UNAIDS PROGRAMME COORDINATING BOARD

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THIRTY-FIFTH MEETING

Date: 9-11 December 2014

Venue: Executive Board room, WHO, Geneva

Agenda item 6

Gap analysis on paediatric HIV treatment, care and support

Additional documents for this item: *none*

Action required at this meeting – the Programme Coordinating Board is invited to:

See decisions in paragraph below:

70. Take note of the report and analysis of gaps in children's access to antiretroviral therapy;

71. Welcome the strategic directions outlined by UNAIDS for closing the paediatric treatment gap and encourage the Joint Programme to initiate implementation of the outlined steps.

Cost implications for decisions: *none*

INTRODUCTION

1. While the last decade has seen remarkable, historic progress in the AIDS response, children are being left further and further behind. The 3.2 million [2.9 – 3.5] children living with HIV are substantially less likely than adults living with HIV to obtain life-saving antiretroviral therapy. Due to gaps in basic commodities and diagnostic technologies as well as serious obstacles to the effective use of the health tools currently available, many children are needlessly dying. In 2013 alone, 190 000 [range = 170 000 – 220 000] children died of AIDS-related causes worldwide.[1]

2. The UNAIDS Programme Coordinating Board has recognized this profound gap in the global AIDS response and is determined to leverage the Joint Programme's influence to reverse it. At its 33rd meeting in December 2013, the Board requested UNAIDS to "prepare a discussion paper and a gap analysis on paediatric HIV treatment, care and support with specific, time-bound targets for getting all children living with HIV on treatment and a strategy on how this would be achieved."

3. Following up on this request, the UNAIDS Secretariat, in collaboration with the Elizabeth Glaser Paediatric AIDS Foundation (EGPAF), UNICEF and WHO, hosted a global consultation on paediatric HIV treatment in Geneva in June 2014 that focused on strategic actions to close the treatment access gap for children. Attendees at the consultation included health ministry representatives from 12 countries, implementers of paediatric HIV treatment programmes, non-governmental organisations and other civil society representatives, United Nations partners, and donor agencies. During the consultation, working groups made extensive recommendations to improve health outcomes for children living with HIV including the initial formulation of new paediatric HIV treatment targets for 2020. In welcoming new targets for children, participants also emphasized the continuing need to test *all* HIV-exposed children and to initiate treatment for *all* HIV-exposed children who are diagnosed with HIV infection.

4. At its 34th Meeting in July 2014, the Programme Coordinating Board called on Member States and the Joint United Nations Programme on HIV/AIDS (Joint Programme / UNAIDS) to pursue '*in line with the common vision of the three zeros a clear commitment in the post-2015 development agenda to ending the AIDS epidemic as a public health threat and an obstacle for overall sustainable development by 2030, provisionally defined as the rapid reduction of new HIV infections, stigma and discrimination experienced by people living with HIV and vulnerable populations and key populations , and AIDS-related deaths by 90% of 2010 levels, through evidence based interventions to include universal access to HIV prevention, treatment, care, and support, such that AIDS no longer represents a major threat to any population or country*'.

5. Since the December meeting of the Programme Coordinating Board, a fast-track initiative has been launched that advocates for a concerted push to close the access gap to HIV treatment and prevention by reaching key populations at higher risk in these countries. So as to realize the UNAIDS Board commitment to ending the AIDS epidemic by 2030, this initiative proposes targets on treatment to be achieved by 2020. Known as '90-90-90', the treatment targets would enable: 90% of people living

[1] UNAIDS 2013 estimates.

with HIV to know their HIV status, 90% of people who know their status to access HIV treatment and 90% of people on HIV treatment to achieve viral suppression by 2020.

6. Also since the December meeting of the Programme Coordinating Board, new data have become available regarding HIV testing and treatment coverage for children. In responding to the request of the 33rd Programme Coordinating Board, the Joint Programme has taken account of the most recent epidemiological estimates regarding children living with HIV, as well as reports from countries through the Global AIDS Response Progress Reporting (GARPR) system and from diverse partners engaged in addressing the HIV testing and treatment needs of children.

7. Building on actions and initiatives presented within the broader context of retargeting the HIV response, this report responds to the Programme Coordinating Board's request at its 33rd meeting, assessing and analysing the paediatric HIV treatment gap; outlining specific, time-bound targets to identify children living with HIV and link them with life-saving treatment services; and describing strategic direction for the way forward to ensure timely and effective implementation of the new targets. After describing these targets, the report outlines the obstacles and challenges that will need to be overcome, emerging new opportunities that will need to be seized and effectively leveraged, and action steps to be taken to rapidly accelerate progress towards ending the AIDS epidemic among children.

