High-Level Dialogue to Assess Progress on and Intensify Commitment To Scaling Up Prevention, Diagnosis and Treatment of Paediatric HIV and TB

December 2022, Vatican City State

Introduction

On 5-6-7 December 2022, leaders of major pharmaceutical and medical technology companies, United Nations (UN) and other international organizations, donors, governments, organizations providing or supporting services for children living with HIV and TB as well as their mothers, participated in a *High-Level Dialogue to Assess Progress on and Intensify Commitment to Scaling Up Prevention, Diagnosis and Treatment of Paediatric HIV and TB*. The Dialogue was convened by His Excellency Archbishop Vincenzo Paglia, President of the Pontifical Academy for Life, and hosted, in the Pontifical Academy of Science, by His Eminence Peter Kodwo Appiah Cardinal Turkson, Prefect of the Dicastery for the Promotion of Integral Human Development. The Dialogue was organized by the World Health Organization (WHO), the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), the President's Emergency Plan for AIDS Relief (PEPFAR), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the Stop TB Partnership, in collaboration with Faith-Based-Organizations (FBOs). The High-Level Dialogue provided an opportunity for stakeholders to build on previous similar consultations on ending paediatric HIV and TB, as well as assess progress on the commitments made as part of the November 2017, December 2018, November 2020 Pediatric HIV & TB Rome Action Plan. The Dialogue was also an opportunity to adopt specific commitments and present research considerations for advancing R&D and registration of HIV and TB medicines for pregnant and breastfeeding women.

The goal of this High-Level Dialogue was to determine the most effective ways to improve the research and development, registration, introduction and roll-out of HIV and TB preventive tools, diagnostics and optimal treatment for children living with HIV and/or with TB, with the ultimate objective of reducing morbidity and mortality among these highly vulnerable groups. In addition, participants put forward a variety of steps they have taken or could take to expand access to new and better drugs to improve HIV and TB treatment among pregnant and breastfeeding women; to preventing TB among children; for early infant diagnosis (EID) and viral load testing, as well as to identify more HIV and TB-exposed children and quickly link them to prevention, testing and treatment services. They also presented further steps that need to be taken to accelerate the development and roll-out of priority paediatric formulations for HIV and TB, including streamlining regulatory processes, improving financing for the whole spectrum of paediatric formulations development, the introduction, and research of optimal products for pregnant and breastfeeding women with HIV and/or TB, as well as ensuring wide availability and uptake of such optimal formulations and diagnostics.

These action points were translated into a set of commitments made by all groups of stakeholders present as well as by individual organizations. **The commitments complement those made during the 2017, 2018 and 2020 High-Level Meetings, most of which are still being implemented and remain valid. The ensemble of action points will be referred to collectively as the Rome Action Plan on Paediatric HIV & TB, with each set applying only to the actors present at the relevant Vatican High-Level Dialogues.** WHO and EGPAF, with the

support of the Rome Action Plan monitoring team[1] have the responsibility for tracking progress on the Action Plan and to promote full and timely implementation of the action points, including following progress towards milestones, and communicating regularly with participants about progress on their commitments and overall implementation of the Plan.

2022 Action Points & Asks

HIV MEDICINES DURING PREGNANCY AND BREASTFEEDING

Academic partners, research institutes and networks, and product development partners

HIV Clinical Trials Research Networks[2] enrolling adults into phase 2/3 clinical trials of new antiretroviral drugs for treatment or prevention, commit to:

1. Implementing the Call to Action[3] principles and advocate for other research networks to do the same including reporting of incident pregnancies occurring during the conduct of such studies; permitting women who become pregnant in trials to consent to stay on study drug; and collecting outcomes of pregnancies as well as pregnancy and breastfeeding PK data in women who become pregnant on study.

The Eunice Kennedy Shriver National Institute of Child Health and Human Development [4] commits to:

2. Continue to co-fund NIAID's relevant efforts through IMPAACT and HPTN.
3. Provide new funding that leverages their clinical trial networks to which investigators, both within the networks and not within, can apply.[5]
4. Continue to support the Maternal-Fetal Medicine Units (MFMU) Network and the Neonatal Research Network (NRN), also during the new seven-year cycle starting in 2023[6].
5. Continue to support the Global Network for Women's and Children's Health Research in the new seven-year cycle to start in 2023.
6. Continue to support the Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub and Centers of Excellence in Therapeutics

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[1] The Action Plan monitoring team is composed of representatives from co-organizing agencies as well as the FBOs sector.

[2] The Eunice Kennedy Shriver National Institute of Child Health and Human Development, and The National Institute of Allergy and Infectious Disease

[3] Research for informed choices: Accelerating the study of new drugs for HIV in pregnant and breastfeeding women. At: call-to-action-to-accelerate-study-of-new-arv-for-pregnant-breastfeeding-women.pdf (who.int)

[4] NICHD Strategic Plan includes this one (of five) scientific research themes– "Advancing Safe and Effective Therapeutics and Devices for Pregnant and Lactating Women, Children, and People with Disabilities." Therefore, NICHD supports several resources that can and do aid pediatric drug development and drug studies in pregnant and lactating persons. Here is a summary of some of those resources.

[5] Multisite Clinical Research: Leveraging Network Infrastructure to Advance Research for Women, Children, Pregnant and Lactating Individuals, and Persons with Disabilities (U01 Clinical Trial Optional)

[6] https://www.nichd.nih.gov/research/PPB/research_funding/FAQs_MFMU-NRN-22

7. Initiate the MPRINT Translational Research Resource Platform in 2023, to support concerted multidisciplinary team science that leverages existing and prospective resources to advance therapeutic research for maternal and pediatric therapeutics.
8. Renew/extend funding opportunity announcement - Translational Research in Maternal and Pediatric Pharmacology and Therapeutics (R01 Clinical Trial Optional)
9. Promote training opportunity - NICHD Research Education Programs (R25 Clinical Trial Not Allowed). Priority areas include virtual skills development courses and supporting resources for researchers on best practice topics such as inclusion and retention of pregnant and lactating persons and/or pediatric patients and their families in clinical research
10. Supporting a National Academies of Science, Engineering, and Medicine (NASEM) study to conduct an evaluation of real and perceived liability around research conducted in pregnant and lactating persons, and develop a framework for addressing medicolegal and liability issues when planning or conducting research specific to pregnant and lactating persons[7].

The National Institute of Allergy and Infectious Disease commits to:

11. Continue to support completion of HPTN 084 pregnancy sub-study (CAB-LA for prevention) in a timely manner.
12. Continue to support completion of enrolment and timely dissemination of results from IMPAACT 2026 for new ARVs for use in pregnancy and postpartum.
13. Support NIAID funded clinical trial research networks to continue to report incident pregnancies occurring during the conduct of studies and collect outcomes of pregnancies as well as pregnancy and breastfeeding PK data in women who become pregnant on study.
14. Support NIAID clinical research networks to continue to ensure appropriate consultation and engagement of community members and community-based organizations through the research cycle for new therapeutics.
15. As appropriate, facilitate completion of embryo-fetal development (FEED/EFD) studies as needed for priority ARVs for use in pregnant and lactating women with established pharma partnerships by end of Phase 2 by applying available contract resources.
16. As appropriate, facilitate completion of pre- and post-natal development studies (PPND) as needed for priority ARVs with established pharma partnerships by the time of early Phase 3 clinical trial enrolment by applying available contract resources.

The French Research Agency on HIV, Viral Hepatitis, STI, TB and Emerging Infectious Diseases commits to:

17. Support greater inclusion of pregnant and breastfeeding women and contribute to a more equitable investigation of new HIV agents in clinical research studies in accordance to the Call to Action[8].
18. Support prevention and ARVs research in pregnancy (address insurance issues).
19. Facilitate development of clinical research on broadly neutralizing antibodies for neonates and pregnant women.

[7] Currently assembling the committee; recommendations anticipated in 2024.

[8] Research for informed choices: Accelerating the study of new drugs for HIV in pregnant and breastfeeding women. At: call-to-action-to-accelerate-study-of-new-arv-for-pregnant-breastfeeding-women.pdf (who.int)

20. Continue to support and facilitate generating, analysing, sharing data on pregnancy, birth, and infant safety outcomes issued from the ANRS-MIE promoted clinical research studies.
21. Support data sharing in the international network under WHO umbrella through a platform to strengthen active surveillance of safety of HIV agents in pregnancy, building harmonization and linkages between surveillance networks;
22. Continue to support involvement of the civil society in research activities and scientific board.

Access to Medicine Foundation commits to include appropriate metrics to capture alignment with the Call To Action[9] principles in their next access index for pharmaceutical companies, and specifically:

23. Complete a review of how pregnant and lactating women are represented in the 2023 Access to Medicine Index Methodology and make subsequent changes to the methodology, as required to continue to reflect their unique needs by Q4 2023.
24. Highlight key opportunities for the pharmaceutical companies within the scope of its research pertaining to pregnant and lactating women as an inclusion in its collaborative engagement work aimed at moving the pharmaceutical industry further and faster on key topics by Q4 2025.
25. Explore the unique needs of pregnant and lactating women in the consultation process and the subsequent development of new frameworks for evaluation, as part of its 5-year Strategic Direction.

Pharmaceutical Companies

Gilead, ViiV Healthcare and MSD commit to implement the principles of the Call to Action (CTA)[10] launched on 1st December 2021 by stakeholders[11] involved in studying antiretroviral agents for treatment and prevention of HIV to support greater inclusion of pregnant women and breastfeeding and contribute to a more equitable investigation of new HIV agents. This includes:

26. Committing to complete embryo-fetal development (EFD) studies for new antiretroviral (ARV) drugs by end of Phase 2 clinical trials.
27. Committing at aiming to complete pre- and post-natal development studies (PPND) for new ARV drugs by the time of early Phase 3 clinical trial enrolment.
28. Committing to generate pharmacokinetic (PK) and early safety data in pregnancy for new drugs by end of Phase 3 clinical trial completion, in the assumption that there are no contraindications to use in pregnancy from pre-clinical studies.

Gilead, building on the progress made by removing contraception requirements for ongoing long acting lenacapavir (LEN) prevention studies and allowing women who become pregnant in LEN HIV prevention trials to consent to stay on study drug, commits to:

29. Provide PK and safety data for lenacapavir in lactating and pregnant women from ongoing prevention studies by 2026.
30. Remove contraception requirements from other ongoing and planned treatment studies with LEN, and permit women who become pregnant in LEN trials to remain on study drug upon consent (contingent on supportive safety data for the agent(s) partnered with LEN).

[9] See Annex section Rome 6 - https://www.paediatrichivactionplan.org/high-level-dialogues
[10] Idem 7
[11] Idem 8

31. Support conducting a dedicated safety study in pregnant women to evaluate potential adverse effects of LEN used for treatment in pregnant women, birth outcomes, and at least short-term follow-up of infants after birth (contingent on supportive safety data for the agent(s) partnered with LEN).

ViiV Healthcare, building on ongoing work to support generation of data during implementation research of CAB LA, commits to:

32. Support investigators to allow women who become pregnant while taking CAB LA to continue CAB LA in pregnancy, following a discussion with their healthcare provider on the benefits and risks, and guided by the approved label.
33. Collect and report safety and birth outcomes (including pregnancy and neonatal outcomes) in women who receive CAB LA PrEP or CAB/RPV LA treatment during pregnancy.
34. Support, facilitate and generate data on pregnancy, birth, and infant safety outcomes for CAB-LA in pregnancy and during lactation via ongoing clinical, non-interventional and implementation science studies and if needed with rapid initiation of additional dedicated studies.
35. Collect PK and safety data in women who become pregnant and elect to stay in the Phase 3 clinical study.

MSD commits to:

36. Should a woman become pregnant, continue to permit participants enrolled in the doravirine and islatravir phase 3 program to continue in the clinical trial, if they reconsent to do so.
37. Collect doravirine and islatravir PK as part of the phase 3 development program in participants who become pregnant and reconsent to remain in the clinical trial. Birth outcomes will also be collected, and infant follow-up will be conducted through the first year of life.
38. Facilitate studies that generate data on pregnancy, birth and infant outcomes for doravirine and islatravir in pregnancy and lactation via MSD-supported studies.

Johnson & Johnson, for the long-acting formulation CAB LA + RPV LA, commits to:

39. Support investigators to permit women who become pregnant during a study to continue taking CAB LA + RPV LA during their pregnancy, if they wish to, following a risk benefit discussion with their provider, and according to local regulatory approval and label.
40. Support and facilitate data collection of pregnancy, birth, lactation, and infant safety outcomes for CAB LA + RPV LA via ongoing research (clinical trials and implementation research), and if needed, with rapid initiation of additional dedicated studies.
41. Collect and report safety and birth outcomes (including pregnancy and neonatal outcomes) from post-marketing surveillance in women who receive CAB LA + RPV LA treatment during pregnancy.

Regulatory Authorities

EMA and USFDA[12] commit to:

[12] The USFDA has committed to be an active participant of the Expert Working Group (EWG), a group tasked to develop a new ICH guidance on Clinical Trials in Pregnant & Breastfeeding People. USFDA has published several guidance, including Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials, and Informed Consent Information Sheet, Guidance for IRBs, Clinical Investigators, and Sponsors; and encourages Sponsors, IRBs, and investigators to consider the contents of the

42. Work with other regulatory authorities within the International Council for Harmonisations of Technical Requirements for Pharmaceuticals for Human Use (ICH) 11 to advance development of supportive regulatory guidance in alignment with the Call To Action principles.
43. Encourage sponsors to consider innovative approaches (i.e., combination DART study designs, as outlined in ICH S5(R3), Section VII) to help expedite DART data collection.
44. Continue to consider the benefit and risks of new molecular entities under development to determine, on a case-by-case basis, and provided that the nonclinical safety data are supportive, whether participants who become pregnant during a clinical trial can remain in the clinical trial and continue to receive the investigational drug. The agencies will continue to proactively engage with sponsors throughout the drug development period to discuss and consider the benefit/risks of an investigational drug when used in women who become pregnant during clinical trials. In addition, to facilitate approaches to increase enrolment of certain underrepresented populations, The FDA has published a guidance, Enhancing the Diversity of Clinical Trial Populations –Eligibility Criteria, Enrolment Practices, and Trial Designs, accessible at https://www.fda.gov/regulatory-information/search-fda-guidancedocuments/enhancing-diversity-clinical-trial-populations-eligibility-criteria-enrollmentpractices-and-trial
45. Continue to encourage sponsors to collect pharmacokinetic (PK) data in pregnant women to characterize effect of pregnancy on drug exposures (e.g., AUC, Ctrough). PK data maybe collected in pre-approval clinical trials when appropriate for pregnant participants to remain in the trial, or through post-approval clinical studies in pregnant women.
46. Continue to work with sponsors to update USPI/EMA PI as additional data become available.
47. To the extent feasible, continue to collaborate with other regulatory agencies on aspects of drug development, including trial designs, endpoints, safety monitoring plans, and patient eligibility criteria (such as pregnant status) for inclusion in clinical trials.

