



STRATEGIC FRAMEWORK

PEDIATRIC HIV TREATMENT INITIATIVE (PHTI)

Accelerating Development of Paediatric ARV Formulations to Close the Treatment Gap

June 2016

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This document provides PHTI's strategic directions and current set up. A provisional framework was presented by PHTI's representatives in different occasions, especially at the 20th International AIDS Conference (IAS), in Australia, in 2014, and at the 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention, in Canada, in 2015.

1. Background

In June 2013, the World Health Organization (WHO) released new guidelines for paediatric HIV care, significantly increasing the number of young children recommended for treatment¹. Appropriate and affordable formulations, specifically as fixed-dose combinations (FDCs), are needed to adhere to these treatment guidelines and to simplify treatment in a way that contributes to treating more children living with HIV. Although the WHO had initiated the process of identifying key missing formulations and appropriate dosing schedules, greater coordination among various players, including industry, was necessary to ensure rapid development and market uptake.

UNITAID, the Medicines Patent Pool (MPP), and the Drugs for Neglected Diseases initiative (DNDi) thus proposed an initiative, the Paediatric HIV Treatment Initiative (PHTI), to meet this need. PHTI was launched in May 2014 during the 67th World Health Assembly and later the Clinton Health Access Initiative (CHAI) was invited to join PHTI². In coordination and collaboration with the WHO, PHTI strives to identify and overcome potential barriers to developing, producing and making available medicines considered to be a priority, with a particular focus on intellectual property (IP), research and development and, if needed, market shaping.

The PHTI provides a dynamic platform for the exchange of information and contributes to creating the synergies among key partners necessary to accelerate the development of WHO recommended paediatric formulations and convening groups of experts, mainly the Paediatric ARV Drug Optimization (PADO), and the Paediatric ARV Working Group (PAWG); see Annex 1. Pharmaceutical companies, regulatory/normative agencies, clinical trials networks/ research centres, United Nations Agencies, National Programs, civil society organizations, financing organizations —and initiatives and organizations such as the ones identified in Annex 1 —are among the key partners of PHTI.

2.

PHTI: Objective, Vision, Mission and Scope

Building upon the expertise and the work of the convening partners, the PHTI aims to work in close collaboration with WHO to create synergies and promote coordination among various key partners and stakeholders to develop the identified product priorities and meet the clinical needs of children living with HIV.

2.1 OBJECTIVE

The objective of the PHTI is to catalyse development of, and accelerate access to, new, better-adapted paediatric ARVs and formulations to improve treatment for all children living with HIV. These formulations specifically include FDCs that are appropriate for children across a broad range of weight and age-bands. In this way, the PHTI seeks to contribute to closing the treatment gap between number of children living with HIV that need treatment and those that currently receive it.

Simpler, child-friendly adapted paediatric formulations, if possible in the form of FDCs, have eased rapid scale-up of treatment as documented by WHO³. New adapted formulations, together with other interventions, increased efforts to identify all cases and the improvement of delivery models for example, will contribute to closing the treatment gap for children.

PHTI WILL BUILD UPON AND COMPLEMENT CURRENT INITIATIVES, ESPECIALLY IN FOUR AREAS:

1. Lead Coordination of Drug Development:

facilitating the link between technical recommendations and the development, production and marketing of priority products and combinations (i.e. encouraging the prioritization of WHO recommended products in manufacturers' and product development organizations' pipelines) as well as collaborating with research networks in conducting the studies needed;

2. Lead Intellectual Property (IP):

Ensuring IP and knowledge sharing;