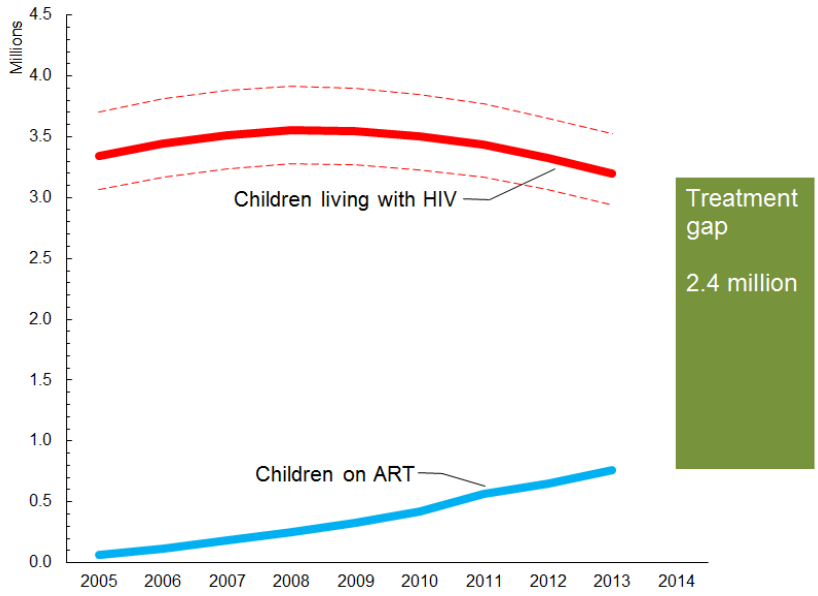
SITUATION ANALYSIS

The paediatric treatment gap: A status report on children living with HIV

8. While 38% [36-40%] of adults living with HIV obtained antiretroviral therapy in 2013, only 24% [22-26%] of children (ages 0-14) living with HIV received HIV treatment.[2] Paediatric treatment coverage is exceptionally low in a number of high-burden countries. In Nigeria, home to the largest estimated number of children living with HIV, only 12% [10-13%] of children living with HIV received antiretroviral therapy in 2013.[3] In the Democratic Republic of Congo, treatment coverage among children was 8% [6-9%] in 2013.[4] A mere one in seven children living with HIV (14% [10-22%]) received antiretroviral therapy in Angola.[1] In 16 countries in sub-Saharan Africa, less than 10% of children living with HIV obtained antiretroviral treatment in 2013.[5]

[2] UNAIDS 2013 estimates.
[3] UNAIDS 2013 estimates.
[4] UNAIDS 2013 estimates.
[5] UNAIDS 2013 estimates.

Treatment gap in children, global



Treatment coverage for children varies among regions. Paediatric treatment coverage in 2013 was 64% [42-84%] in Latin America, 32% [25-35%] in Asia and the Pacific, 24% [20-28%] in the Caribbean, 22% [20-24%] in sub-Saharan Africa, and 11% [8-15%] in North Africa and the Middle East.[6] Within sub-Saharan Africa, HIV treatment coverage for children is generally lower – often substantially so – among countries in West and Central Africa compared to Eastern and Southern Africa.[7]

9. Globally, 3.2 [2.9-3.5] million children under age 15 were living with HIV in 2013.[8] Even with continued success in preventing new infections among children, the number of children requiring HIV treatment will remain substantial. Assuming continued scale-up of services to prevent mother-to-child transmission, a UNAIDS and WHO analysis estimates that in 2020[9], 1.67 million children living with HIV will still need antiretroviral therapy in the 21 priority countries of the *Global Plan towards the elimination of new infections among children by 2015 and keeping their mothers alive* (Global Plan).

[6] UNAIDS 2013 estimates.
[7] UNAIDS 2013 estimates.
[8] UNAIDS 2013 estimates.
[9] WHO, March 2014 Supplement to the 2013 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treatment Preventing HIV Infection. Geneva: WHO, 2014.

10. Persistent treatment gaps have immediate life-or-death consequences for children with early perinatal-acquired infection. Half of all children living with HIV will die by age two without antiretroviral therapy, with peak mortality occurring at 6-8 weeks, highlighting the urgent need to diagnose children at or as soon as possible after birth and to initiate appropriate therapy.[10] [11] Initiating HIV treatment within 12 weeks of birth reduces children's HIV-related child mortality by 75%.[12] Due to the failure to adequately address paediatric HIV treatment needs, the rate of decline in AIDS-related deaths among children is much smaller than the drop in new HIV infections among children. Children, who represent 9% of all people living with HIV, accounted for almost 13% of AIDS-related deaths in 2013.

Reasons why the paediatric treatment gap exists

11. Children's disadvantage in accessing life-saving treatment stems from a series of programmatic gaps and shortcomings, extending across each stage of the paediatric treatment continuum.