EMA commits to:

48. Update the CHMP guideline EMEA/CHMP/203927/2005 Guideline on risk assessment of medicinal products on human reproduction and lactation: from data to labelling.
49. Engage in dialogue with medicine developers regarding timing of non-clinical developmental and reproductive toxicity studies to identify opportunities and challenges for completing them earlier.
50. Promote and support use of standardized and harmonized methods for signal detection and post-authorisation safety studies of medicines in pregnancy and lactation.

National Regulatory Authorities, in countries where CAB LA implementation projects are being undertaken, commit to:

51. Discuss supporting guidance to enable the generation of appropriate PK and safety data in pregnancy and breastfeeding.

guidance. USFDA will continue to work with Sponsors on the specifics of the Informed Consent Form (ICF) language included to communicate potential risks identified from the nonclinical data.

Donors

Funders commit to promote the implementation of the Call To Action principles through their investments, this includes:

52. Fund clinical trials of adequate size to assess the safety in pregnancy of high priority new agents with expected broad use by young women for treatment and prevention of HIV such as CAB LA, LEN and ISL.
53. Support country action and a global platform to strengthen active surveillance of safety of HIV agents (such as TAF, DRV/r and CAB LA) in pregnancy, building harmonization and linkages between surveillance networks, with a focus on the most-affected countries and populations.

Unitaid commits to:

54. Continue to provide funding through the WHO enabler grant to support the work on the development of the R&D framework for studying ARVs during pregnancy and breastfeeding to ensure that mothers and their offspring benefit from most optimized treatments.

UN & International Organizations

WHO commits to:

55. Continue to convene and facilitate a standing expert group to enable timely prioritization of new HIV agents and provide guidance on research priorities and surveillance for use of HIV agents in pregnant and breastfeeding women as integral part of the Conference for ARV Drug Optimization (CADO) process.
56. Continue to support and host the HIV, Hepatitis and STIs Pregnancy and Breastfeeding Therapeutics Working Group (HHS PTWG) to ensure development and updating of appropriate standards, tools and policies to support implementation of accelerated approaches in research and innovations in surveillance to generate high-quality evidence for new HIV agents in pregnancy.
57. Continue to convene and develop norms and standards for new indications for the use of new ARVs for HIV treatment and prevention in pregnant and breastfeeding women in the updating process of the WHO guidelines on the use of ARVs for HIV prevention and treatment – Within a public health approach.
58. Continue to convene and implement a collaborative framework for strengthening the surveillance of existing and new ARVs during pregnancy (including regular reporting to the WHO Advisory Safety Committee of Medical Products).
59. Build on existing accountability frameworks, such as The Global R&D Observatory or the Global R&D Hub, to monitor R&D efforts to promote earlier generation of evidence to support use of new antiretrovirals in pregnant and breastfeeding women.
60. Ensure alignment and represent WHO activities in the discussion and work of the ICH informal working group E21 on "Inclusion of Pregnant and Breastfeeding Individuals in Clinical Trials".

WHO and Research networks[13] commit to:

[13] Engaged in supporting the CTA principles (see section under research networks above and in annex section (Rome 6) https://www.paediatrichivactionplan.org/high-level-dialogues

61. Working together to collaboratively develop standards to strengthen systematic population data collection, registries, and master protocols to promote alignment and harmonization of studies in pregnant women across studies within the work of the WHO HIV, Hepatitis and STIs Pregnancy and Breastfeeding Therapeutics Working Group (HHS PTWG) .
62. Ensure appropriate consultation and engagement of community members and community-based organizations through the research cycle for new therapeutics.

Implementing Partners, Communities, Civil Society Organizations and Faith Based Organizations

Community based organizations commit to support design, implementation and messaging of research conducted according to CTA principles:

63. Engaging as partners in each stage of the HIV treatment and prevention research and surveillance process, including identification of the research questions, protocol development, study implementation, and results interpretation and dissemination.
64. Taking the lead in building community literacy, peer education and advocacy on the inclusion of pregnant women in clinical trials and active surveillance programmes for HIV agents.
65. Partnering with researchers to develop tools to aid in communication about the need for clinical trials and surveillance in pregnancy and the interpretation and application of their findings when they are available.

The CATALYST Study under the MOSAIC consortium commits to:

66. Support study participants who are or who become pregnant while taking CAB LA or dapivirine vaginal ring to stay on the study drug during pregnancy, if they choose to and in accordance with the drug regulatory approval.
67. Collect and report safety and birth outcomes (including pregnancy and neonatal outcomes) in participants who use CAB LA PrEP or dapivirine ring during pregnancy.

AFROCAB commits to:

68. Advocate with governments, the private sector, international regulatory bodies (IRBs), ethicists, researchers and other stakeholders for policies and an enabling environment that facilitates participation of Pregnant and Breastfeeding Women in research.
69. Work with researchers to develop contextually appropriate and palatable materials for Pregnant and Breastfeeding Women in trials including relevant communities.
70. Improve literacy on research (and products under research) including the process, stages, safety, and outcomes among community members including Pregnant and Breastfeeding Women.
71. Hold the researchers and governments accountable for safety, access, and continuity of care for for Pregnant and Breastfeeding Women during and post-trial.

The 4M Network of Mentor Mothers living with HIV (UK), alongside other Community Based Organisations commits to:

72. Supporting the design, implementation and messaging of research conducted according to Call to Action principles. More specifically, to ensure representation of women living with HIV and, as such, to:
    i. Engage as partners in each stage of the HIV treatment and prevention research and surveillance process, including identification of research questions, protocol development, study implementation & results interpretation and dissemination.

ii. Take the lead in building community research literacy, peer education and advocacy on the inclusion of pregnant women in clinical trials & active surveillance programmes for HIV agents.
iii. Partner with researchers to develop tools to aid in communication about the need for clinical trials & surveillance in pregnancy, the interpretation & application of their findings, when they are available.

GNP+[14] commits to:

73. Mobilize the PLHIV (people living with HIV) and KP networks, in particular adolescents and women living with HIV, to increase treatment literacy, demand generation, advocacy, and monitoring to increase access to services for prevention and treatment of HIV during pregnancy and breastfeeding
74. Raise awareness and advocacy for research and policy that support the needs of women and children during pregnancy and breastfeeding.

Catholic Relief Services commits to:

75. Continue working with in-country partners and stakeholders to raise awareness, demand, and support for women and children during pregnancy and breastfeeding, and support policies and standards of practice improving maternal retesting.

HIV DIAGNOSTICS

Commitments should all be achieved by the end of 2023, unless noted otherwise.

Diagnostic manufacturers

Diagnostic manufacturers commit to:

76. Implement and adhere to global access pricing reflective of global demand volumes that ensures consistent reagent pricing across governments and partners within all 145 low- and middle-income countries and regions, and provide a transparent breakdown of pricing for the products and services sold.
77. Implement more consolidated and flexible all-inclusive bundled, or other novel, pricing models that incorporate the menu of any essential molecular tests critical to public health (ie. HIV, TB, HBV, HCV, HPV, MPXV, SARS-CoV-2, etc) instead of separate instrument, consumable, and service procurement models.

[14] The GNP+ commitments are aligned to GNP+ new strategy 2023-2025. The commitments herein shall be reviewed from time to time as appropriate and to adapt to external environmental changes.

78. Reconsider current volume commitment numbers for transitioning to flexible all-inclusive bundled, or other novel, pricing models as current mechanisms are limiting country participation, access, and benefit to novel procurement approaches.
79. Improve oversight and transparency of authorized distributors/representatives under service level agreements that address poor service and lack of adherence to global access pricing schemes.
80. Offer payment terms that better reflect the capability and structures of buyers.
81. Introduce available and upcoming assays on all available proprietary devices, including obtaining the necessary regulatory approvals.
82. Implement a standardized template for service level agreements that clearly spell out minimum performance indicators, including target up-time and failure rate thresholds (with consideration for different causes), plus a mitigation plan when thresholds are exceeded, while committing to improve response times for maintenance and repair programs.
83. Ensure instruments, both laboratory-based and point-of-care, include data connectivity options or are compatible with and can be exported to standard dashboards or databases used in LMICs.
84. Rapidly communicate stock shortages with major buyers and work on joint mitigation strategies. During pandemics or other outbreaks, continue to produce and supply essential tests in order to ensure supply security for critical diseases, such as HIV and TB.
85. Include and standardize multi-lingual display interfaces.
86. Provide three-year advance warning of device discontinuation and transition plans to ensure smooth and cost-minimal transitions to new platforms, including end-of-life equipment removal.

Abbott commits to:

87. Development of additional high-performance assays to support integration of infectious disease screening and testing across programmes including for TB, viral hepatitis and syphilis across Abbott's diagnostic platforms.
88. Offering affordable and accessible all-inclusive per test price (covering the instrument, connectivity, service and maintenance) for m-PIMA assays based on minimum volume thresholds.
89. Continue the all-inclusive, transparent global access ceiling price across Alinity and m2000 molecular assays (HIV, HCV, HBV, HPV, STIs and SARS-CoV-2 assays) and transparently provide volume thresholds for volume-based pricing.
90. Support smooth and cost-minimal transition from m2000 devices to Alinity platforms.

Cepheid commits to:

91. Prioritize transparent global access price both directly and with our distribution partners across all molecular assays in the HBDC program, not limited to HIV and TB but also HPV, HCV, and HBV.
92. Create a transparent & open time bound application process for AccessCare service and maintenance to all 145 high-burden low- and middle-income countries.
93. Rapidly implement an indeterminate range for infant diagnosis, per WHO guidelines, within product software.
94. Consider free replacements of Xpert 6-colour modules with new 10-colour modules when systems are covered under a service agreement.
95. Commit to a rapid roll out of hybrid software to enable a 6C & 10C module to run side by side in the Gene Xpert system.

Hologic commits to:

96. Remain committed to providing all-inclusive, transparent pricing, based on eligibility criteria and volume tiers, that is available in many low- and middle-income countries (published under Hologic's Global Access Initiative (GAI)), is inclusive of reagents, consumables, instrument charges, maintenance, and freight, and available for the following list of assays, which continues to grow as needs arise: HIV-1 plasma, DBS, and EID, HCV, HBV, HPV & GT, SARS-CoV-2.
97. Continue to report quarterly Key Performance Indicators that monitor the quality and timeliness of our product delivery and service and support of our instrument fleet.
98. Submit for WHO prequalification for HCV in 2023.

Molbio commits to:

99. Finalization and market entry of the HIV viral load and infant diagnosis assays along with submission to WHO prequalification.

Roche commits to:

100. Work towards reducing disease silos for diagnostics in order to encourage and support diagnostic integration and multiplex testing to allow use of current platforms to address multiple diseases.
101. Work towards accelerating multi-disease diagnostic network optimization at the national level to support increased access to diagnostic tests, testing and network efficiencies and improvement in specimen-to-clinical action turnaround.
102. Continue the transparent global access ceiling price across molecular assays (HIV, TB, HCV, HBV, HPV, SARS-COV2 assays) and transparently provide volume thresholds for further volume-based price reductions.
103. Ensure the plasma separation card is affordable and consider expanding accessibility to other, non-proprietary technologies.
104. Support smooth and cost-minimal transition from CAP/CTM devices to new platforms.

Donors

Donors[15] commit to:

105. Work towards reducing disease funding silos for diagnostics in order to encourage and support more comprehensive diagnostic strategies, including person-centred care, diagnostic integration and network optimization.
106. Support improved global and national coordination across donors, including funding mechanisms, pooling procurement volumes in negotiations with diagnostic manufacturers, and other activities.
107. Prioritize and re-invigorate paediatric-specific funding for strengthened implementation of HIV and TB diagnostics and support of person-centred diagnostic technologies (ie. point-of-care infant diagnosis, simplified TB sample types).
108. Support current efforts to transition from outright instrument procurement to all-inclusive bundles, or other novel pricing model to ensure in-country harmonization of commodity procurement.
109. Support in a transparent manner, including key performance indicators, the procurement of commodities and operational costs to maintain and further scale-up POC infant diagnosis, as

[15] PEPFAR and Unitaid

well as viral load testing for infants, children, and pregnant and breastfeeding women and advanced HIV disease diagnostics, including TB, as an integral part of optimized and integrated national diagnostic networks and in accordance with national plans and targets.

110. Continue (and expand) support to WHO PQ to broaden their mandate as planned and to shorten timelines for review and minimize time to national registration.

The Global Fund to Fight HIV, TB and Malaria commits to:

111. Support the procurement of commodities and operational costs to maintain and further scale-up POC infant diagnosis, as well as viral load testing for infants, children, and pregnant and breastfeeding women and advanced HIV disease diagnostics, through cross-cutting diagnostic and health systems strengthening interventions as an integral part of optimized and integrated national diagnostic networks and in accordance with national plans and targets.
112. Continue to work with the WHO PQ Team to expand supplier base of quality assured products.
113. Encourage and support countries to adopt innovative contracting mechanisms designed to improve maintenance and servicing of laboratory devices (including those used for paediatric HIV and TB diagnosis and management); a shift towards all-inclusive pricing and reagent rental programs should be explored whenever possible.
114. Support improved global and national coordination across donors to reduce disease funding silos for pediatric HIV and TB diagnostics, and where possible, pooling procurement volumes in negotiations with diagnostic manufacturers, and other activities.
115. Support national, multi-disease diagnostic network optimization mapping exercises to maximise efficiency and increase access to paediatric HIV and TB diagnostic services.

