GLOBAL POLICY BRIEFING

AMPLIFYING GLOBAL LEADERSHIP TO END PAEDIATRIC AIDS

Summary

Ending paediatric HIV and securing an AIDS free future for infants, children, adolescents, and young people is an urgent public health priority and is enshrined in the United Nations' Sustainable Development Goals (SDGs);[a] associated with health, addressing gender equality, reducing inequalities and promoting global partnerships. Globally, recognised as a neglected disease, paediatric HIV requires global and national political leadership, dedicated investment, innovation in research and development (R&D), as well as implementing novel and effective HIV prevention, treatment, and care options.[1]

In 2015, 'Start Free, Stay Free, AIDS Free' targets were established by UNAIDS and its global partners to significantly reduce AIDS as a public health threat for paediatric populations by 2020. The targets included:[2]

- reducing new infections in children (from birth to the age of 14) to **20,000**
- reducing the number of new infections to less than **100,000** among adolescent girls and young women (AGYW)
- providing **1.4 million** CLHIV with antiretroviral therapies (ART)

These ambitious but attainable targets have yet to be reached. In 2019, **150,000 children were newly diagnosed with HIV** and only **950,000 (53%) CLHIV were receiving ART**. Of the **840,000 undiagnosed CLHIV**, an estimated **33% are believed to be between the ages of 5 and 14.**[5]

Where the burden of paediatric HIV in sub-Saharan Africa is particularly high[3]

Nigeria, the United Republic of Tanzania, South Africa, and Mozambique accounted for **50% of HIV incidence in children aged between 0-14 years**

AGYW in sub-Saharan Africa **represented 25% of new infections**, yet they only constituted approximately 10% of the overall regional population[4]

Key obstacles to addressing paediatric HIV include: the availability of appropriate diagnostics. This includes family-based index testing (providing HIV test to the families of PLHIV) and targeted community-based testing to improve HIV case finding.[6] Barriers to eliminating paediatric HIV also includes: vertical transmission (during gestation, delivery, or breastfeeding), slow initiation of treatment, poor availability of optimised paediatric antiretroviral formulations and the challenges associated with delivering family-centred care to support CLHIV and those vulnerable to HIV.[7,8]

As the only global pharmaceutical company 100% dedicated to HIV, ViiV Healthcare is at the forefront of researching and delivering innovative HIV medicines, solutions and programme partnerships which aim to improve the lives of people living with and those most vulnerable to HIV including paediatric populations. Ending paediatric AIDS forms part of our mission and investing to address chronic infectious diseases in children and young people is a global health strategic priority for both ViiV Healthcare and GSK, our majority shareholder. To this end, ViiV Healthcare works collaboratively with diverse partners to advocate for and commit to the following policy principles:

To drive HIV research innovation in drug development which seeks to improve paediatric health outcomes. This ensures we prioritise R&D efforts and pursue bold public health commitments focused on appropriate medicines and formulations for young infants through to young people under the age of 18. These essential 'first line' medicines are identified as high priority by the World Health Organisation (WHO)-led Paediatric Antiretroviral (ARV) Drug Optimisation (PADO) group - made up of global public health experts.[9] We worked with diverse research partners including the National Institutes of Health (NIH), the International Maternal Paediatric Adolescent AIDS Clinical Trials Network (IMPAACT) and PENTA child health research networks to generate robust and reliable data to support regulatory dossier submissions.

To champion the power of partnerships essential to create an enabling environment to speed-up access to, and improve delivery of, priority child-friendly HIV prevention and treatments options by:

- **Accelerating the development, registration,** and availability of paediatric antiretroviral formulations in developing countries **through technology transfer and voluntary licensing** partnerships with global health agencies and generic manufacturers.