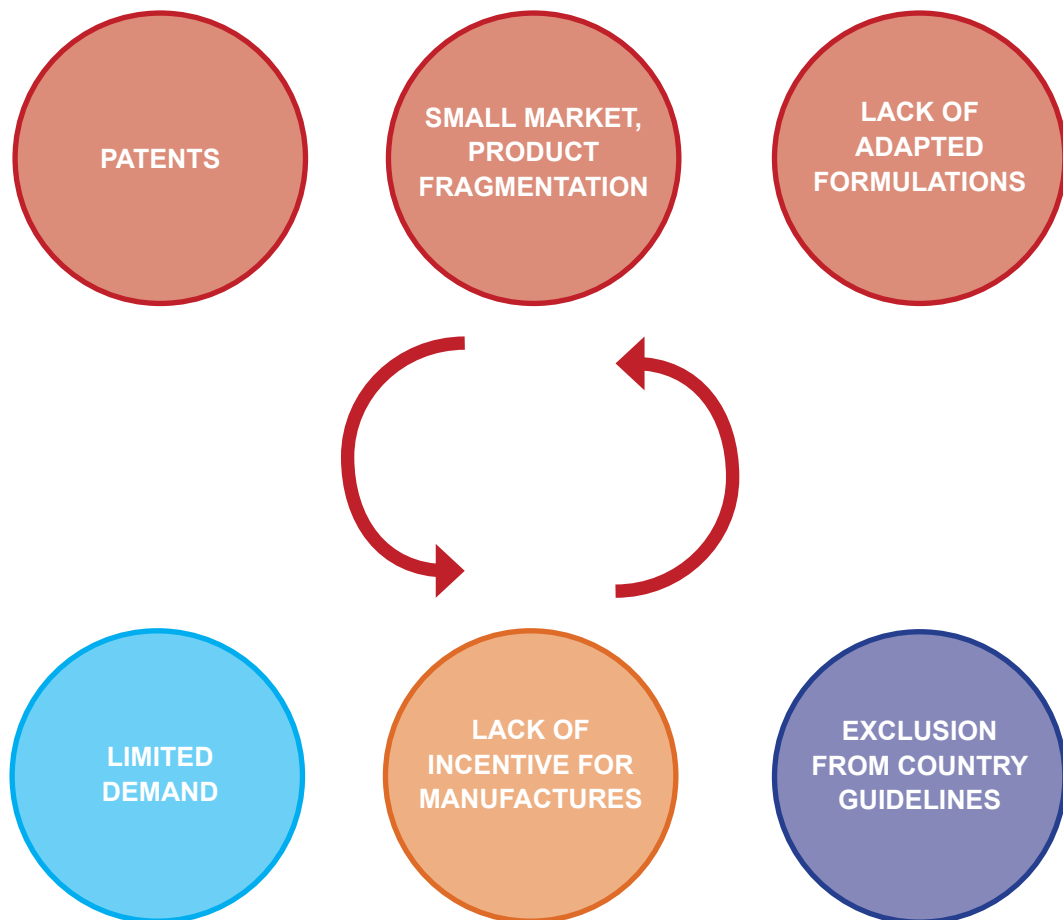
3. Seek External Funding:

facilitating the financing mechanisms for the development, manufacture, quantification of needs (i.e. forecasting the number of children requiring treatment) and market uptake; as well as collaborating with other partners to mobilise resources and identify innovative and sustainable funding mechanisms to support formulation development;

4. Support Market Adoption:

raising awareness of the challenges in the global health community and eventually assessing the acceptability of proposed formulations.

CHALLENGES OF DEVELOPING NEW PAEDIATRIC FORMULATIONS



2.2 VISION

In alignment with the global target to end the AIDS epidemic by 2030, the PHTI aims to deliver by 2020 the paediatric ARV formulations needed to meet the treatment targets for children living with HIV⁴. Through its specific work, PHTI will also contribute to the Sustainable Development Goals (SDGs) Target 3.3 in the SDG health goal calls on the world to end the epidemics of AIDS, Tuberculosis, Malaria, and Neglected Tropical Diseases by 2030, and to combat hepatitis and other communicable diseases⁵.

2.3 MISSION

Using the expertise of its member organisations (CHAI, DNDi, MPP, UNITAID and WHO), the PHTI will lead coordination of drug development and access activities to bridge the gap between the need and operational delivery of paediatric HIV treatments.

2.4 SCOPE

PHTI does not exist as a legal entity, but is the name given to a collaborative agreement between the member organizations. As such, it has no power to enter into agreements, and holds no funds. Any contracts required in the execution of the objectives will be between one or more of the members and the necessary third parties.