PEPFAR commits to:

116. Work towards reducing disease funding silos for diagnostics in order to encourage and support diagnostic integration and multiplex testing to allow use of current platforms to address multiple diseases.
117. Accelerate multi-disease diagnostic network optimization at the national level to support increased access to testing and network efficiencies, decrease total cost per test, and improvement in specimen-to-clinical action turnaround.
118. Continue engaging governments for policy change in support of all-inclusive pricing models and accelerated complementary use of point-of-care and centralized platforms.
119. Ensure implementing agencies and partners are aware of current paediatric diagnostics that can be procured with PEPFAR funds and ensure safe and ethical HIV testing services are offered to all biological children of parents living with HIV and biological siblings of children living with HIV This can include further scaling appropriate/approved use of HIVST assays including caregiver assisted oral self-testing for screening children at home.
120. Expanding case finding modalities to find undiagnosed children and conducting audits of children newly testing positive for HIV—to inform new approaches to find the missing children, including improving demand generation linked to clinical services through multiple avenues.
121. Working with partners to improve CLHIV estimates through innovative data collection methods in tandem with household surveys.
122. Work with African based institutions to strengthen their capacity for regional regulatory approval of products.

Unitaid commits to:

123. Continue work on accelerating the availability and affordability of innovative diagnostic tools, including those that benefit children living with HIV, TB and other co-infections – either through funding late-stage development or product adaptations (including sample approaches) that will adapt to the settings these tools are needed.
124. Continue direct support to WHO within the enabler grant for diagnostic activities, as well as direct support to WHO PQR for quality and regulatory priorities.
125. Pursue opportunities to strengthen regional manufacturing of diagnostics, as part of Untaid's new strategy (2023 – 2027).

UN & International Organizations

WHO commits to:

126. Continue to work with countries and partners to implement and scale-up access to key diagnostics for infants and children, especially including point-of-care infant diagnosis, viral load, and diagnostics for advanced HIV disease, encouraging an optimized, integrated diagnostic network while doing so.
127. Develop and publish additional guidance on the treatment monitoring algorithm and associated thresholds for viral suppression and treatment failure.
128. Support users to detect product problems for IVDs (including through external quality assessment and 3rd party quality control) to enhance post-market surveillance for IVDs.
129. Support development of national Essential Diagnostics Lists to include HIV and TB diagnostics, particularly point-of-care infant diagnosis and LF-LAM in decentralized non-laboratory settings.
130. Implement and prioritize a sustainable and affordable collaborative registration procedure for diagnostics and support national regulatory bodies to make use of it to streamline their national regulatory procedures.
131. Subject to support from donors (see 15 above), reinforce the capacity of its Prequalification of In Vitro Diagnostics programme, so that additional resources can help to expand its mandate and support efficient review of HIV-related diagnostic products (including advanced HIV disease diagnostics).

Global Alliance[16] commits to:

132. The Global Alliance and members commit to work with regional and national partners to support Alliance member countries to roll out their national action plans in line with normative guidance and implementation best practice, including increasing access to pediatric and adolescent HIV diagnosis to ensure that by 2025, 95% of children and adolescents living with HIV know their status.

UNICEF commits to:

133. Increase access to child testing and case finding. Specifically in 2023 UNICEF will:
    i. Host a technical consultation with key global partners around enhanced strategies to identify undiagnosed children living with HIV

[16] https://www.childrenandaids.org/global-alliance

ii. Ensure that in emergency contexts (eg currently in Ukraine), children and families have access to a continuous supply of essential HIV diagnostics

134. Support decentralized multi-disease POC antenatal testing to advance dual and triple elimination of HIV.
135. Strengthen diagnostic literacy and work in partnership with CSOs, CBOs and/or FBOs to support advocacy for diagnostics and generate demand for testing.
136. Support data-driven optimization of national diagnostics networks including laboratory-based, near point-of-care and point-of-care technologies and to optimize investment and create an enabling environment for diagnosis of HIV and other conditions.

Implementing partners, Communities, Civil Society Organizations and Faith Based Organizations

CHAI commits to:

137. Enable access to affordable commodities through increasing pricing transparency especially of supply chain markups, improving inclusiveness of global access pricing across countries, and exploring improved distribution options to minimize price variability and excess costs.
138. Facilitate timely infant diagnosis and VL monitoring through prioritizing point-of-care solutions and integrated diagnostic networks with efficient sample referral and data management systems.
139. Accelerate pediatric case-finding through scaling proven testing strategies, expanding targeted testing and innovation in facility and community settings, and optimizing use of diagnostic technologies such as POC EID/VL and HIVST.

EGPAF commits to:

140. In EGPAF programs, strive to achieve 95% of all HIV-exposed infants receive an EID test within 2 months of birth and, if negative, 95% are retested at 9 months and 95% at the end of exposure (post-breast-feeding), preferably using a same visit POC test, and 95% receive immediate linkage to care with ART initiation using an optimal formulation for those testing HIV positive.
141. Ensure that 95% of pregnant and breast-feeding women attending ANC in EGPAF-supported facilities with unknown HIV status and who are at risk for acquiring HIV are offered frequent HIV screening throughout pregnancy and breast-feeding, with linkage to PrEP services for those testing negative and immediate linkage to care with ART initiation using an optimal formulation for those testing positive.
142. In EGPAF programs, strive to achieve 95% of infants, children and pregnant and breast-feeding women on ART are offered viral load testing, as per the WHO recommended treatment monitoring algorithm, preferably using a same-visit POC test, with prompt initiation of adherence counselling and switch to second-line ART, as needed, for those who are persistently unsuppressed.
143. Annual data gathering and analysis on inequalities between children and adults in access to testing, treatment and viral load suppression across EGPAF programs.

FIND commits to:

144. Provide technical support to low-and middle-income countries to develop national Essential Diagnostics Lists including point-of-care tests for HIV and TB.
145. Optimize use of current diagnostics through diagnostic network optimization including integrating priority HIV viral load and infant diagnosis testing with TB testing on GeneXpert platforms.

AFROCAB commits to:

146. Engage with diagnostic manufacturers to develop robust pediatric diagnostics and negotiate for lower prices for diagnostics readily available.
147. Equip communities with correct information and literacy on pediatric diagnostics to generate demand and utility.

GNP+ commits to:

148. The Global Network of People living with HIV (GNP+) committed to mobilize the PLHIV and KP networks, in particular adolescents and women living with HIV, to increase diagnostic literacy, strengthen advocacy for diagnostics, address stigma, and promote demand generation and monitoring to increase access to diagnostics for children living with HIV – including Point of Care diagnostics.
149. Promoting peer to peer support structures to promote greater use of HIV prevention, treatment and care services among children. point of care early infant diagnosis.

Pangaea Zimbabwe commits to:

150. Engage and involve communities in the design, planning, monitoring and implementation of people centred services, priorities and references for paediatric diagnostics.
151. Increase community literacy and generate demand for quality client centred paediatric diagnostic services.
152. Foster the development and implementation of evidence-based policies aligned to emerging paediatric diagnostics priorities.

Faith Based Organizations commit to:

153. Equip, mobilize, and support faith leaders, FBOs, people in places of worship, and the wider community to create demand for testing of infants and children.
154. Combat stigma and discrimination among faith leaders and within communities of faith.
155. Further collaborate and coordinate community mobilization, education and outreach to find otherwise hard-to-reach children, adolescents, youth and adults for age-appropriate prevention education, testing and linkage to treatment, health and social support services and integrate into the national system.

Caritas Internationalis[17] commits to:

156. Strengthen its engagement with young people in fighting HIV and TB related stigma and discrimination and to work with them and the communities to spread awareness about the importance of HIV and TB prevention, testing and treatment.

Catholic Relief Services commits to:

[17] Caritas Internationalis (CI) re-commits to the actions adopted in the 2017, 2018, 2020 Action Plan for both HIV and TB.

157. Continue working with in-country partners and stakeholders to improve case-finding and optimize testing strategies for children, adolescent girls and young women, and adults.
158. Continue to advocate for and support efforts to strengthen community-facility linkages, and improved collaboration and integration between health and social welfare service providers.

Catholic Medical Mission Board commits to:

159. Double down on paediatric and adolescent case finding, emphasizing the focus on identifying contacts of index patients – specifically children – and focusing on the use of risk assessment tools to identify likely cases as part of general care in project-supported facilities.
160. Support and participate in national efforts to improve and integrate the use and impact of pediatric diagnostics for HIV and to working to develop national strategies to optimize the use of new technologies and interventions.
161. Continue to emphasize identification of pregnant women in supported communities (relying on catchment community health workers to know the pregnancy intentions and status of each woman of reproductive age in the catchment). Ongoing focus on ensuring that all identified are tested for HIV, enrolled on ART if positive, and supported to adhere to treatment, and on following their HIV-exposed infants for testing at specified intervals until final status confirmation at 18 months.

Zimbabwe Association of Church-Related Hospitals commits to:

162. Advocate for infrastructure, simplified and user-friendly diagnostic equipment provision for rural settings.

All partners commit to:

163. Address inequities by tackling the stigma and discrimination in communities, schools, and healthcare settings that prevent children living with HIV from accessing testing and treatment.
164. Increase literacy about CD4 testing and viral load and promote a client-centred approach to support expansion of access to viral load for pregnant and breastfeeding women and children on treatment, including at the point-of-care.
165. Review and assess emerging co-infections for immunocompromised infants and children, including those with advanced HIV disease, such as severe bacterial infections, fungal infections, and others for country consideration and implementation.
166. Engage affected communities for input and guidance on investment and programmatic priorities, provide support to in-country civil society organizations to engage in advocacy and demand creation for new tools, and ensure data is publicly available to support communities and civil society to monitor progress regarding uptake and implementation of essential diagnostic tools.

TB DIAGNOSTICS

Academic partners, research institutes and networks, and product development partners

FIND commits to:

167. Support the development and assessment of child-friendly samples for TB and promising new TB diagnostics to support decentralised testing and case finding in children and families.
168. Support data generation to enable regulatory assessments, national and global policy review for novel diagnostics for TB infection.
169. Generate child-specific data to support the expansion of use cases for TB diagnostics.

Stellenbosch University and FIND commit to:

170. Incorporate the development of paediatric specimen banks/repositories, including non-sputum sample types, into studies to support faster clinical evaluation of new TB diagnostics and ensure open access to academic groups and manufacturers.
171. Stellenbosch University also commits to evaluate and validate CAD for TB in children in collaboration with other global partners.

NIAID commits to:

172. Support grants funded to explore TB biomarkers in children to eventually better diagnose children and to better understand those who will progress to active TB disease.
173. Engage in discussions with FIND and others on whether NIAID can be helpful in achieving the goals of having better understanding of paediatric chest x-ray reading for more accurate TB diagnosis.

Diagnostic manufacturers

Diagnostic manufacturers[18] commit to:

174. Generate data on new and existing WHO-recommended tests where evidence is lacking for children, including evidence on using alternative (non-sputum-based) sample types.
175. Develop quality-assured, affordable, less invasive alternative specimen processing methods or products (not based only on sputum) that can be used for the paediatric population at the primary health care level, such as urine, stool, tongue swabs or saliva.
176. Work with procurers to monitor stock levels and consumption rates to improve forecasting aimed at minimising the likelihood of stockouts, maintain sufficient regional buffer stock levels and have mitigation plans in place to ensure service continuity
177. Begin moving from a separate instrument, consumable, and service procurement towards more consolidated, all-inclusive pricing models that pool volumes across diseases (i.e. TB, HIV, HBV, HCV, HPV, MPXV, SARS-CoV-2, etc.) and that include service and maintenance.
178. Provide service level agreements to all countries that are monitored according to standardised key performance indicators for all technology types and their offered service plans

[18] Abbott, Cepheid, Hologic, Molbio, Roche.

179. Ensure TB molecular products that are WHO recommended achieve WHO pre-qualification by 2024 and the required post-marketing surveillance is in place.

Abbott commits to:

180. Develop and bring to market in the shortest possible time a new, more sensitive lateral flow TB LAM RDT with a broader indication for use, including those without HIV co-infection in adults and children.
181. Support and strengthen integrated diagnostic networks with comprehensive diagnostic solutions, including data analytics, to improve efficiencies, optimise resource utilisation and maximise the multi-disease capability (HIV, TB, HBV, HCV, HPV, STI and SARS-COV2) on current and future instrumentation.

Cepheid commits to:

182. Reduce the price of Xpert MTB/XDR ($19.80) to promote access and support the implementation of decentralised drug-susceptibility testing.
183. Consider the creation of a new bundle deal with 10C instruments & XDR for 2023
184. Deliver the rollout of new hybrid software in 2023 that enables the running of 6C & 10C modules side by side on the Gene Xpert platform.
185. Evaluate the blood-based host response test for TB for potential use in children as either a diagnostic or screening test
186. Create a transparent Access Care application process & time bound inclusion roadmap to all 145 high-burden low- and middle-income countries
187. Evaluate the blood-based host response test for TB for potential use in children as either a diagnostic or screening test
188. Offer global access pricing to both NTP and non-NTP/private sector in high-burden TB countries via a public-private partnership mechanism and provide a transparent breakdown of pricing for the products and services sold.

Hologic commits to:

189. Continue development of a TB diagnostic and resistance assay on Panther

Molbio commits to:

190. Prioritise the development of resistance markers for TB as well as multiple sample types and to work on a TB+COVID test.
191. Offer global access pricing to both NTP and non-NTP/private sector in high-burden TB countries via a public-private partnership mechanism.

Roche commits to:

192. Support and strengthen a shared and integrated diagnostic network maximising the multi-disease capability (HIV, TB, HBV, HCV, HPV, SARS_COV2, etc.) on current instrumentation.
193. Introduce transparent global access ceiling prices across molecular assays (TB, HIV, HCV, HBV, HPV assays, SARS_COV2, etc.) and transparently provide volume thresholds for further volume-based price reductions.

Donors

The Global Fund to Fight HIV, TB and Malaria commits to:

194. Prioritise funding investments aimed at improving case detection by increasing access (new procurement and improved networks) to molecular WHO-recommended diagnostics (including the use of non-sputum testing, devices and consumables for non-sputum sample types), LF-LAM assays, and digital x-ray technologies for screening for adults and children
195. Support implementation of Global Fund Program Essentials and operational and implementation research aimed at increasing case-finding through new tools, testing procedures and algorithms, and the scale-up of WHO recommended guidelines and product procurement in high TB burden countries.
196. Encourage and support countries to adopt innovative contracting mechanisms designed to improve maintenance and servicing of laboratory devices (including those used for paediatric HIV AND TB diagnosis and management); a shift towards all-inclusive pricing and reagent rental programs should be explored whenever possible.

