligence on needs and demand for therapeutic products in many disease areas (e.g. TB, hepatitis C, and hepatitis B) (23). In some cases, stigma and discrimination are additional barriers to the treatment of children affected by certain diseases (28).

- Paediatric drug research, development and delivery are not supported by broad dedicated funding mechanisms and targeted intervention programmes. When actions and resources are not aligned across the full product development process, a single gap that prevents or stalls the transition from one phase to another can bring progress to a halt (Fig. 2). Transparency and coordination of funding are desperately needed as research has shown that the available funding is concentrated mainly in Europe and the United States (29).
Fig. 2. Siloed product development efforts by different stakeholders can delay development of adapted paediatric drug formulations

Advocating for possible solutions
Creating strong momentum and mobilizing leadership to trigger implementation of existing policies and/or the improvement of the policy landscape for paediatric drug development is key to achieving better health for children. This advocacy brief proposes a set of solutions and framing narratives for partners and stakeholders to use in their conversations when advocating for the #BetterMeds4Kids agenda (Fig. 3).

Fig. 3. Five proposed solutions and framing narratives

1. PRIORITIZE EFFORTS
Focus on priority drugs and formulations that are in the pipeline.

2. COORDINATE
Strengthen coordination to accelerate access to prioritized medicines and formulations for children.

3. INCENTIVIZE ACTION
Address regulatory challenges and facilitate market entry to incentivize R&D investments and initiatives.

4. ENSURE ACCESSIBILITY
Accelerate introduction of and sustain access to better and affordable medicines for children in country.

5. INVEST MORE AND SMARTER
Mobilize resources to accelerate research and development of better formulations for children.
Solution 1 – Prioritize efforts

Focus on priority drugs and formulations that are in the pipeline

The Paediatric Drug Optimization (PADO) process is a critical mechanism to identify priority drugs and formulations that need to be developed and delivered to fill important access gaps (30). The process has been applied to prioritize products and research questions across various therapeutic areas: antibiotics; childhood cancer (applied to the six Global Initiative for Childhood Cancer diseases: acute lymphoblastic leukaemia, Burkitt lymphoma, Hodgkin lymphoma, retinoblastoma, Wilms tumour, and low-grade glioma); COVID-19; hepatitis C; HIV; neglected tropical diseases (applied to five NTDs: human African trypanosomiasis, onchocerciasis, scabies, schistosomiasis and visceral leishmaniasis); TB (13). Each disease area and product require specific advocacy support at different levels to ensure that these priorities move forward in the product lifecycle and become available to children in a timely manner.

Possible actions to implement solution 1

• Promote alignment around priority paediatric medicine formulations. This includes support and political attention to the outcomes of WHO-led PADO processes (30).
• Ensure systematic assessment of age-appropriateness of paediatric formulations included in national essential medicines list, taking into account the WHO Model List of Essential Medicines (including the WHO Model List of Essential Medicines for Children) and advocate for accessibility and affordability of those essential medicines.

Solution 2 – Coordinate

Strengthen coordination to accelerate access to prioritized medicines and formulations for children

With a fragmented landscape of paediatric drug innovation and delivery, efforts often focus on tackling just one part of the product life cycle, with insufficient attention paid to upstream or downstream activities (Fig. 2). This is exacerbated by the lack of a global priority-setting mechanism across many areas of paediatric health product development. The lack of regular and consistent tracking and mapping of needs, gaps, actors, and funding flows significantly reduces the options for aligning actors and efforts, targeting interventions, benefiting from potentially cross-cutting technologies (e.g. for taste masking and administration) and achieving more coherent and seamless funding streams that allow translation across phases from early research and development to access.