3.

PHTI: How it Works

The development of adapted paediatric formulations requires the involvement of multiple players. The PHTI will support a coordinated effort towards the development and production of appropriate products by ensuring that technical guidance from WHO experts translates into real medicines available in the market.

Pharmaceutical companies have the expertise in developing paediatric formulations. Negotiating agreements to share patents and know-how is thus the critical first step. Once voluntary licences are in place, the IP on new medicines and formulations will be sublicensed to generic manufacturers and subsequently developed using the MPP's mechanism for out-licensing and product development. This will catalyse manufacturing of high-quality priority formulations.

PHTI works as a focused and light structure. To support its initial work in 2014-2015 Product Specific Teams (PSTs) were formed. The PSTs were a fundamental element helping PHTI to work on the formulations. The PSTs included clinical and formulation experts, regulators and other relevant specialists; PSTs members provided their expertise for free. Confidentiality agreements were signed when deemed necessary to help exchange of relevant information. In the future, in the case that it is needed, specific teams could be created to address issues identified by PHTI.

3.1 STRUCTURE, RESPONSIBILITIES AND DECISION- MAKING

The PHTI is now moving into a more operational phase for which faster responsiveness is required. Two decisions were taken in 2015 to support this change:

- The creation of a new Coordination & Strategy Group (CSG), chaired by UNITAID⁶. The CSG provides strategic directions to PHTI, oversees its activities, and ensures coherence of the projects; see Annex 2
- Members of the CSG will be in charge of running the projects identified so far; see Annex 3.

3.2 COORDINATION WITH KEY PARTNERS

Achieving the objective of accelerating the development of better drugs for children would rely to a certain extent on other on-going initiatives such as the technical work conducted by WHO and the Paediatric ARV Working Group (PAWG) to recommend best therapeutic options, develop dosing recommendations and identify needed missing formulations; and the Inter-Agency Task Team (IATT) for Prevention and Treatment of HIV Infection in Pregnant Women, Mother and Children's work to select optimal⁷ existing paediatric formulations (and incorporate new ones as they are developed) in an effort to reduce market fragmentation. Research networks are also a critical partner of PHTI.