PEPFAR commits to:

197. See the HIV commitments

Unitaid commits to:

198. Catalyse the evaluation and uptake of new tools and approaches to reduce the case detection gap through market acceleration, accuracy trials, operational research, and optimised implementation algorithms.
199. Support operational and implementation research to increase case-finding through new tools, testing procedures and algorithms, and the scale-up of product procurement in high TB burden countries.
200. Continue work on accelerating the availability and affordability of innovative diagnostic tools, including those that benefit children living with HIV, TB and other co-infections – either through funding late-stage development or product adaptations (including sample approaches) that will adapt to the settings these tools are needed.
201. Ensure that catalytic pilots for diagnostic introduction will promote efforts for diagnostic network optimization to accelerate a multi-disease approach, as part of efforts to further integrate laboratory networking and reduce disease silos.
202. Continue direct support to WHO within the enabler grant for diagnostic activities, as well as direct support to WHO PQR for quality and regulatory priorities.

UN & International Organizations

WHO commits to:

203. With appropriate evidence, prioritise the review of additional urine-based lateral flow assays, molecular technologies (point-of-care and laboratory-based), alternative (non-sputum based) specimen types, and novel testing approaches to provide better tools for paediatric TB detection and encourage and introduce market competition.
204. Timely processing of submissions by WHO pre-qualification of molecular TB diagnostics and expand to include other tests while also supporting national regulatory bodies by making WHO assessments available.

205. Generate target product profiles for TB screening and diagnostics with inclusion of specific considerations for children and adolescents.
206. Develop WHO programmatic standards for TB diagnostics that ensure the best available tools are accessible and used to impact patient care.

Implementing Partners, Communities, Civil Society Organizations, Faith Based Organizations and National governments

National governments, with support from implementing partners and FBOs commit to:

207. Adopt and implement WHO TB screening guidelines relevant to infants and children, including the use of the child-adapted symptom-based screening questionnaire as well as the use of chest X-rays for screening.
208. Adopt WHO TB diagnostic guidelines that are relevant to children, including the use of stool and other non-sputum specimens for TB diagnosis by WHO-recommended rapid molecular assays for which the use of those sample types have been recommended, and the use of LF-LAM in accordance with WHO recommendations.
209. Develop and implement comprehensive programs specifically for paediatric TB training, mentorship and supervision (including training on sample collection procedures, stool processing, CXR reading and interpretation, and use of WHO-recommended algorithms for clinical diagnosis) in order to build front-line healthcare workers' capacity to diagnose and manage pediatric TB.
210. Train and promote the capacity of community health workers or other community cadres to conduct household contact tracing, screening of identified paediatric contacts of TB index cases, counselling, initiation of TB preventive treatment (if permitted by national guidelines) and monitoring of treatment adherence.
211. Scale up and improve primary health care level access to timely, quality-assured paediatric TB diagnostics, including molecular WHO-recommended diagnostics and LF-LAM assays, using comprehensive diagnostic network improvements for multi-disease testing and optimised use of all diagnostic resources to maximise paediatric case detection.
212. Incorporate costed and budgeted requests for interventions for paediatric TB screening and diagnosis, including procurement, training, and case-finding interventions, into domestic budgets, bilateral and multilateral grant applications (e.g., Global Fund and PEPFAR).
213. Prioritise and support the scale-up of decentralised and integrated models of care for maternal, infant and child case-finding approaches and systematically ensure household contacts of persons living with TB are screened, tested and linked to treatment, including preventive treatment where appropriate.
214. Remove financial barriers and reduce catastrophic costs to accessing TB screening and preventive treatment for healthy children who are exposed to TB (e.g., provide transport vouchers, home-based screening and treatment, etc.) as well as TB diagnosis (CXR fees, costs related to the course of broad-spectrum antibiotics)
215. Support optimal access and supply to TB diagnostics through streamlined regulatory registration of WHO-recommended screening and diagnostic products and not taxing public goods.

Faith Based Organisations commit to:

216. Support and participate in national efforts to improve the uptake of paediatric diagnostics for TB and HIV, ensuring that communities are educated and informed on health risks and the need for early health access as well as reducing stigma.
217. Introduce initiatives aimed at reducing catastrophic costs on individuals by providing financial and operational support (e.g., sample collection and delivery) to vulnerable populations to access essential screening and diagnostic services.

EGPAF commits to:

218. Through its Unitaid-funded project CaP-TB, improve paediatric TB care, finding more children with latent (TB infection) or active TB (TB disease), and putting them on appropriate treatment. It includes improving the increased access and use of TB preventive treatment in high-risk populations of child contacts <5 and CLHIV.

Academic partners, research institutes and networks

IAVI commits to:

219. Pursue Phase 1 studies of a highly potent, novel bNAbs combination by 2024 to support demonstration of safety and enable subsequent evaluation for a postnatal prophylaxis (PNP) indication.
220. Advance research, advocacy, and contribute to collaboration and coordination designed to ensure more efficient and timely investigation of bNAbs in the context of PNP.
221. Ensure early engagement of communities and local stakeholders in Africa to define a regionally driven clinical development plan for a PNP indication for the bNAbs.

IMPAACT commits to:

222. Determine dosing and safety of DTG dispersible tablets in newborns by third quarter 2024
223. Determine safety, dosing, and acceptability of long-acting injectable ART with cabotegravir and rilpivirine in adolescents by second quarter of 2024 and children over age 2 years by second quarter of 2024.
224. IMPAACT to collaborate with GAP-f partners and appropriate research networks to implement a platform trial to assess innovative options to deliver postnatal prophylaxis

Penta commits to:

225. Setting up a data collection system in collaboration with the Ministry of Health of Uganda to monitor the safety and effectiveness of dolutegravir in the paediatric population.
226. Study the PK, safety and virological/immunological impact of monoclonal anti-HIV antibodies in combination with antivirals in children responding to therapy, by 2025.
227. Promoting the use of real-world data in combination with clinical trial data for regulatory purposes.

Stellenbosch University commits to:

228. Complete investigation of DTG dispersible tablets in neonates by early 2024 with interim results by early 2024 and undertake investigation of DTG dissolvable oral film in neonates by the end of 2024, with support from UNITAID.
229. Collaborate with other GAP-f partners and pharmaceutical companies, to design and set up a platform to enable rapid investigation of neonatal PK of new antiretrovirals as well as key antibiotics and antivirals for inclusion in AHD package.

Pharmaceutical Companies

Gilead commits to:

230. Prioritizing development of low dose F/TAF tablet for oral suspension (TOS) and completing investigation of low dose F/TAF TOS paediatric dose for children 3-<25kg older than 4 weeks by end of 2025.
231. Supporting generic development, manufacturing, and regulatory approval of the prioritized paediatric low-dose F/TAF paediatric formulation (as needed beyond what is already allowed through the MPP-Gilead licence for TAF).

232. Fulfilling ongoing PSPs and PIPs for lenacapavir with collaboration and feedback from the GAP-f partners and collaborating to evaluate the potential investigation of lenacapavir in children with multi-drug resistant HIV infection.
233. Collaborate on the design of a platform trial and development of appropriate neonatal formulation(s) to assess innovative options to deliver postnatal prophylaxis and evaluate neonatal PK.
234. Collaborate with GAP-f partners to develop an enhanced monitoring and safety data platform for new and existing paediatric ARV drugs.
235. Make publicly available synopses of PSPs, similar to publicly available PIP summaries, for PADO priority products to enable a more transparent clinical trial ecosystem.

Janssen commits to:

236. Provision of Janssen DRV PK model data to CHAI and PENTA to support registration of Gx DRV/r 120mg/20mg optimal paediatric fixed dose combination.
237. Enhance collaboration and facilitate knowledge-sharing to promote development of new technologies to enhance effectiveness and acceptability of paediatric medicines, including long-acting injectables for infants, children, and adolescents (Rilpivirine).
238. In collaboration with EGPAF and other key partners, the New Horizons Advancing Paediatric HIV Care Collaborative (NHC) will provide support to its participating countries with health systems strengthening and access to Darunavir (DRV) & Etravirine (ETR) through donations (from Johnson & Johnson subsidiary Janssen Products LP).
    i. New patient enrolments will continue through till Q4 2025 with donation until 24yrs of age or switch to other drug formulations.
    ii. Johnson & Johnson and the NHC team commits to seek additional stakeholders to support the expansion of these NHC critical initiatives.
239. Ensure availability of DRV paediatric formulations (75mg; 150mg) in LMIC countries until DRV/r 120/20mg (fixed dose combination) FDC product is available.

Laurus Labs commits to:

240. Collaborating with regulators and clinicians to obtain data on the ease of administration of oral films in neonates and the paediatric population by 2024.
241. Expanding the oral film technology to other HIV products as well as TB and malaria.
242. Allocating resources to develop DRV and TAF containing FDCs for the paediatric use beginning Q2 2023.

MSD commits to:

243. Make publicly available the PSP for PADO priority products to enable a more transparent clinical trial ecosystem.
244. Explore collaborations with GAP-f partners to accelerate the generation of evidence on child-friendly formulations of ISL, using weight bands and with concurrent testing of age groups making use of PAWG and GAP-f input on PSPs and PIPs.

ViiV Healthcare commits to:

245. Collaborate with key PAWG members and research networks to support ViiV to undertake appropriate modelling to inform the use of CAB LA for perinatal and postnatal prophylaxis.
246. Advance research and collaborate with WHO and research networks on the investigation of CAB LA injectables in the context of PNP and treatment for children and adolescents.
247. Contribute to the implementation of a platform trial to assess innovative options to deliver postnatal prophylaxis.
248. Collaborate with GAP-f partners to design and set up a dedicated platform for neonatal PK studies.
249. Support long-term follow up in the ODYSSEY trial, including long-term safety profile data by Q1 2024.
250. Collaborate with GAP-f partners to develop an enhanced monitoring and safety data platform for new and existing paediatric ARV drugs.
251. Shipping (GSK/ViiV Healthcare) study drugs (DTG) for DOLPHIN Kids in Q1 202319.
252. Advance research and contribute to collaborations and coordination designed to ensure more efficient and timely investigation of bNABs in the context of PNP and paediatric treatment.

Partnerships

GAP-f partners commit to:

253. Sustain and strengthen collaboration among relevant stakeholders to ensure the most efficient development and uptake of novel paediatric ARV formulations, in close consultation with the community of people living with HIV.
254. Collaborate with PAWG to offer technical advice to national Ethics Review Boards to accelerate the process of ethical approval in high burden countries contributing to key paediatric clinical trials.
255. With Penta and IMPAACT scientific leadership, rapidly develop and implement research actions (including carrying out specific studies to generate high quality evidence for regulatory submissions and high-quality pharmacovigilance studies where needed) to accelerate access to innovative, high quality, and affordable drugs for children worldwide.
256. By the end of 2025 and with the support of EDCTP, Penta will partner with Gilead and CHAI to implement the UNIVERSAL project to inform development and use of DRV/r FDC and TAF-containing FDC as prioritized by PADO.
257. With CHAI leadership and the support of Unitaid, partner with Janssen and generic manufacturers to develop and register paediatric DRV/r 120/20 mg tablet by mid-2024.
258. CHAI, with support of Unitaid, will collaborate with PENTA and Gilead to advance the development of generic versions of TAF-containing paediatric formulations.
259. Enhance collaboration and facilitate knowledge-sharing to promote development of new technologies (i.e., Micro Array Patches and dissolvable oral films) to enhance administration, effectiveness and acceptability of paediatric medicines.
260. Identify and facilitate the most suitable financial incentive for a given product included in PADO list, possibly including one or more of the following:
    i. Support to development upon timely achievement of key milestones

[19] DOLPHIN-Kids is primarily a drug interaction study between DTG and the TB drug rifapentine in children and adolescents living with HIVin South Africa. ViiV is supporting this study by drug donation of DTG clinical trials' material.

ii. Catalytic procurement
iii. Advance market commitments.

261. Continue to seek and direct funding to support the additional research and development required to inform development and use of PADO priority products included in GAP-f 2022-2024 business plan.
262. Continue to promote donor coordination to cover the full spectrum of activities required to ensure accelerated research, development, registration, commercialization, roll-out, and appropriate monitoring of PADO priority products.
263. With CHAI leadership, advance research on bitter sensing and bitter blockers in collaboration with Monell, Medicines Malaria Venture, and donors to identify a universal "bitter blocker" that can be used in paediatric formulations to improve palatability.
264. With Stellenbosch University leadership under the PETITE collaboration with Chang Mai University, to design and set up a platform to enable rapid investigation of neonatal PK of new antiretrovirals as well as key antibiotics and antivirals for inclusion in AHD package.
265. Design and pilot test an enhanced monitoring and safety data platform for new and existing paediatric ARV drugs, in collaboration with WHO HIV (HHS) Department.
266. Implement a coordinated plan, in consultation with the community of people living with HIV, to provide technical assistance in support of ALD and co-formulated DRV/r introduction to ensure rapid policy update and effective uptake in priority countries.
267. Carry out a critical review and identify solutions to improve stockout management and "last mile" distribution, in particular for stocks of low volume drug products (e.g., LPVr and DRV/r formulations, neonatal ARV formulations) including ways to improve forecasting, clinical and supply chain collaboration

Regulatory Authorities

EMA commits to:

268. Continue to participate in the Paediatric ARV Drug Optimization (PADO) and Paediatric ARV Working Group (PAWG) meetings and take into consideration the list of priority products in the evaluation of Paediatric Investigation Plans for related medicines.
269. Explore stepwise approach in PIP in agreement of paediatric investigation plans for treatment of HIV to align them to evolving needs of different paediatric age-subgroups.

WHO PQ commits to:

270. Continue to convene the Paediatric Regulatory network to accelerate national registration through reliance and facilitate in-country registration of specific products under the Collaborative procedure established by WHO.

WHO-PQ and US FDA commit to:

271. WHO-PQ and US FDA to collaborate and agree on the next steps for the CRPlite.

US FDA commits to:

272. USFDA is committed to work with sponsors and investigators who may need additional guidance on drug development. USFDA encourages Sponsors to engage in the PreIND consultation program.