- **Building local healthcare capacity.** Since 2012, ViiV Healthcare has collaborated with the International AIDS Society (IAS) to establish the Collaborative Initiative for Paediatric HIV Education & Research (CIPHER). This collaborative supports the development of technical skills and expertise to address key clinical and operational research gaps in paediatric and adolescent HIV, specific to resource-limited countries.[10] As well as seeking to support the next generation of paediatric HIV researchers, the alliance has developed a global paediatric HIV cohort collaboration which now informs global policy updates and key research priorities.

- **Strengthening community-led capacity, through thought leadership and strategic investment, to end paediatric AIDS by 2025.** ViiV Healthcare's Positive Action programme has a well-established track record of strategic partnership engagement with diverse stakeholders to address paediatric HIV. This includes over a decade of programmatic engagement with several international and local partners. Our new 10-year strategy launched in 2020, re-affirms our commitment to tackle paediatric HIV.

- **Engaging and supporting global health policy.** ViiV Healthcare is a strong and active supporter of global and bilateral agencies which are critical to informing community, local, national, regional, and global policy to address paediatric HIV. This includes the Global Fund, the President's Emergency Plan for AIDS Relief (PEPFAR), UNAIDS, the WHO and Unicef, among others. We support the important role played by these organisations and recognise the need for political leadership to ensure they are adequately resourced to effectively fulfil their public health mandates. This includes leaving no child living with or vulnerable to HIV behind.

The Challenge

The complexity in paediatric antiretroviral R&D

The challenges associated with paediatric ARV development and delivery are varied and complex. Paediatric populations are segmented by weight and age which may require multiple dosage formulations that can be complicated to develop with respect to palatability, dispersibility and recommended storage conditions (given the majority of CLHIV live in climates where temperatures and humidity are high). In addition, demand volumes are comparatively low compared to adult ARVs which can be challenging for manufacturing efficiency and sustainability. The gulf in unmet clinical needs for paediatric populations is also often driven by the more complicated and cumbersome diagnostics processes. Infants require a unique HIV test (virological), which is not readily available in most low- and middle-income countries.[11] In addition, conducting clinical trials to establish drug safety and efficacy are also fraught with difficulty due to a lack of data and delays in the completion of clinical studies. Understandably, parents are also reluctant to provide consent for their children to participate in clinical trials. Furthermore, the introduction and uptake of novel child-friendly health products remains challenging. This includes national registration of medicines, national treatment guidelines, demand generation and adequate training to deliver appropriate child-centred care.[12]

ViiV Healthcare collaborates with diverse partners to address many of these challenges in ambitious and innovative ways. This is steered by the strategic leadership provided by the Global Accelerator for Paediatric Formulations (GAP-f), a WHO-led initiative which seeks to advance progress across the full spectrum of drug development aiming to prioritise, evaluate, develop and deliver optimal formulations for paediatric populations. The GAP-F collaborative framework works to delivers a more rapid, efficient and targeted approach to paediatric drug formulation development. This includes simplifying the generation of robust clinical evidence, incentivising manufacturers, accelerating product development and introduction as well as coordinating procurement.[13]

The Power of Partnership

The challenge of addressing paediatric HIV, eliminating preventable AIDS-related paediatric child deaths, and securing paediatric HIV targets cannot be met without diverse and multisectoral partnerships across the public, private and not-for-profit sectors. Efforts need to focus on: accelerating the development, registration and availability of priority medicines; building local healthcare capacity; strengthening community-led initiatives and prioritising global policy engagement to end paediatric AIDS by 2025; given the 2020 target has been missed.

To this end, ViiV Healthcare has collaborated with partners, with whom we share our bold ambition to challenge convention. Together we seek to proactively build trust as well as promote open and transparent engagement which enables us to work innovatively to address paediatric HIV.