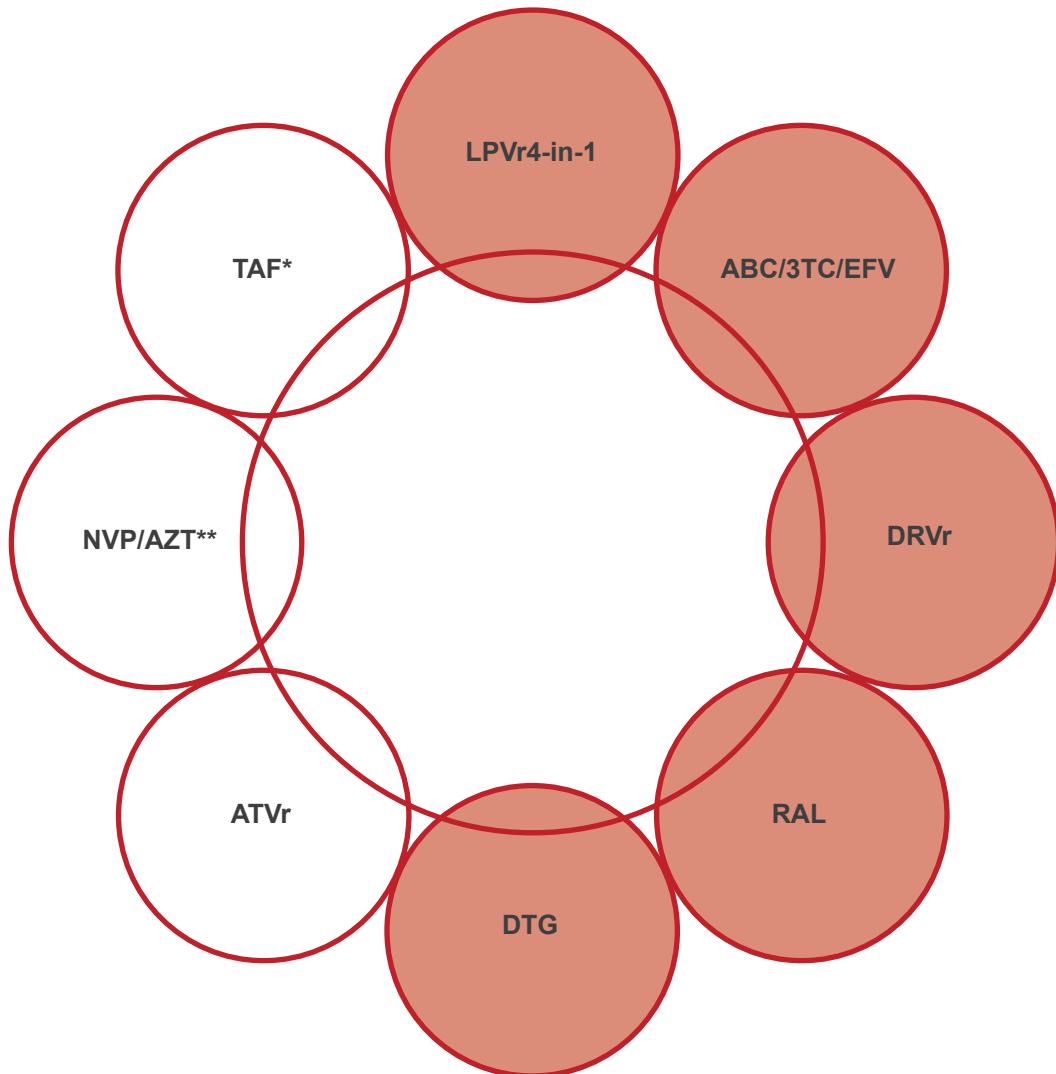
3.3 HOW TO ENGAGE WITH PHTI

PHTI aims to work closely with key partners and relevant stakeholders to ensure broad participation in the initiative as well as a more participatory engagement; see Annex 1.

3.4 PHTI'S TARGET FORMULATIONS

The dearth of simple, child-friendly HIV formulations continues to stall the full implementation of the WHO's 2013 and 2015 treatment guidelines⁸ and contributes to the slow phase out of less effective and more toxic drugs no longer recommended. Simpler treatment options, if possible in FDCs, are required to reduce the gap between children in need of treatment and those who receive ARVs. WHO convenes the PADO meetings to among other things, establish priorities for drug and formulation development and identify research gaps on the use of ARVs for infants, children and adolescents⁹.

The graphic below presents PADO priorities and in white the formulations for which there are not PHTI active projects as of now¹⁰



* Preferably combined with DTG.

** For infant prophylaxis.

Development and production of better quality medicines would address closing the gap to provide treatment for children living with HIV by directly increasing the availability, acceptability/ adaptability and delivery, and indirectly by impacting affordability.

BASED ON THE WHO/PADO RECOMMENDATIONS THE FORMULATIONS LISTED BELOW ARE PRIORITIZED BY PHTI:

ABC or AZT/3TC/LPV/r Lead: DNDi	Important combination in first and second lines. It is currently unavailable in FDC form. Formulation work under way by DNDi/Cipla ¹¹
ABC/3TC/EFV Lead: MPP	Important combination in first line that is recommended as a preferred regimen for children from three to 10 years old. Technical and regulatory support already ongoing. MPP sub-licensees already working on this formulation
DRV/r Lead: CHAI	This combination is needed for second line for children failing on LPV/r-based combinations. Plans to pursue efficiencies with adult formulation development since the ratio for second adult with DRV resistance-associated mutations is the same as pediatric ratio (6:1)
RAL Lead: MPP	Use in infants and young children. PK model to establish weight-band dosing already conducted by Merck and MPP. Evidence may be required to support use of the existing formulations in the younger age group. Main activities would be coordination and support to manufacturers to facilitate development of products. MPP sub-licensees already working on this project
DTG Lead: CHAI	Identified as key drug in first line with potential for harmonization across the full age spectrum. Coordination and support to manufacturers to facilitate development of products will be needed
ABC/3TC/DTG Lead: CHAI	Development of this FDC will be pursued in parallel with the single with input from the originator. Coordination and support to manufacturers to facilitate development of products will be needed
TAF/XTC/DTG Lead: CHAI	Key product to potentially enable alignment with adult regimen. Clinical work data is needed for pediatric populations, if possible in alignment with adults. Licences have been signed for both TAF and DTG