Donors

The Global Fund to Fight HIV, TB and Malaria commits to:

273. Support GAP-f partners' plan for the accelerated introduction and rollout of the DTG 10mg dispersible tablet formulation, paediatric ALD, and paediatric darunavir/ritonavir in priority countries to ensure early and wide uptake.
274. The Global Fund commits to streamline and shorten critical quality assurance processes (such as sample testing) to accelerate the GF's ability to place a first order via the Pooled Procurement Mechanism for a new paediatric product.

PEPFAR commits to:

275. Procuring only optimal Paediatric ART formulations (per optimal formulary) and ensuring implementing Agencies and partners are informed of the formulations that can be procured with PEPFAR funding.
276. Ensuring implementing agencies and partners are prepared for the introduction of pALD by not overstocking ABC/3TC 120/60 mg and DTG 10 mg.
277. Ensuring implementing agencies and partners are prepared for co-formulated DRV/r introduction and transition from other PI based regimens in children 3 and older.
278. Addressing preventable deaths in CLHIV by implementing the STOP AIDS WHO package of care for all children with AHD; supporting mortality surveillance systems and cause of death audits, in collaboration with country governments, to allow for targeted mortality prevention efforts; ensuring CLHIV newly initiating on ART are provided with intensive case management until VLS is achieved; and ensuring malnutrition is diagnosed and treated early in CLHIV.

NIAID commits to:

279. Continue to support IMPAACT to determine dosing and safety of DTG dispersible tablets in newborns by third quarter 2024.
280. Continue to support IMPAACT to determine safety, dosing, and acceptability of long-acting injectable ART with cabotegravir and rilpivirine in adolescents by second quarter of 2024 and children over age 2 years by second quarter of 2024.
281. Continue to support the PAVE Martin Delaney Collaboratory to completion in Q2 2026. The major research goals of the grant includes defining the establishment and evolution of the HIV latent reservoir in perinatal infection and enhancing bNab delivery to achieve post treatment control of HIV-1 off of ART.
282. Continue to support IMPAACT to complete IMPAACT 2037, which is assessing safety and PK of bNabs in infants exposed to HIV.
283. Support increasing the understanding of concurrent dosing of ARVs and TB medications.
284. When appropriate and unmet needs exist, leverage NIAID resources to support development and evaluation of optimized paediatric formulations for priority ARVs and TB prevention and treatment medications.
285. Contribute to address potential funding gaps for the development of a universal bitter blocker by leveraging contract resources in 2023.
286. Engage in discussions with IAVI and pharmaceutical partners on criteria for advancement of bNAbs for postnatal prophylaxis.
287. Contribute to stakeholder consultations convened by WHO on bNabs for treatment and prevention in 2023.

Unitaid commits to:

288. Support the study of appropriate dosing and safety of DTG dispersible tablets and the DTG oral film in neonates, as well as acceptability amongst care-givers by the end of 2024.
289. Continue to support WHO and partners on the development and introduction of optimal ARV formulations, such as generic ALD, paediatric DRV/r FDC and paediatric TAF, and on the roll out of a paediatric Advanced HIV Disease (AHD) package of care – including associated treatment literacy and training, and enhanced monitoring & safety data platform for new and existing paediatric ARV drugs.

UN & International Organizations

WHO commits to:

290. Continue to host the Paediatric ARV Drug Optimization (PADO) process and update the list of priority products with a view to providing a consistent, clear, and harmonized set of products for communication to industry and regulators in a timely manner, with inclusion in the WHO Expression of Interest list as soon as dosing is provided.
291. Continue to use the Paediatric ARV Working Group (PAWG) mechanism to provide recommendations on optimal dosing and ratios for HIV paediatric drug formulation development.
292. In collaboration with other partners, continue to revise the Optimal ARV Formulary and ensure its inclusion in the WHO Model List of Essential Medicines List for Children by end of 2023 and 2024 respectively.
293. By the end of 2023, update treatment guidelines on sequencing ART regimens for children and adolescents with treatment failure to ensure that more effective drugs in age-appropriate formulations are recommended for children who experience treatment failure.
294. Promote and facilitate operational and implementation research on treatment failure and HIV drug resistance that may adversely impact WHO preferred regimens for infants, children and adolescents, including acquired and transmitted resistance and selected drug resistance in infants exposed to maternal ART and post-natal infant antiretroviral prophylaxis (PNP).
295. Promoting and gathering evidence from research on continuation of abacavir when changing a failing NNRTI or PI-based regimen to a DTG regimen in children below 30 kg.
296. By the end of 2023, in collaboration with appropriate partners, undertake forecasting exercises for antiretroviral drugs and formulations for sequencing of the regimens in children and adolescents with confirmed treatment failure following adherence interventions.
297. Define, in collaboration with PAWG members, principles to guide evidence generation for policy revision to include novel agents, innovative delivery methods and strategies for PNP.
298. Convene and promote coordination and collaboration among key stakeholders engaged with investigation and development of broadly neutralizing antibodies (bNabs) for treatment and prevention of HIV in infants and children by Q1 2023.
299. Convene efforts to facilitate generation and gathering of evidence on causes of mortality in children living with HIV and on how to optimize the package of care in diagnosis, prevention and treatment of advanced HIV disease (AHD) in children and adolescents.
300. Work via its regional offices and in collaboration with all partners (Global Fund, PEPFAR, GAP-f, etc.) to support transition plans and ensure rapid uptake of optimal ARVs globally, including low burden and lower volume countries.

301. With PAHO leadership, leverage PAHO Strategic Fund to support rapid country adoption of ALD and DRV/r novel Paediatric formulations.
302. Convene and collaborate with MOHs and all partners (PEPFAR, Global Fund, GAP-f and other implementing partners) to strengthen and expand efforts to rapidly monitor safety and effectiveness of novel Paediatric ARVs including DTG, ALD and co-formulated DRV/r.
303. Continue supporting the implementation of the STOP-AIDS toolkit for the AHD in children.

UNICEF commits to:

304. UNICEF SD commits to support uptake of novel paediatric treatment options by inclusion of fixed dose ALD (expected to be prequalified 6/2023) and other new products when available, in long term agreements with manufacturers that offer flat pricing for children everywhere living in LMICs.
305. Work with countries to increase uptake of newer drugs and formulations through demand creation for paediatric treatment services and generation of age disaggregated data to inform supply planning and forecasting.
306. UNICEF commits to collaborate with GAP-f partners to develop and validate a product-agnostic toolkit to support and accelerate the introduction of new paediatric drugs and formulations. The toolkit will include stakeholder planning and advocacy elements and will be disseminated by October, 2023.
307. UNICEF commits to collaborate with GAP-f partners to review and update the pDTG transition tracker and expand the countries covered by the tracker from 30 to 59 by Q3 2023.

UNAIDS commits to:

308. Continuing to support countries to produce estimates of children newly infected with HIV, children living with HIV, and AIDS related deaths among children, along with key indicators around treatment coverage and prevention of vertical transmission, towards the UNAIDS Global report in July. In addition, in collaboration with UNAIDS' Reference Group on Estimates Modelling and Projections, UNAIDS will continue to pursue methods for collecting robust data on children and HIV.

CHAI commits to:

309. Support product development and introduction of paediatric ABC/3TC/DTG (pALD), paediatric darunavir/ritonavir (pDRV/r), and paediatric TAF (pTAF) once regulatory approvals are received.
310. Scale implementation of the WHO recommended STOP-AIDS toolkit for children living with HIV to identify more children in need and provide a comprehensive package of care for children to prevent, diagnose, and treat drivers of morbidity and mortality.
311. Support adoption of best practices for expanding and sustaining uptake of optimal ARVs for children (e.g., granular monitoring, peer support etc.) and innovate to improve continuity in care (e.g., disclosure, mental health).
312. Engage in market shaping activities to accelerate access to optimal generic paediatric treatment products, including long-acting medications and next generation delivery methods.

Access to Medicine Foundation commits to:

313. Completing a review of how paediatric populations are represented in the 2023 Access to Medicine Index Methodology and to making subsequent changes to the methodology, as required to continue to reflect their unique needs by Q4 2023.
314. Highlighting key opportunities for the pharmaceutical companies within the scope of our research pertaining to paediatric populations as an inclusion in our collaborative engagement work aimed at moving the pharmaceutical industry further and faster on key topics by Q4 2025.
315. Exploring the unique needs of paediatric populations in the consultation process and the subsequent development of new frameworks for evaluation, as part of its 5-year Strategic Direction.

MPP commits to:

316. Continue to facilitate access to the best available medicines for children. Specifically, the MPP will continue to work with patent holders to in-license paediatric drugs as prioritized by the WHO/PADO, and to sublicense to generic manufacturers to ensure that appropriate formulations are rapidly developed, registered and made available in as many developing countries as possible.
317. Continue to inform all countries in the paediatric license group on the status of paediatric ARV patents.
318. Expand its quarterly reported information on the progress of priority paediatric drug formulations, sharing not only the list of countries with regulatory filings, regulatory approvals, and supplies of paediatric DTG (10 mg scored dispersible tablets), but also reporting for paediatric ALD (ABC/3TC/DTG 60/30/5 mg) as an important upcoming addition to the paediatric HIV treatment toolbox. In addition, this reporting will include anonymized regulatory filing plans and timelines, as well as quarterly country-by-country volumes of medicines supplied across all countries covered by the MPP-ViiV Healthcare licence for paediatric DTG.

Implementing Partners, Communities, Civil Society and Faith Based Organizations

EGPAF commits to:

319. Work with MoH to contribute to scale up and sustain access to the full portfolio of WHO-recommended paediatric ARVs, including backbone and alternative products, which are needed to deliver optimal first-, second- and third-line treatment regimens.
320. As co-chair of the GAP-f Product Access and Treatment Delivery working group, sustain and strengthen collaboration among relevant stakeholders to ensure quick access to the most optimal paediatric ARV formulations, in close consultation with civil society and the communities, including the community of people living with HIV.
321. Work with MoH, GAP-f partners and other national and international stakeholders to contribute to scale up and sustain uninterrupted access to pDTG 10 mg along with backbone paediatric formulations in EGPAF countries.
322. Support a coordinated plan with key partners, including GAP-f members, to provide technical assistance in support of ALD fixed-dose combination therapy for children 10kg to 25kg introduction to ensure rapid policy update and effective uptake in EGPAF's countries.
323. Continue to support the implementation of the STOP-AIDS package of care for advance HIV disease (AHD) in children and develop a paediatric AHD toolkit and training materials with

support from the Gates Foundation to further strengthen the identification and management of paediatric AHD.

324. As co-chair of the GAP-f Product Access and Treatment Delivery working group, sustain and strengthen collaboration among relevant stakeholders to ensure quick access to the most optimal paediatric ARV formulations, in close consultation with civil society and the communities, including the community of people living with HIV.
325. With the support and in collaboration with Johnson & Johnson (J&J) and other key partners, the New Horizons Advancing Paediatric HIV Care Collaborative (NHC) will provide support to its participating countries with health systems strengthening and access to Darunavir (DRV) & Etravirine (ETR) through donations (from Johnson & Johnson subsidiary Janssen Products LP). The NHC team commits to seek additional stakeholders to support the expansion of these NHC critical initiatives.

Pangaea Zimbabwe commits to:

326. Ensure ongoing quality CSO and community engagement and preparedness for introduction and uptake of optimal paediatric medicines for TB/HIV as they are adopted in country.
327. Increase community literacy and advocacy to generate demand for optimal paediatric TB and HIV medicines as they are introduced.

GNP+[20] commits to:

328. The Global Network of People living with HIV (GNP+) committed to mobilize the PLHIV and KP networks, in particular adolescents and women living with HIV, to increase treatment literacy, demand generation, advocacy, and monitoring to increase access to treatment for children living with HIV.
329. Raising awareness in global fora about the structural barriers to diagnostic and treatment of children with HIV. Including Stigma, discrimination, criminalization, and violence.
330. The Global Network of People living with HIV (GNP+) committed to mobilize the PLHIV and KP networks to address inequities in children by tackling stigma and discrimination in communities, schools, and healthcare settings that prevent children living with HIV from accessing testing and treatment.
331. Raising awareness in global fora about the unmet diagnostic and treatment needs of children affected by HIV including access to Early Infant Diagnostics (EID), Post Exposure Prophylaxis during breastfeeding and access to ARV's.
332. Support treatment preparedness programs, ensure improvement of treatment awareness among caregivers of children of all ages and adolescents, and work jointly with other stakeholders on treatment literacy and demand creation for new paediatric formulations.
333. Promoting peer to peer support structures for mental health support and to promote greater use of HIV prevention, treatment and care services among children.
334. Increase literacy among communities about Advanced HIV Disease (AHD) among children, promote adherence and advocacy to promote a client-centred approach to support expansion of access to viral load for pregnant and breastfeeding women and children on treatment, including at the point-of-care.

[20] GNP+ commitments are anchored in our GIPA principle and will be guided broadly by the 4 key commitments.

335. Support Community Led Monitoring to gather evidence for improved quality of services for children affected by HIV including supporting communities to rapidly communicate treatment disruptions, and shortages with key national and global health actors for rapid response actions.
336. Mobilize PLHIV, KP networks and communities to help build treatment literacy, generate demand, and expand access to ARVs among children.
337. GNP+ commits to convene communities and Civil Society and activists concerned about access to treatment for Children affected by HIV under the End Paediatric AIDS in Children (EPIC) initiative for collaboration and join advocacy work.
338. GNP+ Commits being strategic community partner alongside ICW and Y+ Global in the Global Alliance to end AIDS in Children; being part of the steering committee, working groups and supporting country networks to engage meaningfully to meet the objectives and goal of the Global Alliance.
339. Building strong community voice at global and national level particularly of young people meaningfully representing and advocating for children's access to HIV prevention and treatment.
340. Through The Young Emerging Leaders program, we will recruit 5 YEL –children to support representation and advocacy at global influencing platforms. Additionally, through our EPIC program we will build the capacity of 30 community activists (mama and papa bears) who will engage in national and grassroots level advocacy for children including during national level.
341. Collaborate with Global and national health actors – UN agencies, researchers, funders, program implementers to inform policy, resource and program planning, implementation and monitoring that impact access to HIV diagnostics and treatment among children. – Includes being part of Coalition of Children Affected by AIDS (CCABA), Global Alliance etc

MSF commits to:

342. Support the scale-up optimized, evidence-based TB-HIV case-finding strategies to ensure strong case-finding and identification, diagnosis and treatment among children in the settings where we are working.
343. Support Ministries of Health to scale-up HIV and TB programs including PMTCT, helping overcome barriers to the access of new diagnostic technologies and treatments enabling the implementation of new approaches.
344. Continue working with WHO, Stop TB and other organizations at local, regional and global level; from ensuring the quality-of-care standards, to research, advocacy and policy development and improvements.