Pioneering clinical data generation
ViiV Healthcare has developed a dispersible paediatric tablet formulation of Dolutegravir; a once-daily treatment for neonates as young as four weeks old and children living with HIV. This has been recently be approved by the US Food and Drug Administration. To deliver this ambitious and innovative commitment, we collaborated extensively with partners including the National Institute of Health (NIH), the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network and Paediatric European Network for Treatment of AIDS (PENTA). Together we generated and analysed appropriate clinical data to support regulatory submissions.[14]

a. Accelerating the development, registration and availability of paediatric DTG in developing countries through technology transfer and voluntary licensing partnerships working with global health agencies and generic manufacturers

Since 2018, ViiV Healthcare has collaborated with two global health organisations - the Clinton Health Access Initiative (CHAI), Unitaid (an UN-backed global health initiative) - and two generic manufacturers - Mylan (now a subsidiary of the Viatris group) and Macleods - to accelerate generic development and registration through the transfer of DTG dispersible tablet technology. Through this innovative partnership, Mylan was able to submit their regulatory dossier to the FDA for review in advance of ViiV Healthcare securing regulatory approval from the US FDA. This was the first time this parallel approach (opposed to the conventionally sequential approach) has been adopted for an HIV medicine. Furthermore, in June 2020, Macleods submitted a new drug application for tentative approval under the FDA's PEPFAR[b] scheme within days of ViiV Healthcare receiving FDA approval.[15,16] In addition to Mylan and Macleods, there are 13 other generic manufacturers who have voluntary licences for paediatric DTG formulations with ViiV Healthcare, either directly or via the Medicines Patent Pool (MPP).[17,18] This enables these pharmaceutical companies to develop, manufacture and supply paediatric DTG formulations to 121 developing countries. This represented nearly 99% of children living with HIV across low-and-middle income countries (as classified by the World Bank) at the time of agreement execution.[19,20,21]

ViiV Healthcare also funds an independent collaborative HIV clinical and experimental platform which seeks to identify new therapeutic strategies to treat children infected with HIV, with a goal to achieve HIV remission.

EPIICAL (Early-treated Perinatally HIV-infected Individuals: Improving Children's Actual Life) has been developed by PENTA Child Health Research and 25 other international research partners including the University of Witswatersrand (South Africa), University of Miami (USA), University College London (UK) and Korolinkska Institutet, Sweden, among others.[22] The project seeks to tackle the needs of children and their families by advancing the science of HIV remission developed by clinicians, researchers, the HIV community, regulators and industry. The platform's data and insights have the potential to transform the lives of CLHIV worldwide which could also be applied to treatment of HIV in adults, particularly those who initiate ART early.

b. Building local healthcare capacity

Addressing healthcare system challenges in countries with a high burden of paediatric HIV is critical to end the epidemic. Recognising this, ViiV Healthcare collaborates with diverse partners to help strengthen local technical capacity.

ViiV Healthcare's support enabled the International AIDS Society (IAS) to establish the Collaborative Initiative for Paediatric HIV Education & Research (CIPHER), through funding to accelerate priority research in low and middle-income countries (LMICs). The alliance also seeks to support the development of the next generation of paediatric HIV researchers. It has led to the creation of a global paediatric HIV cohort collaboration which now informs global policy updates and research priorities.[23]

c. Strengthening community-led capacity, through thought leadership and strategic investment, to end paediatric AIDS by 2025

ViiV Healthcare's Positive Action programme has a well-established track record of strategic partnership engagement and investment with diverse partners to address paediatric HIV. Investments focus on access to services for vulnerable groups through strengthening community engagement, improving service delivery as well as tackling stigma and discrimination. Historically, this includes over a decade of programmatic engagement and £50 million invested into the community-based response via the 'Positive Action Children's Fund'. In 2019, our paediatric programmes impacted the lives of almost 640,000 people.[24]

[b] The U.S. President's Emergency Plan for AIDS relief (PEPFAR) is the largest commitment by any nation to address a single disease in history, enables by strong bipartisan support across nine U.S. congresses and three presidential administrations.