WHO recommendations are dynamic and evolve on a continuous basis with new evidence and the implementation of better tools. The PHTI will systematically review the list of WHO recommended pediatric ARV formulations in order to accelerate the development and approval of the WHO's priority products.

3.5 COMMUNICATION APPROACH

PHTI will establish and maintain regular channels of communication, especially emphasising the following:

- Production and dissemination of a Newsletter of PHTI's activities, especially with updates regarding the status and timeline of the development of the formulations, achievements, and challenges;
- In addition to the information already presented at the websites of PHTI's member organizations, a section will be created at UNITAID website where PHTI will be featured;
- As often as possible and when needed, PHTI will hold meetings to present its progress using international gatherings such as the International AIDS Conference (IAS), the Conference on Retrovirus and Opportunistic Infections (CROI), IAS Conference on HIV Pathogenesis, Treatment and Prevention, the International Conference on AIDS & STIs in Africa (ICASA), and the World Health Assembly (WHA);
- When needed, PHTI will publish statements and press releases.

3.6 EXPECTED IMPACT

- **Ensuring that appropriate WHO-preferred regimens are developed and reach children:** It is expected that the initiative will have a significant and immediate impact by ensuring appropriate WHO-preferred regimens are developed and reach the children.
- **Optimization of treatment:** Simpler treatment options are required to reduce the gap between children in need of treatment and those who receive ARVs. These options should: Allow simplified dosing by weight-band; Harmonize paediatric and adult regimens; Ensure suitability for treatment sequencing strategy that addresses challenges in drug procurement and supply chain and that helps in reducing market fragmentation; and Start treating children as early as possible in order to improve their vital prognostic.
- **Availability of treatment regimens for children:** The PHTI will make available quality recommended regimens for children, tackle barriers for treatment and therefore is expected to reduce the gap of HIV positive children needing treatment.
- **Product Introduction:** PHTI use its best efforts to accelerate in-country registration and market introduction of the new developed formulation.

Conclusion

Similar to adults, the provision of antiretroviral treatment for children younger than 15 years has expanded impressively — from an estimated 18 000 in 2000 to 823 000 in 2014 and more than doubled in 2010–2014 alone. However, coverage for children was lower than for adults in 2014, and it was about 30% [28–32%] in the African Region, where 90% of children living with HIV reside¹². Meeting treatment needs of this vulnerable and under-served population will align with the goals of other HIV/AIDS children’s organizations such as the Elizabeth Glaser Paediatric AIDS Foundation (EGPAF), the United Nations Children’s Fund (UNICEF) and WHO joint call for action among concerted stakeholders to end paediatric HIV/AIDS — the Double Dividend initiative¹³.

About PHTI's Member Organizations

PHTI's member organizations have an extensive contribution to pediatric HIV and each of them can offer a unique expertise to make PHTI a reality.



Clinton Health Access Initiative (CHAI) was founded in 2002 with a transformational goal: help save the lives of millions of people living with HIV/AIDS in the developing world by dramatically scaling up antiretroviral treatment. Since then, CHAI has pursued several similarly ambitious goals, from scaling up pediatric AIDS treatment in order to achieve equity with adults in a time frame few thought possible, to rapidly accelerating the rollout of new vaccines. More information available at: <https://www.clintonfoundation.org/our-work/clinton-health-access-initiative>



Drugs for Neglected Diseases initiative (DNDi) became a legal entity in 2003 and it is a collaborative, patients' needs-driven, non-profit drug research and development organization that is developing new treatments for neglected diseases. More information available at: <http://www.dndi.org/about-dndi/>