Catholic Medical Mission Board commits to:

345. Collaborating at all levels and working in communities, schools, and faith and healthcare settings to disseminate the HIV Messages of Hope and to combat HIV-related stigma and discrimination, including among faith leaders.
346. Continue to provide client-centered HIV care and treatment within health facilities as well as community-based treatment, and as part of that commitment, we commit to ensuring that such care is provided free of stigma.
347. Advocate to and support the national and state-level ministries of health to rapidly transition to optimal paediatric formulations per the latest WHO guidelines. We will provide coordinated

support for the development and implementation of transition plans and will ensure that both clinicians and patients understand the benefits of the new formulations and their availability.

348. Support scale-up of access to priority formulations and diagnostics and facilitate their wider rollout by ensuring the availability of guidance, education, and materials, and by working through community health structures. CMMB works with various cadres of community resource people to support follow-up of children living with HIV as well as to prevent mother-to-child transmission of HIV, which remains too high across the countries we serve.
349. Ensure that we are fully implementing differentiated service delivery in all its variations—for example, flexible clinic hours and community drug distribution modalities such as home ARV delivery and community ART groups.
    i. In Zambia, where many children live at their schools during the school year, we will scale up the scholar model, where antiretroviral medications are sent directly to the institution.

350. Mobilize our networks and work with communities to help build treatment literacy, generate demand, and expand access to diagnosis and treatment for both HIV and TB among children, collaborating with other stakeholders. We will work closely with stakeholders at all levels toward this end, including community health workers.
    i. In Kenya, to improve outcomes, over the next year, CMMB will train 249 health workers of various cadres on treatment literacy and any new pediatric ART guidelines. We will support them to follow up with those having poor treatment outcomes and HIV-positive pregnant women for PMTCT. In addition, we commit to training them additionally on human rights and gender issues to address factors impeding optimal adherence.

351. Scaling up both age-appropriate adherence support groups as well as individualized and group support for caregivers, including psychosocial support. We will work with caregivers to strengthen the skills required to meet the needs of their HIV-positive children. Additionally, we will focus on providing support for HIV-positive pregnant women for prevention of mother-to-child transmission and follow-up testing.
    i. In Haiti, we commit to scaling up the use of income-generating activities for adolescents and young adults to increase their economic autonomy, lessen reliance on risk behaviors by young women to provide spending money, and reinforce adherence.
    ii. Also in Haiti, we will continue to implement directly observed therapy (DOT). In this approach borrowed from TB treatment, a project field worker visits the family of an HIV-positive child to directly observe the administration of the child's medication. Currently 82% of unsuppressed paediatric patients have benefited from DOT, with a resuppression rate of 88%.
    iii. As part of adherence support to caregivers, CMMB commits to supporting parents to disclose to their children, as disclosure is a first step toward paediatric adherence. Currently, in our projects in Haiti, 93% of disclosed preteens are virally suppressed.

352. To local, regional, and national governments, CMMB will promote an increase in investments in community HIV prevention, care and support programs that strengthen community-focused interventions to enhance support for children and adolescents living with HIV through the continuum of care. CMMB will also advocate for inclusion of interventions addressing social

determinants of health into existing frameworks for paediatric HIV prevention, care and treatment funding mechanisms.

Catholic Relief Services commits to:

353. Continue supporting in-country partners reaching families, communities, social welfare service providers, and community and facility-based health providers to improve treatment literacy, and provide holistic support and strengthened case management practices to improve treatment coverage, adherence, and viral load suppression for children living with HIV.
354. Continue addressing social and structural barriers inhibiting access to testing and treatment services for children living with HIV.
355. Continue community engagement and empowerment efforts supporting community led quality of service monitoring for children affected by HIV.

Zimbabwe Association of Church-Related Hospitals commits to:

356. Advocate and call upon all Partners who have committed to work with FBOs to honour their commitment to fully engage FBOs in HIV and TB treatment for mothers, children, young girls and adolescents.
357. Follow up on the High-Level Meeting agenda and advocate for Interfaith leadership in prioritizing major commitment for diagnostic and HIV and TB treatment working with Government (Head of States and (MoH) – Church Leadership have direct access to Heads of State and Ministers of Health to speed intervention and policy changes.
358. Advocate for capacitation of FBO Medical supplies Stores for commodity security for diagnostics and HIV/TB treatment including licensing for local production and manufacturing (MEDS, JMS, EPN and other DSOs)
359. Advocate for improved evidence-based data reporting to inform decision making, gaps analysis and financial support.

TB TREATMENT for CHILDREN, PREGNANT, POST-PARTUM AND BREASTFEEDING WOMEN

Specific commitments regarding the development, regulation and introduction and roll out of medicines for TB prevention and TB treatment for paediatric populations as well as pregnant and breastfeeding women

Academic partners, research institutes and networks

Access to Medicine Foundation commits to:

360. Complete a review of how paediatric populations and pregnant and lactating women are represented in the 2023 Access to Medicine Index Methodology and to making subsequent changes to the methodology, as required to continue to reflect their unique needs by Q4 2023.
361. Highlight key opportunities for the pharmaceutical companies within the scope of our research pertaining to paediatric populations and pregnant and lactating women as an inclusion in our collaborative engagement work aimed at moving the pharmaceutical industry further and faster on key topics by Q4 2025.

362. Explore the unique needs of paediatric populations as well as pregnant and lactating women in the consultation process and the subsequent development of new frameworks for evaluation, as part of its 5-year Strategic Direction.

Aurum Institute on behalf of the IMPAACT4TB consortium commits to:

363. Generating evidence for 3HP implementation across different populations and service delivery methods to ensure scale up is ongoing by 2024
    i. DOLPHIN TOO investigating 3HP initiation in ART naïve PLHIV
    ii. TBTC Study 35 to inform dosing of 3HP in children under 2 years old (in collaboration with Desmond Tutu Centre for TB and CDC)
    iii. CHIP-TB investigating 3HP (TPT) for child contacts in Ethiopia and South Africa
    iv. Choice Architecture Study investigating an opt-out strategy to increase TPT uptake within ART clinics
364. Generate further evidence to support adoption of short rifapentine based TB preventive treatment regimens in overlooked populations including paediatrics and pregnant women by adopting a family-centred approach to TPT.
    i. Dolphin Kids (evaluating 3HP with DTG based ART)
    ii. Dolphin Moms (evaluating 3HP & 1HP in pregnant people with HIV)
    iii. One to Three Trial comparing 1HP to 3HP among PLHIV and HHCs
    iv. RPT Crush Study (maybe) – considering Crush to add to options for children as a backup plan if paediatric formulation is not available in time
365. Donation of 300mg singles of rifapentine for use in underserved populations for TPT e.g., household contacts, healthcare workers.
366. Improving contact tracing strategies and linkage to care: countries asking for tests of infection to possibly improve TPT uptake
367. Paediatric formulation – generic manufacturer expected filing in 1st half of 2023, demonstration study in one or two countries to evaluate palatability and acceptance of the formulation. This will likely be in HIV negative children as we will not have evidence for HIV positive children on DTG based ART.

NIH/NIAID commits to:

368. Continue supporting IMPAACT and other funded grants to determine PK, safety and dosing of delamanid, bedaquiline, and short course rifapentine by Q4 2025.
369. Support increasing the understanding of concurrent dosing of ARVs and TB medications.
370. When appropriate and unmet needs exist, leverage NIAID resources to support development and evaluation of optimized paediatric formulations for priority ARVs and TB prevention and treatment medications.
371. Contribute to address potential funding gaps for the development of a universal bitter blocker by leveraging contract resources in 2023.

Stellenbosch University commits to:

372. Completing the TB CHAMP Trial studying TPT in children and adults who are household contacts of people with MDR-TB.
373. Study the use of 3HP using novel formulation in children below 2 years contacts of people with TB and disseminating data during 2023.

374. Study taste-masked novel dispersible formulations of Moxifloxicin and Linezolid in children to inform commercial developed.
375. Study Pretomanid in girls, through the IMPAACT network.
376. Evaluate the short HPMZ regimen (also called the Study 31 regimen) for PK, safety, tolerability and acceptability in children < 12 years with DS-TB, through the TBTC network.
377. Collaborate with WHO and University College London on data collection and curation children, adolescents and pregnant women with drug-resistant TB to inform policy guidelines

Pharmaceutical and generic companies

Johnson & Johnson commits to:

378. Ensuring ongoing access to the 20mg bedaquiline tablet, which Johnson & Johnson, in partnership with Stop TB Partnership's GDF Paediatric DR-TB Initiative, has already made available for over 130 countries, following US FDA approval in May 2020.
379. Continue efforts in exploring additional clinical trial sites to ensure timely completion of study investigating the use of bedaquiline in children below 5 years of age.
380. Engage early and regularly with GAP-f and other WHO-convened expert groups on paediatric drug and regimen development, including target regimen profile consultations for paediatric DR-TB regimens.
381. Make paediatric formulations and data available to research networks advancing paediatric PK and safety studies where appropriate under collaborative agreements. Rapidly submit paediatric data to regulatory authorities and the WHO to facilitate updating of labelling and treatment guidelines.
382. Use the following best practices for the design and implementation of research studies in paediatric populations:
    i. Engage with regulators to explore options for paediatric studies as soon as a given drug shows promising efficacy and safety in Phase IIa adult studies.
    ii. Consider including adolescents when conducting initial adult efficacy trials or conduct parallel trials with the goal of providing information to support licensing for adolescents at or near the same time as adults, when appropriate from a scientific and ethical perspective and allowed by regulations.
    iii. In the design of paediatric PK and safety studies, when appropriate from a scientific and ethical perspective and allowed by regulations, consider studying weight-based dosing and enrolling all children above 4 weeks of age concurrently (i.e., no age de-escalation)
    iv. Assess acceptability and palatability of paediatric formulations, including for use in low-resource settings, at the earliest appropriate stage of the formulation's development.
383. Consider the use of reliance regulatory procedures, including the WHO collaborative Registration Procedure (CRP), for national registration of paediatric TB products.
384. Ensure all drug registration dossiers for paediatrics (including an age-appropriate formulation), meet requirements at the time of filing and that responses to specific queries are complete and provided in a timely manner.
385. Consider providing multilingual paediatric patient information leaflets to facilitate appropriate use by healthcare workers and caregivers.
386. Consider prioritizing registration submission of new TB paediatric products in high burden countries where import waivers cannot be granted.

387. Assuming there are no contraindications to use in pregnancy from pre-clinical studies, Johnson & Johnson supports inclusion of women who become pregnant in clinical trials by allowing them to remain on study drug with consent.

Lupin commits to:

388. Finalize the development of 3-medicine paediatric fixed-dose combination product for treatment of drug-sensitive TB, with an aim of submitting a dossier to WHO PQ and ERP by December 2022.
389. Finalize the development of rifapentine 150mg dispersible tablet for TB preventative treatment with an aim of submitting a dossier to WHO PQ and ERP by May 2023.
390. Finalize the development of a clofazimine 50mg tablet for treatment of drug-resistant TB with an aim of submitting a dossier to WHO PQ and ERP by end of 2023.
391. Finalize development of bedaquiline 20mg dispersible tablet for treatment of drug-resistant TB with an aim of submitting a dossier to WHO PQ and ERP by end of 2024.

Micro Labs commits to:

392. Finalize the development 3-medicine paediatric fixed-dose combination product (RHZ) for treatment of drug-sensitive TB, with an aim of submitting dossier to WHO PQ by Q3 of 2023.

Otsuka commits to:

393. Facilitate access to its child-friendly delamanid formulation in collaboration with the Stop TB Partnership's GDF Paediatric DR-TB Initiative, national TB programmes, and other stakeholders.
394. Finalise technology transfer and continue knowledge sharing that can expediate child-friendly delamanid formulations used to treat DR-TB by generic companies.
395. Initiate and/or support stakeholders and pharmaceutical companies to apply to national drug regulatory authorities for approval of paediatric formulation of delamanid.
396. Expedite development and regulatory submission of paediatric versions of new TB compounds already in the Otsuka R&D pipeline, with an aim to have paediatric versions available shortly after regulatory approval of the adult formulation.
397. Prioritize the development, registration, and commercialization of priority TB products in research and development plans.
398. Make paediatric formulations and data available to research networks and WHO advancing paediatric PK and safety studies.
399. Timely submit data to regulatory authorities and the WHO to facilitate updating of labelling and recommendations.
400. Use the following best practices for the design and implementation of research studies:
    i. Initiate preparation for paediatric studies as soon as a given drug shows promising efficacy and safety in Phase IIb/c adult studies.
    ii. Assess acceptability and palatability of formulations, including for use in low-resource settings, at early stages of the formulation’s development.
401. Develop drug susceptibility testing (DST) and methods in parallel to new molecule development and make pure drug substance available for DST at the same time as the introduction of a new molecule.
402. Explore regulatory options to allow access to TB paediatric formulations in other regions and countries currently without access.

403. Ensure all drug registration dossiers meet requirements at the time of filing and that responses to specific queries are complete and provided in a timely manner.
404. Provide multilingual Patient Information Leaflets or Instructions for Use to facilitate appropriate use by healthcare workers and caregivers.
405. Register new TB paediatric products timely in countries where registration is required and import waivers cannot be granted for procurement (regardless of source of funding).

Sanofi commits to:

406. Continue to support research networks conducting studies to confirm rifapentine dosing in young children, including children living with HIV, guaranteeing supply and availability of the product.