In 2020, ViiV Healthcare embarked on a new Positive Action strategy which reaffirms the company's commitment to address paediatric HIV. We have formed a three-year partnership focused on ending paediatric AIDS by 2025 in Mozambique, Nigeria and Uganda by harnessing the unique strengths of leading programme implementing organisations such as Aidsfonds, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), ELMA Foundation, the Paediatric-Adolescent Treatment Africa (PATA), and Unicef. The partnership seeks to support and scale-up implementation of sustainable and high-quality impact interventions to improve paediatric HIV service delivery. Informed by the Unicef Paediatric Service Delivery Framework[c], the partnership aims to work alongside governments, civil society and the wider communities to identify gaps in services and interventions to address unmet needs. This includes supporting access to treatment and ensuring mothers and children living with HIV and the most vulnerable are retained in care.

d. Global policy engagement

Investing in innovative science to address infectious diseases affecting children and young people is a key strategic global health priority for ViiV Healthcare. [25] We are strong and active advocates of key organisations investing in global health resources and technical capacity such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF)[d], PEPFAR, UNAIDS, Unicef and the WHO, among others.[26] We support the important role played by these organisations and recognise the need for robust political support to fulfil their critical global public health mandates as well as to ensure they are adequately resourced, to deliver epidemic and pandemic control. This is essential to ensure no child living with or affected by HIV is left behind.

Since 2016, ViiV Healthcare's CEO has been a key and active participant in the annual Vatican Platform for High-Level Dialogues; the Rome Action Plan[e] on Paediatric HIV. The meeting series is convened by His Eminence Peter Kodwo Appiah Cardinal Turkson, Prefect of the Dicastery for the Promotion of Integral Human Development. The dialogue series is organised by the WHO, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), PEPFAR, UNAIDS, Caritas Internationalis, the World Council of Churches – Ecumenical Advocacy Alliance (WCC-EAA). Other participants include senior representatives from global health organisations, manufacturers (innovators, generics, and diagnostic companies), clinical experts, political leaders, regulators, multilateral funders and civil society. The Plan aims to drive ambitious acceleration, collaboration, and commitment in order to expedite clinical product development and registration.[27]

Ending the paediatric AIDS epidemic

Given that paediatric AIDS can be averted, and paediatric HIV is both preventable and treatable; strong political leadership, targeted resources and ambitious partnerships are critical to ensure infants, children and young people secure an AIDS free future. As the world grapples with improving the global response to address current and future pandemics, it is important to underline the fact that no one infectious disease can be fought at the expense of another. Despite the current COVID-19 pandemic, protecting resources needed to address paediatric HIV is critical to avert avoidable new infections and AIDS-related deaths. The importance of improving access to treatment through community-led delivery is critical. In addition, youth-focused services to improve retention in care and increase public awareness about HIV prevention options cannot be overstated.

[c] The paediatric service delivery framework presents strategies to address bottlenecks across the continuum of care for each population: infants, children and adolescents. t describes comprehensive and targeted service delivery models, which emphasize strong linkages between testing, treatment and care, and between communities and facilities - http://www.childrenandaids.org/Paediatric-Service-Delivery-Framework

[d] The Global Fund is a partnership designed to accelerate the end of AIDS, tuberculosis, and malaria as epidemics. The Global Fund raises and invests more than US$4 billion a year to support programs run by local experts in more than 100 countries.

[e] The 'Paediatric HIV: Rome Action Plan' represents commitments by diverse key stakeholder which seeks to accelerate research, development, registration, initiation and uptake of HIV diagnostics and optimal antiretroviral drugs (ARVs) for children living with HIV.

ViiV healthcare global policy briefings series:
Making HIV a smaller part of people's lives
ViiV Healthcare has developed a series of global policy briefings which outline our commitments through diverse partnerships to tackle key global public health priorities affecting the global, regional, national and community HIV response. We aim to inform public policy and healthcare delivery to ensure no person living with HIV is left behind, by supporting communities affected by HIV.

About ViiV Healthcare
Established in November 2009, we are the only pharmaceutical company solely focused on combating, preventing and ultimately curing HIV & AIDS. ViiV Healthcare is dedicated to researching and delivering innovative HIV medicines and solutions which make HIV a smaller part of people's lives.
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