Medicines Patent Pool (MPP) is a United Nations-backed organization, established in 2010, offering a public-health driven business model that aims to lower the prices of HIV medicines and facilitate the development of better-adapted HIV treatment and special formulations for children, through voluntary licensing, patent pooling and coordinating and product development. More information available at: <http://www.medicinespatentpool.org/about/>



UNITAID was established in 2006 by Brazil, Chile, France, Norway and the United Kingdom to provide an innovative approach to global health. UNITAID plays an important part in the global effort to defeat HIV/AIDS, tuberculosis and malaria, by facilitating and speeding up the availability of improved health tools, including medicines and diagnostics. More information available at: <http://www.unitaid.org/en/who/about-unitaid>



World Health Organization/HIV Department is part of the Cluster for HIV, TB, Malaria and Neglected Tropical Diseases. It consists of the following units: the Global Hepatitis Programme, HIV Treatment and Care; Key Populations and Prevention; Technologies and Commodities; Strategic Information and Planning; and Programme Development and Implementation. More information available at: <http://www.who.int/hiv/aboutdept/en/>

Annex 1

PHTI's Main Partners

As listed below, so far three levels of collaborators are identified: key partners, stakeholders and observers.

Key Partners

The list of key partners includes paediatric AIDS initiatives as well as organizations dedicated to pediatric AIDS.

1. Pediatric ARV Drug Optimization (PADO):

WHO convenes the PADO meetings to among other things, establish priorities for drug and formulation development and identify research gaps on the use of ARVs for infants, children and adolescents. PADO 1 took place in Dakar in October 2013, and PADO 2 in Geneva in December 2014, as a result of these meetings, a list of missing formulations have been identified. More information available at: <http://www.who.int/hiv/pub/toolkits/flyer-peadriatic-hiv-dec2014.pdf>; and: <http://www.who.int/hiv/pub/toolkits/brief-optimizationpaedriatic-art.pdf?ua=1>

2. Pediatric ARV Working Group (PAWG):

A subset of PADO. More information available at: <http://www.who.int/hiv/pub/toolkits/brief-optimization-paedriatic-art.pdf?ua=1>

3. The Inter-Agency Task Team (IATT)

for Prevention and Treatment of HIV Infection in Pregnant Women, Mother and Children is a group of 28 multilateral, government, and non-governmental organizations that are committed to strengthening global, regional and national partnerships and programs that address the survival of pregnant women, mothers and children living with HIV. Established in 1998, the IATT is co-chaired by UNICEF and WHO and has recently been reconfigured to optimally support country-led implementation of the Global Plan towards the Elimination of New HIV Infections among Children by 2015 and Keeping their Mothers Alive (Global Plan). More information available at: <http://www.emtct-iatt.org/>

4. Paediatric ARV Procurement Working Group (PAPWG)

was established in 2011 to adopt a coordinated approach to the procurement of paediatric ARVs to secure the paediatric ARV market and to support sustained treatment scale-up. The PAPWG's approach to improving supply security has been so successful that some paediatric ARVs no longer require the same level of support that they have previously received. Thus, in January 2016, the group approved the expansion of the scope of the PAPWG to include additional products facing similar market conditions. This is aligned with the Global Fund's Market Shaping Strategy and efforts of other member organisations. To reflect its broadened mission and scope, the PAPWG has adapted its name from the Paediatric ARV Procurement Working Group (PAPWG) to the ARV Procurement Working Group (APWG).

5. The Double Dividend Initiative.

Launched in 2013 by EGPAF, UNICEF and WHO, the Double Dividend initiative is intended to catalyse accelerated action toward the dual goals of ending paediatric HIV and AIDS and improving child survival. More information available at: http://www.unicef.org/aids/files/Action_Framework_Final.pdf

6. Accelerating Children's HIV/AIDS Treatment (ACT) Initiative

was established in August 2014 by PEPFAR in partnership with the Children's Investment Fund Foundation (CIFF). ACT is a \$200 million initiative to double the total number of children receiving ART by the end of 2016 across nine African countries. This investment intends to enable at least 300,000 more children (0-19 years of age) to receive ART. The countries are: Cameroon, Democratic Republic of the Congo, Lesotho, Kenya, Malawi, Mozambique, Tanzania, Zambia and Zimbabwe. More information available at: <http://www.pepfar.gov/press/releases/2014/230334.htm>