ViiV commits to:

407. Support the study the possible interaction between Dolutegravir and Rifapentine.

Regulatory Authorities

European Medicines Agency commits to:

408. Participate in PADO TB and continue the review of Paediatric Investigation Plans (PIPs) specifically taking into account the following points, always bearing in mind that PIPs are evaluated on a scientific case-by-case basis:
    i. Paediatric formulation development must be considered in an integrated way right from the beginning of the planning process together with the whole paediatric drug development after completion of phase 1 studies in adults, taking into account dose finding and clinical studies.
    ii. Adolescents should be included in adult trials or adolescent trials should be conducted in parallel with adult trials unless scientifically justified.
    iii. Studies of medicines across the paediatric spectrum of ages/weights should be conducted in parallel rather than in a serial age-staggered approach, taking into account for example the pharmacological characteristics of the particular medicinal product, e.g. specific safety or drug disposition factors which may warrant a different approach.
    iv. PIPs for new TB medicines should consider systematic inclusion of children with HIV and other common co-infections found in children, taking into account safety or drug-drug interaction issues.
409. Provide guidance about when clinical trials for efficacy have to be done in children and adolescents and when extrapolation of efficacy based on PK is sufficient.
410. For planned regulatory submissions to provide guidance on pathways for paediatric drug development programmes without reference products and/or TB indication in adults.
411. Continue to work with other non-EU regulatory authorities and WHO to foster alignment on development programmes for prevention and treatment of TB in children and adolescents.
412. Identify specific mechanisms as defined by the legal framework to facilitate access to WHO Prequalified paediatric TB formulations in their countries/regions through specific mechanisms as defined by the legal framework.
413. Continue to offer the opportunity to target countries to participate as observers in the EMA evaluation.

US Food and Drug Administration commits to:

414. Observe the following principles in regulatory review processes:
    i. Extrapolating efficacy from adults to children is acceptable for most children and adolescents with TB. Extrapolation of adult efficacy to paediatric populations for the treatment of pulmonary TB may be appropriate for most paediatric populations, other than the very young as they can have different clinical and pathophysiologic characteristics. Pharmacokinetic (PK) and safety information in paediatric patients will be needed to support the appropriate dose for treatment of children.
    ii. Adolescents with pulmonary TB can be included in phase 3 clinical trials, if appropriate.
    iii. Paediatric patients can be enrolled in trials if sufficient safety and antimycobacterial activity data in adults are available and appropriate dosing regimens have been characterized.
    iv. Studies of drugs across the paediatric spectrum of ages/weights can be conducted in parallel rather than sequentially unless there are specific safety or pharmacokinetic properties that warrant a different approach.
    v. Paediatric development plans for new TB medicines could include children living with HIV and other common co-infections or conditions provided there are no safety or drug-drug interaction issues.
    vi. Cohorts for paediatric studies can be defined based on chronological age or weight-based criteria, particularly for oral drugs.
    vii. Paediatric formulation development should begin soon after adult Phase 2-b trials and dose selection.
415. Continue to work with other regulatory authorities to seek alignment on development of products for TB in children and adolescents.
416. Remain engaged in the development of products and age-appropriate formulations for treatment of TB in children and adolescents.

Partnerships

GAP-f and partners commit to:

417. Provide a platform to support work led by key TB stakeholders in order to accelerate investigation, development, introduction and roll out of paediatric TB priority formulations when needed.
418. Promote coordination and collaboration and, mobilize resources if needed, to cover the full spectrum of activities required to ensure accelerated research, development, registration, commercialization, roll-out, sustainable access to paediatric TB priority formulations.
419. Support the CHEETA Task Force to engage with key stakeholders including donors, researchers, industry partners, regulators to accelerate paediatric clinical trials of TB drugs, including through an innovative platform trial.

Donors

Global Fund to Fund HIV, TB and Malaria commits to:

420. Support the procurement of child-friendly formulations for all TB treatments (DSTB, DRTB and TPT) in line with the Program Essentials promoting short, all oral regimens.
421. Encourage countries to use pool procurement mechanisms, such as GDF, for quality assured paediatric products.

PEPFAR commits to:

422. Through COP, closing the remaining gap in contact investigation and TPT for household contacts and for all children and adolescents living with HIV.

Unitaid commits to:

423. Extend its funding to IMPAACT4TB project to generate evidence on co-administration of rifapentine and dolutegravir among children under the age of five who are exposed to TB.
424. Invest in studying the dosage and safety of rifapentine in HIV-infected and HIV-uninfected children (0-12 years of age) with TB infection.
425. Promote a head-to-head comparison on use of 3HP versus 1HP in HIV-infected and HIV uninfected children
426. Support the rapid adoption of shorter TPT preventive treatment, reducing the price of rifapentine and rolling out 3HP and 1HP in 12 project countries and beyond, and facilitating supplies of 1 HP.
427. Continue to invest through the BENEFIT Kids Project in improved formulations to treat drug-resistant TB including moxifloxacin (MFX), linezolid (LZD), optimization of dosing of drug-resistant TB, and testing the effectiveness of levofloxacin as prevention of MDR-TB in children.
428. Support WHO on the rapid adoption of new shorter all oral regimens for DR-TB using new drugs (i.e., bedaquiline, pretomanid, and delamanid) assuring availability of adaptations and options for children and adolescents.

UN, International Organizations

MEDECINS SANS FRONTIERES commits to:

429. Continue working to overcome the lack of technical solutions to the existing challenges to combat paediatric TB and HIV, through program implementation, community engagement, advocacy and operational research.
430. Support national programmes and local health care workers to gain competence and confidence in managing paediatric HIV and TB patients.
431. Support the scale-up optimized, evidence-based TB-HIV case-finding strategies to ensure strong case-finding and identification, diagnosis and treatment among children in the settings where we are working.
432. Fast-track the implementation of PMTCT, the new WHO Treatment decision algorithms, short regimen for children and adolescents with non-severe TB and prevention of TB in eligible children to save many lives.
433. Support Ministries of Health to scale-up HIV and TB programs including PMTCT, helping overcome barriers to the access of new diagnostic technologies and treatments enabling the implementation of new approaches.
434. Continue working with WHO, Stop TB and other organizations at local, regional and global level; from ensuring the quality-of-care standards, to research, advocacy and policy development and improvements.

Stop TB Partnership's Global Drug Facility commits to:

435. Ensure priority formulations are appropriately communicated to suppliers, including in regular meetings with suppliers, GDF tenders, and at GDF's supplier meetings.

436. Ensure the TB Medicines Dashboard reflects current priority formulations and is updated regularly
437. Identify and implement mechanisms to de-risk suppliers who invest in development of child-friendly formulations.
438. Continuously monitor and project demand for paediatric formulations to identify when the market would benefit from additional suppliers.
439. Lead the external review of the TB section for each Global Fund's Expert Review Panel Expression of Interest (GF ERP EOI) through TPMAT and suggest prioritization of formulations for expedited review.
440. Monitor the development pipeline and work with the Global Fund to expedite access to new formulations and medicines.
441. Lead the TB Procurement and Market-Shaping Action Team (TPMAT) to coordinate global TB stakeholders and develop implementation roadmaps for new formulations.
442. Work to build, stabilize and maintain access to small-volume products including child-friendly formulations for drug-resistant TB.
443. Continue to use the Launchpad Approach to support the introduction and scale-up of paediatric formulations in programmes.
444. Provide technical assistance to support country TB programmes to quantify and forecast child-friendly formulations based on programmatic needs

TB Procurement and Market Shaping Action Team commits to:

445. Assess proposed formulations against the intended use(s), available research results, and the market to ensure the final formulation will fulfil as many intended uses as possible minimizing market and supply chain barriers to introduction and scale-up.
446. Review the TB Medicines Dashboard and facilitate coordination and alignment across all stakeholders contributing lists and guidance documents to the dashboard.

The Union commits to:

447. Continue to support countries to prioritize the identification, diagnosis, and scale-up of TB preventive treatment, including children living with HIV, including via the Union Sub Saharan Africa Centre of Excellence for Child and Adolescent TB as well as in countries where we are working with National TB programmes -keep
448. Support the scale-up of access to priority formulations and diagnostics and to take steps to facilitate their wider roll-out including by performing operational research and ensuring The Union's existing paediatric publications and training tools are up to date and disseminated widely in a number of languages to promote the highest standard of care for all children with or at risk of TB.
449. Advocate for the rights of all children, including those living with HIV, to receive TB care and treatment and promote a human-rights based approach to TB; to urge governments to ensure that all children have access to the latest formulations and models of care for TB prevention and care; and to work together to reduce stigma and discrimination that stops children from accessing care that they need. – keep.

UNAIDS commits to:

450. Support countries to collect and report data on TB-HIV co-infection, TB treatment initiation and outcomes in children living with HIV.

UNICEF commits to:

451. Advocate and support Governments for increased paediatric TB case-finding and access to child-friendly treatment as a core member of the TB Child and Adolescent Working Group and the TB PADO.
452. Support national governments to optimize the integration of TB with child health, HIV, and nutrition services.

WHO (GTB) commits to:

453. Wide dissemination and country support for implementation of the 2022 WHO consolidated guidelines and operational handbook on the management of TB in children and adolescents, in collaboration with the WHO Civil Society Task Force on TB and technical partners.
454. Consider new evidence for possible updating of the WHO guidance on the management of TB in children and adolescents, when it becomes available.
455. In collaboration with Stop TB Partnership/Global Drug Facility (GDF) and the TB Procurement and Market-Shaping Action Team (TPMAT), continue to revise the minimum set of paediatric formulations to guide national procurement and ensure their inclusion in the Essential Medicine List for Children (EMLc).
456. Update the list of priority medicinal products and related research agenda and ensure that the outcome of the prioritization process is communicated in through the WHO PQ Expression of Interest and other relevant fora as soon as dosing is identified.
457. Continue to support countries to collect, and report and use data on children and young adolescents with TB tested for HIV, % of co-infection and access to ART, in collaboration with UNAIDS, UNICEF and other partners, and to publish data in the WHO Global TB Report.
458. Update the 2018 WHO Roadmap towards ending TB in children and adolescents, in collaboration with partners, and consider including maternal and infant TB in the 2023 version.
459. Advocate for data collection on the safety and efficacy of TB preventive treatment and TB treatment during pregnancy and post-partum, to fill research gaps.
460. Facilitate the collection of data on DR-TB in pregnancy and post-partum, linked to infant outcomes as part of the WHO DR-TB Individual Patient Database (IPD).

WHO (PQ) commits to:

461. Ensure that new paediatric formulations are prioritized for WHO PQ review.
462. Promote the use of the WHO Collaborative Registration Procedure based on PQ or SRA approval to expedite national review of paediatric TB drugs and formulations.
463. Expand CRP Light beyond the pilot sites and discuss with USFDA the choice of products.

Implementing Partners, Communities, Civil Society Organizations and Faith Based Organizations

EGPAF commits to:

464. Improve the proportion of children and adolescents living with HIV (CALHIV) initiating and completing TB preventive treatment (TPT) among newly diagnosed CALHIV who access care at EGPAF supported facilities.

465. Improve the proportion of CALHIV that are identified as presumptive TB as well as the proportion finally diagnosed with TB among the CALHIV who access care at EGPAF supported facilities. Improve the linkage to TB treatment initiation among those diagnosed with TB.
466. Develop a paediatric and adolescent TB monitoring and evaluation framework for patient level and programmatic level indicators.
467. At least three public events and/or advocacy products led or co-led by EGPAF in collaborations with other TB stakeholders to sensitize, increase awareness and advocate for childhood TB at the national, regional and global levels in 2023.
468. Provide technical support to National TB Programs for policy change to adopt the new child and adolescents TB guidelines and recommendations released by WHO in 2022.

Global Coalition of TB Advocates commits to:

469. Advocate for accelerated and uninterrupted TPT roll out for children of HHCs through advocacy, community capacity building on TPT and demand generation
470. Advocate for the inclusion of children and pregnant women in TB R&D as members of CABs and CAGs
471. Pursue efforts to end stigma and discrimination associated with TB by supporting partners involved in the TB response and through the development of tools to address stigma

KNCV Tuberculosis Foundation commits to:

472. Work with country stakeholders to develop a platform and mechanism to ensure all commitments turn into action
473. Support countries to develop national strategic plans and Global Fund concept notes that are data driven and addressing the needs of children in the entire patient pathway.
474. Collaborate and coordinate with in-country professional and regulatory bodies to ensure countries are prepared for early uptake of new innovations/medicines and develop a plan for scale up.
475. Produce high quality documentation of our best practices and evidence to share at global platforms to guide global policies and guidelines.
476. Engage with civil society to create sense of urgency at country level to ensure all children needs related to TB/HIV are implemented
477. Support countries in scaling up the stool test with GeneXpert for TB diagnosis in children including development of generic SOP's and training materials.
478. Support countries to self-assess and quantify the programmatic implementation of WHO recommendations on the management of TB in children and adolescents

Catholic Medical Missions Board commits to:

479. Collaboration at all levels and working in communities, schools, and faith and healthcare settings to disseminate messages of Hope for TB and to combat TB-related stigma and discrimination, including among faith leaders.
480. Working to mobilize community leaders and their faith communities in support of efforts to reduce stigma and discrimination efforts via evidence-based education and training.
481. Fostering and actively participating in coordinated and collaborative advocacy at regional and national levels to increase funding for TB research and development and the introduction and scale-up of priority paediatric drugs and formulations; to accelerate regulatory processes for

rapid adoption and uptake of optimal paediatric TB drugs and formulations; and to ensure sustainable access to optimal TB testing and treatment for infants and children.

482. Mobilizing our networks and work with communities, in close collaboration with other stakeholders, to expand access to TB diagnosis and TB treatment initiation (new and retreatment) and adherence among children, adolescents, and families, including among those living in hard-to-reach places and in contexts affected by conflict and crisis. Specifically, we will support health facilities in their catchments, and ensure that assessment and diagnosis of TB among paediatric and adolescent HIV patients is routine and institutionalized. We will also incorporate TB screening and referral into training and task lists assigned to community health workers associated with our HIV projects. Additionally, community health workers in CMMB-supported health facilities' catchments will be trained and empowered to visit households with under-five TB patients to provide health education, do contact screening, and refer those with presumptive TB. CMMB will provide treatment support and assist with finding children who have interrupted TB treatment.
483. Supporting and participating in national efforts to improve and integrate the use and impact of paediatric diagnostics for TB and to develop national strategies to optimize the use of new technologies and interventions.
484. Ensuring that all paediatric and adolescent patients receive TB preventive treatment, with provision of treatment support if necessary for the household.