Barriers to timely diagnosis of HIV in children

12. As children born to mothers living with HIV carry maternal HIV antibodies for up to 18 months, more sophisticated tests that identify the presence of viral DNA or RNA are required to diagnose HIV in very young children. As such testing primarily relies on centralized laboratories, health settings typically use dried blood spots, which are then transferred to laboratories for analysis.

13. HIV testing needs to occur soon after infants of women living with HIV are born, as peak mortality for infants living with HIV occurs at 6-8 weeks.[13] Testing should be repeated throughout the breastfeeding period, when the risk of HIV transmission is still substantial. WHO recommends virological testing at 4-6 weeks or at the earliest opportunity thereafter[14], noting that the algorithms for infant testing are currently being reviewed.

14. In 2013, however, only 42% of HIV-exposed infants received early infant diagnostic services within the first two months of life.[15] Compounding this problem, children who are missed by normal testing procedures are often never offered subsequent opportunities for testing, even though children in low- and middle-income countries frequently access a broad array of health, educational and social services. HIV testing is not routinely offered to children who access child-focused services (e.g., immunization, nutrition, in-wards, social protection). Consequently, children who

[10] Penazzato M et al. Optimization of antiretroviral therapy in HIV-infected children under 3 years of age: a systematic review. AIDS, 2014, 28(Supp. 2):S137-S146.
[11] Newell ML et al. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. Lancet, 2004, 364:1236–43.
[12] Cotton MR et al., Early time-limited antiretroviral therapy versus deferred therapy in South African infants infected with HIV : results from the children with HIV early antiretroviral (CHER) randomised trial, Lancet, 2013, 382 :1555-1563.
[13] Bourne DE et al. Emergence of a peak in early infant mortality due to HIV/AIDS in South Africa. AIDS, 2009, 23:101–6.
[14] WHO, Diagnosis of HIV infection in infants and children: WHO recommendations. Geneva: WHO, 2010.
[15] WHO, Global update on the health sector response to HIV. Geneva: WHO, 2014.

have breastfed often do not receive a conclusive HIV test after breastfeeding has stopped.

15. Although development of the dried blood spot specimen collection technique for early infant diagnosis represented a transformative step forward in addressing the diagnostic needs of young children living with HIV, the necessary reliance on centralized laboratories for virological testing is associated with increased transport costs, substantial turnaround time for results and other challenges. Multi-country studies indicate that up to 51% of infants who test positive on these specialized tests never receive their test results.[16]

16. Although the testing gap for children is considerable, there are some encouraging trends on which to build. Since 2007, the number of facilities collecting specimens for early infant diagnosis worldwide has risen from 200 to more than 10 000. In 2013, more than 1 million early infant diagnostic tests were performed in low- and middle-income countries.[17] Prices for early infant diagnostic technologies have fallen, and a highly fragmented market has been consolidated into a limited number of bundled products.

17. Among the most promising developments with respect to early infant diagnosis is the emergence of an active pipeline of new diagnostic tools with the potential to overcome some of the challenges associated with the current laboratory-based DNA tests. One viral load test that can be performed at the point of care is already on the market, although it has not been prequalified by WHO, and several additional point-of-care viral load tests are likely to become available in the next two years.[18] Three point-of-care tests specifically for early infant diagnosis are in development, including two that will enter the market in the coming months.[19] Such point-of-care technologies could potentially obviate the need to send dried blood spot specimens for remote testing at centralized labs, largely eliminating turnaround times and helping minimize early loss to follow-up. Ultimately, a mix of centralized laboratories and point-of-care tools is likely to be needed to ensure timely diagnosis of children living with HIV diverse resource-limited settings.

Service delivery challenges

18. Substantial delays occur in linking children diagnosed with HIV infection to treatment and care services.[20] [21] [22] [23] A study in Botswana found that median time from birth until initiation of HIV treatment was 23 weeks – substantially beyond the period of

[16] Chatterjee A et al., Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programmes in four countries, BMC Pub Health, 2011, 11:553.
[17] Katz. Scaling up infant diagnosis: market-related challenges and enabling linkage to care. UNITAID HIV Market Forum, April 2014.
[18] Katz, 2014.
[19] Katz, 2014.
[20] Chamla D et al. Evidence from the field: missed opportunities for identifying and linking HIV-infected children for early initiation of ART. AIDS, 2013, 27(Supp. 2):S139-S146.
[21] Anaky MF et al. Scaling up antiretroviral therapy for HIV-infected children in Cote d'Ivoire: determinants of survival and loss to programme. Bull World Health Organ. 2010, 88:490–9.
[22] Phelps BR et al.. Linkage, initiation and retention of children in the antiretroviral therapy cascade: an overview, AIDS. 2013, Suppl 2:S207-13.
[23] Fenner L et al. Early mortality and loss to follow-up in HIV-infected children starting antiretroviral therapy in Southern Africa, J Acquir Immune Defic Syndr, 2010, 54:524–32.