7. Global Pediatric Antiretroviral Commitment-to-Action (CTA)

was launched on World AIDS Day 2014 by PEPFAR, PHTI, and the Global Fund. The CTA brings together leading organizations to accelerate the development of high-priority pediatric ARV co-formulations for first and second-line treatment by 2017. More information available at: <http://www.pepfar.gov/press/235353.htm>; <http://unitaid.org/en/event/16-home/1499-global-pediatric-antiretroviral-commitment-to-action>

- 8. Industry Liaison Forum (ILF)/International AIDS Society (IAS).**
The ILF is a mechanism to constructively engage stakeholders on issues in line with IAS Member Priorities. It is designed to take advantage of the IAS's key strengths: its well-respected convening power; its acknowledged independence from industry and other key partners and stakeholders; and its diverse working groups composed of some of the world's top thought leaders and scientific experts in a wide array of fields. More information available at: <http://www.iasociety.org/What-we-do/Industry-Liaison-Forum/About>

- 9. Collaborative Initiative for Paediatric HIV Education and Research (CIPHER)/IAS.**
CIPHER is aimed at optimizing clinical management and delivery of services to infants, children and adolescents affected by HIV in resource-limited settings through advocacy and research promotion. More information available at: <http://www.iasociety.org/CIPHER>

- 10. Elizabeth Glaser Pediatric AIDS Foundation (EGPAF).**
Founded in 1988, EGPAF seeks to end pediatric HIV/AIDS through research, advocacy, and prevention and treatment programs. More information available at: <http://www.pedaids.org/features/our-work>

Stakeholders

The list of stakeholders includes: Donors, Industry, Clinical Trials Networks/Research Centres, United Nations Agencies, Implementers, National Programs, Civil Society organizations, including organizations of people living with HIV can play a crucial role in the PHTI through advocacy activities, and Pharmaceutical partners.

Observers

The list of observers includes basically representatives of Regulatory and Normative Agencies such as the U.S. Food and Drug Administration (US FDA), the European Medicines Agency (EMA), and the Pre-qualification Programme of the WHO.

Annex 2

PHTI's Coordination & Strategy Group

(as of June 2016)

Organization	Representative	Alternate
UNITAID (Chair PHTI)	Robert Matiru, Director, Operations	Team Lead , HIV Portfolio (TBC)
CHAI	David Ripin, Executive Vice-President Access and Chief Scientific Officer	Melynda Watkins, Director of Product Development and Regulatory Affairs
DNDi	Bernard Pécou, Executive Director	Marc Lallemand, Head Pediatric HIV Program
MPP	Greg Perry, Executive Director	Sandeep Juneja, Business Development Director; and Fernando Pascual, Medical/Pharmaceutical Advisor
WHO	Gottfried Hirschall, Director of the HIV/AIDS Department of WHO	Meg Doherty, Coordinator, Treatment and Care Unit, HIV/AIDS Department; Martina Penazzato, Medical Officer, Treatment and Care Unit, HIV/AIDS Department

Annex 3

Acronyms and Abbreviations

3TC:	Lamivudine
ABC:	Abacavir
ACT:	Accelerating Children's HIV/AIDS Treatment Initiative
AIDS:	Acquired Immune Deficiency Syndrome
ART:	Antiretroviral Treatment
APWG:	ARV Procurement Working Group
ATVr:	Atazanavir/ritonavir
AZT:	Azidothymidine (Zidovudine)
CHAI:	Clinton Health Access Initiative
CIFF:	Children's Investment Fund Foundation
CIPHER:	Collaborative Initiative for Paediatric HIV Education and Research
CROI:	Conference on Retrovirus and Opportunistic Infections
CSG:	Coordination & Strategy Group
CTA:	Global Pediatric Antiretroviral Commitment-to-Action
DNDi:	Drugs for Neglected Diseases initiative
DRV:	Darunavir
DTG:	Dolutegravir
EFV:	Efavirenz
EGPAF:	Elizabeth Glaser Pediatric AIDS Foundation
EMA:	European Medicines Agency
EOI:	Expression of Interest
FDC:	Fixed-dose Combination
FTC:	Emtricitabine
HIV:	Human Immune Deficiency Virus
IAS:	International AIDS Society