MINISTRIES OF HEALTH: HIV & TB PREVENTION, DIAGNOSIS and TREATMENT for CHILDREN, PREGNANT, POST-PARTUM AND BREASTFEEDING WOMEN

Cameroon commits to:

485. Take the appropriate actions (such as mobilize resources, identify sites, create capacity, prioritize for EMR set up, analyse, and share data) to support surveillance for birth defects and other birth outcomes in pregnant women living with HIV or at risk of HIV who are receiving antiretroviral drugs periconception and/or during pregnancy. This is particularly needed for TAF, DRV/r and the long-acting ARVs for prevention and treatment, such as CAB LA, where drug exposure can occur even if the drug is stopped up to a year prior to conception.
486. Accelerate transition to more optimal regimens and formulations much as described in 2021 WHO Guidelines and Optimal formulary by:
    i. Enhancing efforts to fully roll out pDTG for 1st and 2nd line so that uptake is completed by Q2 2023
    ii. Actively transition All stable infants and children to DTG-based regimen irrespective of VL availability by Q2 2023
    iii. Securing appropriate quantities of LPVr granules for the small proportion of children who don't tolerate DTG
487. Improve communication and capacity between MOH, Paediatric TWG, supply chain colleagues, and healthcare workers to improve forecasting of Paediatric ARVs and anticipate shortages and stockouts by establishing routine collaboration pathways. A routine communication plan should also be established between facilities to allow for stock to move more readily between facilities in situations of stock out or low stock.
488. Undertake preparatory work to:
    i. Accelerate the introduction of pALD by not overstocking ABC/3TC 120/60 mg and DTG 10 mg.
    ii. Facilitate co-formulated DRV/r introduction and transition from other PI based regimens in children 3 and older.

Kenya

TB and HIV Diagnostics

489. Expand access to appropriate, timely, high quality, cost-effective infant diagnosis, and viral load technologies, as well as urine-based LF-LAM and geneXpert Ultra for TB diagnosis in children, using comprehensive diagnostic mapping and use of all available di gnostic resources, recognizing the significant patient benefits of point-of-care infant diagnosis and ART initiation and optimized diagnostic networks possible when using multiplex, integrated technologies.
490. Introduce a national Essential Diagnostics List that includes HIV and TB diagnostics, particularly point-of-care infant diagnosis and LF-LAM in decentralized non-laboratory settings.
491. Prioritize an optimized strategy of effective, evidence-based case-finding testing approaches to increase demand for testing of children of all ages and improve patient identification, including

HIV testing all children attending malnutrition, TB, and inpatient wards, tracking of mother-infant pairs and opportune testing points, scaling up index testing, etc.

492. Integrate TB screening at all service delivery points and enhance the use of TB diagnostic algorithms to ensure early clinical diagnosis for TB in children hence averting mortality due to TB.
493. Support EMTCT, viral suppression and retention in treatment and care (of pregnant and breastfeeding women and HIV-positive infants and children) through consistent viral load testing and consideration for point-of-care viral load for prioritized populations, including infants and children, pregnant and breastfeeding women.
494. Develop more accurate, transparent, and consolidated forecasts (through data collection and public reporting on diagnostics uptake and implementation) to support manufacturing, improve supply chain management and reagent availability, and support national, regional or global pooled procurement and related activities and to track progress.
495. Support current efforts to transition from outright instrument procurement to all-inclusive bundles or other novel pricing models for centralized and point-of-care platforms to address issues around stock-outs, sample backlog, high cost per test and long turn-around time.
496. Prioritize implementation and documentation of the final diagnosis/outcome after the period of risk for transmission of HIV-exposed infants (at 18 months of age or 3 months' post-cessation of breastfeeding, whichever is later)
497. Implement legal provisions and national programs for post-market surveillance of diagnostic products, including procedures and tools for supplier responsibilities and reporting incidents, adverse events and field safety corrective actions promptly to the national regulator.

TB and HIV Treatment

498. Accelerate the transition to more optimal regimens and formulations much as described in 2021 WHO Guidelines and Optimal formulary by:
    i. Enhancing efforts to fully roll out DTG for 1st and 2nd line.
    ii. Actively transition All stable infants and children with a valid viral load to DTG- based regimen irrespective of VL availability by Q4 2023.
    iii. Securing appropriate quantities of LPVr granules for the small proportion of children who don't tolerate DTG.
    iv. Adoption of the 2022 WHO guidelines on the management of tuberculosis in children and adolescents that includes the use of a shorter regimen four-month treatment regimen for those children with drug-sensitive non-severe TB, and all oral regimen for children with multi-drug-resistant TB with the new molecules, Bedaquline/Delamanid as applicable.
    v. Accelerate scale-up of TB preventive therapy with child-friendly fix d-dose combination medication. This includes lobbying for fast-tracking the child-friendly fixed-dose combination of the weekly rifapentine and lsoniazid.

499. Mobilize resources, plan, and implement a national HIVDR survey on HIV-expose infants to monitor the selection of drug resistance in infants and children by the end of 2 24.
500. Support and contribute to strengthening monitoring of uptake, safety and effectiveness for all Paediatric products for treatment and prevention of HIV and TB in infants and children by

fostering data collection and use as well as by joining global efforts to accelerate safety and effectiveness monitoring.

501. Enhance efforts to implement the STOP AIDS AHD package by optimizing diagnosis and management of severe bacterial infections, malnutrition, and cotrimoxazole (CTX) prophylaxis delivery.
502. To collaborate in fast-tracking registration of ALD and co-formulated DRV/r for children and adolescents where possible (via the WHO Collaborative Registration Procedure and other reliance mechanisms).
503. Develop a last-mile distribution strategy for Pediatric ARVs that includes an early warning system that rapidly addresses supply issues that arise at the facility level (the drug is in the country but not necessarily at all facilities).
504. Improve communication and capacity between MOH, Pediatric TWG, supply chain colleagues, and healthcare workers to improve forecasting of Pediatric ARVs and anticipate shortages and stockouts by establishing routine collaboration pathways. A routine communication plan should also be established between facilities to allow the stock to move more readily between facilities in stock-out or low-stock situations.
505. Establishing unified data systems that allow monitoring (VL/regimen, stocks, number of children by weight and age bands, etc.) by regimen across all country data platforms.
506. Ensure collaboration between Implementing partners and Country Government in putting surveillance systems and cause of death audits in place to allow for targeted mortality prevention efforts.
507. Working with partners to improve CLHIV estimates through innovative data collection methods with household surveys.

Ghana[21] commits, by the end of 2025, to:

Diagnostics

508. Optimize Diagnostic Networks through digitization.
509. Initiating and scaling up stool examination for tuberculosis detection.
510. Supporting current efforts to introduce from outright instrument procurement to all-inclusive bundles, or other novel pricing model for both centralised and point-of-care platforms to address issues around stock-outs, sample back-log, high cost per test and long turn-around time.
511. Introducing a national Essential Diagnostics List that includes HIV and TB diagnostics, particularly point-of-care infant diagnosis and LF-LAM in decentralized non-laboratory settings.

Programme Implementation

512. Enhanced integration of Reproductive and Child health and Nutrition services with TB/HIV services to improve coverage of maternal and paediatric TB/HIV
513. Supporting MTCT, viral suppression and retention in treatment and care (of pregnant and breastfeeding women as well as HIV-positive infants and children) through consistent provision of viral load testing and consideration for point-of-care viral load for prioritized populations (ie. infants and children, pregnant and breastfeeding women).

[21] Cross-cutting for HIV and TB

514. Pre and post services Continuous Medical Education Program on Paediatric TB/HIV twice in a year for clinicians to improve on knowledge.
515. Support and improve on the sample transportation through the enhanced DNO. At the moment POC is at 5%. Ghana commits to 50% by 2025
516. Expand the use of e-learning Platforms to rapidly scale-up the building capacity of service providers in innovative HIV/TB health care delivery services

Data Capture and Transfer

517. Developing more accurate, transparent, and consolidated forecasts (through data collection and public reporting on diagnostics uptake and implementation) to support manufacturing, improve supply chain management, and reagent availability as well as to support national, regional or global pooled procurement and related activities and to track progress.

The Federal Republic of Nigeria[22] commits to:

518. Ending Paediatric AIDS by 2030 by active collaboration with relevant global, regional and in-country stakeholders including communities.
519. Using the Rome Action Plans as the bedrock used to develop other national plans that will help eliminate paediatric AIDS by 2030.
520. Considering Prevention of Mother to Child Transmission of HIV (PMTCT) as a critical area where progress will contribute to ending paediatric AIDS by 2030.
521. Enhancing efforts to fully roll out pDTG for 1st and 2nd line so that uptake is completed by Q2 2023.

[22] The Federal Ministry of Health (FMOH) through National AIDS/STIs Control Program (NASCP) in collaboration with the National Tuberculosis and Leprosy Control Program (NTBLCP) held a consultation meeting to develop a joint Paediatric Action Plan for both TB and HIV in 2021. The Joint Paediatric Action Plan is a five-year plan (2021-2025) with interventions based on identified gaps in paediatric HIV & TB Treatment. The plan, which is still ongoing focuses on the following interventions:

- Scale-up screening and case finding among children and adolescents
- Improve the quality of documentation and reporting
- Capacity building to scale up treatment and diagnostics
- Strengthen the referral system between the peripheral facilities and tertiary/secondary institutions to improve case management of complications and more severe forms of TB in children

To further strengthen this commitment, the FMOH established Paediatric coordination structures at the Sub-National levels geared towards ensuring the sustainability of the HIV response in Nigeria. This further led to the National AIDS/STIs Control Program (NASCP) inaugurating the Paediatric/Adolescents Focal Persons across the 36 States plus the Federal Capital Territory (FCT) with the mandate of closing the gaps in paediatric/adolescent HIV.

Most of the States now have Technical Working Groups (TWGs) solely for:

i. Coordinating paediatric/adolescent activities
ii. Care for infants, children, and adolescents living with HIV and children exposed to HIV
iii. Closing the treatment gap for pregnant and breastfeeding women living with HIV and optimizing continuity of treatment towards eliminating vertical transmission
iv. Preventing and detecting new HIV infections among pregnant & breastfeeding adolescents and women
v. Addressing rights, gender equality and social/structural barriers that may hinder access to services.

522. Actively transition all stable infants and children to DTG-based regimen irrespective of VL availability by Q2 2023.
523. Support and contribute to strengthening monitoring of uptake, safety and effectiveness for all paediatric products for treatment and prevention of HIV in infants and children by fostering data collection and use as well as by joining global efforts to accelerate safety and effectiveness monitoring.

South Africa commits to:

524. Updating the national TB guidelines on the management of TB in children and adolescents in line with the most recent WHO guidance.
525. Improving access to TB diagnostics (mWRDs including Urine LAM and CXR) in particular for children living with HIV as well as treatment decision algorithms to support a clinical diagnosis in children.
526. Promote the use of stool on Expert MTB/RIF or Xpert Ultra.
527. Enhancing reporting and recording on TB by age groups as well as their analysis and use.
528. Establishing a national TB and pregnancy register as many women with MDR-TB are of reproductive age.
529. With support from SAPHRA, promoting the use of shorter TB regimens in children and adolescents and scale up access to child-friendly formulations of second line drugs to treat RR-/MDR-TB.
530. Scale up contact investigation and provision of TPT

United Republic of Tanzania commits to:

Diagnostics

531. Prioritize an optimized strategy of effective, evidence-based case-finding testing approaches to increase demand for testing of children of all ages and improve patient identification, including HIV testing all children attending malnutrition, TB, and inpatient wards, tracking of mother-infant pairs and opportune testing points, scaling up index testing, etc.
532. Support MTCT, viral suppression and retention in treatment and care (of pregnant and breastfeeding women as well as HIV-positive infants and children) through consistent provision of viral load testing and consideration for point-of-care viral load for prioritized populations (ie. infants and children, pregnant and breastfeeding women, etc).
533. Develop more accurate, transparent, and consolidated forecasts (through data collection and public reporting on diagnostics uptake and implementation) to support manufacturing, improve supply chain management, and reagent availability as well as to support national, regional or global pooled procurement and related activities and to track progress.
534. Prioritize implementation and documentation of the final diagnosis / outcome after the period of risk for transmission of HIV-exposed infants (at 18 months of age or 3 months post-cessation of breastfeeding, whichever is later).
535. Implement legal provisions and national programs for post market surveillance of diagnostic products that include procedures and tools for supplier responsibilities and reporting incidents and field safety corrective actions promptly to the national regulator.
536. Increase availability and coverage of point-of-care infant diagnosis and viral load through expansion of devices from 130 to 340 by December 2023.

537. Strengthen sample transportation through modalities whereby Tanzania Postal Transportation will urgently engage PPP modalities and hire private vendors to fast-track sample transportation and reduce the turnaround times.
538. Complete the diagnostic network optimization assessment, including cost analyses, for HIV infant diagnosis, HIV viral load, and tuberculosis.
539. Expand identification of HIV-exposed infants through integration with child immunization and nutrition programs through implementation of a countrywide standard operating procedure for rapid registration.

Treatment

540. Accelerate transition to more optimal regimens and formulations as described in WHO Guidelines and 2018 Optimal formulary by:
    i. Developing transition plans by Q1 2019
    ii. Introducing DTG 50 mg for children above 25 kg by Q2 2019
    iii. Fully phasing out NVP based regimens by Q3 2019 in children older than 3 years and by Q2 2020 in children younger than 3 years.
    iv. Optimizing the use of LPVr solid formulations by prioritizing infants and children that most need them as well as using LPVr tablets as soon as a child can swallow them
    v. Transitioning stable children to optimal regimens as outlined by in the WHO treatment guidelines and in the Optimal Formulary and Limited Use List
541. Increase viral load monitoring of children and ensure linkage of children failing first line drugs to 2nd and 3rd line drugs, working with donors and manufacturers to ensure availability of drugs in line with WHO guidelines.
542. Support MTCT, viral suppression and retention in treatment and care (of pregnant and breastfeeding women as well as HIV-positive infants and children) through consistent provision of viral load testing and consideration for point-of-care viral load for prioritized populations (ie. infants and children, pregnant and breastfeeding women, etc).