Possible actions to implement solution 2

• Ensure access to better medicines for children remains on global, regional and national agendas through advocacy and high-level political engagement. This can be done by ensuring accountability in the context of the World Health Assembly and with WHO Member States; by advocating for access to medicines for children as part of global political debates (such as the G20 and G7), and regional institutions (including the African Union and African Medicines Agency among others); and through active engagement in national-level debates and policy deliberations.
• Ensure accountability at all levels through the development and follow up of action items from specific resolutions, agreements, debates and policies, and leverage clinical trials and diagnostics resolutions to advocate for access to care for vulnerable populations.

• Leverage pandemic prevention, preparedness and response processes (such as those of the Intergovernmental Negotiating Body on a pandemic treaty) and integrate language on vulnerable populations in high-level policy outcomes.

Solution 3 – Incentivize action

Address regulatory challenges and facilitate market entry to incentivize research and development investments and initiatives

In 2021, only an estimated 7% of pharmaceutical companies’ research and development (R&D) investment was focused on products targeting children under 12, despite significant gaps in paediatric treatment options (3).

Possible actions to implement solution 3

• Invest in clinical research capacity and accelerate the development of guidelines, norms and standards for clinical research in neonates and children, and ensure feasibility and implementation of results as well as the gathering of real world data to report on the outcomes. Also incentivize research and manufacturing in the context of support to local production, including investment funds and support to companies that commit to paediatric medicines development.

• Streamline regulatory procedures for priority paediatric medicines by helping to identify the most efficient regulatory routes at the national and regional levels, including through the use of collaborative registration procedures (31). Harmonize regulatory guidance for the development and introduction of paediatric medicines, including working towards ensuring that regulatory procedures from one therapeutic area or drug type can be applied to others, and facilitate the development of enabling norms, standards, regulations and policies. Also simplify and incentivize the paediatric R&D process by, for example, identifying and overcoming inefficiencies in regulatory procedures, and establishing targeted economic incentives such as market entry rewards.

• Ensure availability, supply and affordability by fully integrating access planning across all stages of the paediatric medicines development processes. Leverage pooled procurement (global and regional) to address small market challenges through strong coordination mechanisms. This includes joint price negotiations and efforts to reduce transaction and operational costs, using multi-year agreements, accurate forecasting and demand creation, and strong advocacy to bring attention to, prevent and solve stock outs and supply disruptions.

Solution 4 – Ensure accessibility

Accelerate introduction of and sustain access to better and affordable medicines for children

Introducing and transitioning to optimal treatments for children at the country level faces various challenges. Policy updates, capacity building, demand creation, quantification, budgeting, procurement, distribution and pharmacovigilance are, among others, key issues that national
implementers need to anticipate and plan for to ensure system readiness for introducing and sustaining optimal therapies for children.

Possible actions to implement solution 4

- Develop/update national essential medicine lists for children. The development of a National Essential Medicine List for Children is an important step, facilitating inclusion of optimal paediatric medicines in pharmacy stocks, reimbursement schemes and hospital lists, as well as their effective distribution and availability across various parts of health care systems.

- Ensure affordable prices for medicines for children through price negotiations or increased competition (including through the use of voluntary licensing agreements) (32). Also ensure that public insurance coverage schemes cover medicines designated as essential for children.

- Strengthen national paediatric medicine action plans and their implementation across national health systems, including through training health workers and caregivers on the use and/or administration of optimal paediatric drug formulations and monitoring safety of medicines use in children (33). This should include adequate training of health care workers and caregivers regarding new product administration. Clarity around any changes to dosage and dosing schedules as children grow is important and can help ensure appropriate use and intended health outcomes and benefits.

- Enhance community preparedness and engagement of civil society, communities and patient groups (including children), which contributes to successful introduction and sustainability of drugs through, treatment literacy, demand creation, service delivery and accountability.

Solution 5 – Invest more and smarter

Mobilize resources to accelerate research and development of better formulations for children

Support for research, development and introduction of optimal formulations for children is limited. The GAP-f investment case estimates that the resource needs for a product portfolio of 10 formulations in six disease areas will be more than US$ 100 million by 2030, in order to positively impact over 16 million children’s lives (1).