IATT: Inter-Agency Task Team for Prevention and Treatment of HIV Infection in Pregnant Women, Mother and Children
ICASA: International Conference on AIDS & STIs in Africa
ILF: Industry Liaison Forum
IP: Intellectual Property
LPV/r: Lopinavir/ritonavir
MPP: Medicines Patent Pool
NVP/AZT: Nevirapine/zidovudine
PADO: Paediatric ARV Drug Optimization
PAPWG: Paediatric ARV Procurement Working Group
PAWG: Paediatric ARV Working Group
PEPFAR: U.S. President's Emergency Plan for AIDS Relief
PHTI: Paediatric HIV Treatment Initiative
PST: Product Specific Team
RAL: Raltegravir
TAF: Tenofovir Alafenamide Fumarate
UNAIDS: Joint United Nations Programme on HIV/AIDS
UNICEF: United Nations Children's Fund
USFDA: United States Food and Drug Administration
WHA: World Health Assembly
WHO: World Health Organization
XTC: 3TC (Lamivudine) or FTC (Emtricitabine)

End notes

¹**WHO. 2013.** *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach.* Available at: http://apps.who.int/iris/bitstream/10665/85321/1/9789241505727_eng.pdf?ua=1

²**Paediatric HIV Treatment Initiative:** *Closing the Treatment Gap through Innovation.* 2014. Document prepared for the launch of the PHTI during the 67th World Health Assembly. Available at: http://unitaid.org/images/publications/PEDS_ARV_INITIATIVE_HR.PDF

³“Scored dispersible fixed-dose combinations for children with dosage based on weight bands can support the scaling up

⁴**UNAIDS. 2015.** *On the Fast-Track to end AIDS by 2030: Focus on location and population.* Available at: http://www.unaids.org/sites/default/files/media_asset/WAD2015_report_en_part01.pdf

UNAIDS. 2014. 90–90–90 - *An ambitious treatment target to help end the AIDS epidemic.* Available at: http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf

⁵**WHO. 2015.** *Accelerating progress on HIV, tuberculosis, malaria, hepatitis and neglected tropical diseases*

A new agenda for 2016-2030. Available at: http://apps.who.int/iris/bitstream/10665/204419/1/9789241510134_eng.pdf?ua=1

⁶**After the launch,** it was agreed that PHTI’s coordination would be with the MPP; in November 2015, the coordination moved to UNITAID.

⁷**Optimal paediatric formulations** are those that meet certain criteria, specifically ones that allow simple administration, transport and distribution.

⁸**WHO. 2015.** *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: what’s new.* Available at: http://apps.who.int/iris/bitstream/10665/198064/1/9789241509893_eng.pdf?ua=1

⁹**PADO 1** took place in Dakar in October 2013, and PADO 2 in Geneva in December 2014, as a result of these meetings, a list of missing formulations have been identified.

¹⁰**Paediatric ARV Drug Optimization 2.** *Meeting Report, December 2014.* Available at: <http://www.who.int/hiv/pub/meetingreports/paediatric-arv-optimization/en/index1.html>

¹¹**See DNDi** update published on World AIDS Day 2015. Available at: <http://www.dndi.org/2015/media-centre/news/paediatric-hiv-status-update/>

¹²**WHO. 2015.** *Global health sector response to HIV, 2000-2015: focus on innovations in Africa: progress report.* Available at: http://apps.who.int/iris/bitstream/10665/198065/1/9789241509824_eng.pdf

¹³**UNICEF, WHO & EGPAF.** *The Double Dividend.* 2013. Available at: http://www.unicef.org/aids/files/Action_Framework_Final.pdf