Possible actions to implement solution 5

- Advocate for increased investments by multilateral and bilateral donors, the private sector and initiatives that contribute to accelerating access to better medicines for children. This includes increased investments in and from public, private and philanthropic sectors.

- Leverage government funding, development assistance and philanthropic finances by shaping local paediatric medicines markets, attracting impact investors, and increasing the funding available for innovative approaches to expand access to paediatric products in LMICs, thereby mobilizing additional resources for research, development and introduction of better medicines for children.

- Advocate for organizations investing in research, development and introduction of adult medicines to extend their support to include paediatric medicines and child-friendly formulations.
Delivering adapted therapies to children: Five areas of action

Access to medicines for children is essential to reduce child mortality and to achieve better health for all. The fact that children die due to lack of access to optimal medicines should be a call to action to all stakeholders working on health.

This document is intended to support stakeholders within, around and outside the GAP-f network who believe that #BetterMeds4Kids are essential to advocate for accelerated access to better medicines for children. It proposes five areas of action:

- **Prioritize efforts:** Focus on priority drugs and formulations that are in the pipeline.
- **Coordinate:** Strengthen coordination to accelerate access to prioritized medicines and formulations for children.
- **Incentivize action:** Address regulatory challenges and facilitate market entry to incentivize R&D investments and initiatives.
- **Ensure accessibility:** Accelerate introduction of and sustain access to better and affordable medicines for children in country.
- **Invest more and smarter:** Mobilize resources to accelerate research and development of better formulations for children.

This paper calls on WHO Member States and other relevant stakeholders to share good policy practices and solutions, and collaborate to address remaining gaps through existing platforms and mechanisms, including WHO governing bodies, and advocate for the prioritization of children's needs in global, regional and national debates on access to medicines.

Approach to development

GAP-f is a WHO network created to respond to the paediatric medicines gap. Following adoption of the World Health Assembly resolution Promoting innovation and access to quality, safe, efficacious and affordable medicines for children (10), GAP-f was conceived to build on and formalize the model developed within the HIV community to provide a sustainable mechanism ensuring that safer, more effective and more durable paediatric formulations are developed and made available to children against an accelerated timeline.

This advocacy brief was developed through a consultative process with the GAP-f Strategy and Coordination Committee and with the GAP-f Civil Society and Community Engagement (CSCE) dialogue, which is led by partner organizations: Elizabeth Glaser Pediatric AIDS Foundation and Medicines Patent Pool. The CSCE group includes nongovernmental organizations, community representatives and civil society organizations, as well as GAP-f network partners. The CSCE supports and catalyses civil society and communities’ contributions to the paediatric drug optimization continuum. Peer-reviewed publications were used to inform the introduction and narrative components of the brief. Stakeholder consultations informed the key priorities as well as the language and overall direction of the brief.

Declarations of interest

All technical contributors and participants in relevant advisory groups were individually required to complete standardized WHO declaration of interest statements. These declarations were thoroughly reviewed by the WHO secretariat. Following this review process, no conflicts of interest were identified that could compromise the objectivity or integrity of this brief.

A list of GAP-f member organizations is available at: [https://www.who.int/initiatives/gap-f/members](https://www.who.int/initiatives/gap-f/members)
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About the GAP-F network

The Global Accelerator for Paediatric Formulations (GAP-F) is a collaborative initiative aimed at addressing the critical need for equitable access to paediatric medicines tailored to the specific needs of children, particularly in low- and middle-income countries. Established in response to the fragmented landscape of paediatric drug development, GAP-F seeks to overcome barriers that hinder the timely development, approval, and distribution of age-appropriate formulations for children. By leveraging the expertise and resources of a diverse network of partners, GAP-F focuses on accelerating research, development, regulatory approval, and market introduction of essential paediatric medicines. Its work is crucial in ensuring that children receive effective, safe, and affordable treatments, ultimately contributing to the achievement of Sustainable Development Goal 3 (Good Health and Well-being) and universal health coverage.

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