peak mortality – with an average three-week interval between receipt of test results and treatment initiation; of 79 children in the study who died, 56 died before receiving HIV treatment.[24]

19. Numerous service delivery factors contribute to poor outcomes for children living with HIV. Many health care workers are reluctant to recommend HIV testing or referral to care for children, due in many cases to lack of knowledge regarding the importance of early infant diagnosis and treatment initiation for children or fears that antiretroviral administration for children is especially complex.[25]

20. Although data from Malawi, Uganda and Zimbabwe indicate that stockouts of antiretroviral medicines occur more frequently for paediatric formulations than for adult medicines[26], steps are being taken to prevent stockouts of paediatric antiretroviral medicines from occurring. The Global Fund has assumed leadership of the Paediatric ARV Procurement Working Group and Procurement Consortium, managing a project initiated by the Clinton Health Access Initiative (CHAI) with UNITAID funding. The consortium, which involves leading partners, officially endorses the updated paediatric formulary approved by the Inter-Agency Task Team on the Prevention and Treatment of HIV Infection in Women, Mothers and Children in order to streamline access to medicines. The consortium also undertakes multi-partner demand forecasting the results of which are shared with suppliers, and orders among more than 50 countries are coordinated, helping ensure that low-volume orders can be addressed in a timely manner. With UNITAID support, CHAI is implementing a programme to support countries in commodity procurement and uptake and to coordinate with manufacturers to maximize the reliability of supply.

21. To be effective, treatment services for children need to be comprehensive and integrated. Children living with HIV often live in communities with limited access to essential health services. Even with access to HIV diagnostic testing and antiretroviral therapy, many children living with HIV are at risk of common infectious diseases such as pneumonia, diarrhea, malaria and measles, as well as malnutrition and failure to thrive. [27] Improving health outcomes for children living with HIV requires provision of a basic package of effective interventions for prevention and treatment of common conditions – immunizations, screening and management of under-nutrition, malaria prevention with insecticide treated nets, and access to basic treatment for pneumonia, diarrhea and malaria. Children have several contacts with the health system through different service delivery points, and identifying points of convergence for integrated HIV and child survival services are required to accelerate and sustain actions to improve overall health outcomes for children.

[24] Motswere-Chira C et al. Follow-up of infants diagnosed with HIV – Early Infant Diagnosis Program, Francistown, Botswana, 2005-2012. MMWR, 2014, 63:158-160.
[25] Phelps BR et al., 2013.
[26] Gibb D, Streamlining investments in clinical trials regulatory pathways, UNITAID HIV Market Forum, April 2014.
[27] WHO. Global Health Observatory (http://www.who.int.gho.child_health/en/index.html)

Inadequate spectrum of antiretroviral medicines for children

22. Due to differences in medicine delivery needs, changing medicine metabolism and difficulties swallowing pills, children require medicine formulations that differ from those prescribed for adults. For children living with HIV, WHO recommends different regimens depending on the child's age, with protease-based first-line regimens recommended for children under age three.

Children and the 2013 WHO guidelines

WHO's 2013 consolidated antiretroviral guidelines call for immediate initiation of HIV treatment among children under age five, regardless of CD4 count or clinical staging. Among children under age three, the 2013 guidelines recommend more potent regimens (specifically, regimens including ritonavir-boosted lopinavir). The 2013 guidelines call for increased use of viral load monitoring. With respect to service delivery, WHO recommends task-shifting, service decentralization and service integration.

23. However, initial clinical trials for new antiretroviral medicines almost invariably focus exclusively on adults, with children and pregnant women typically excluded. This practice results in substantial delays in the availability of paediatric formulations, as lengthy and costly follow-up studies are required to validate the safety and effectiveness for children of medicines that have proven effective for treatment of HIV in adults. As of mid-2014, only 12 of the 29 antiretroviral medicines approved for use in adults had also been approved for children.[28] Currently, the only protease-based regimen available for use in young children, ritonavir-boosted lopinavir, is accessible as a syrup that tastes unpleasant, is not approved for use at birth, and requires refrigeration down to the point of delivery. Neither of two extremely promising new antiretrovirals – dolutegravir and TAF (a pro-medicine of tenofovir) – has been validated for use in children.[29] For young children who do not respond to recommended protease inhibitor based first-line regimens, second-line options are limited. The lack of fixed dose combinations increases medication burdens, which in turn reduces adherence; currently, there is only one single-tablet first-line regimen for children, although no single-tablet formulation exists for WHO's preferred regimens.[30] There are also interactions between antiretrovirals and treatments for other diseases in children, most notably tuberculosis.

24. Other factors contribute to the sub-optimal array of antiretroviral medicines for children. For example, regulatory pathways are more complicated for paediatric medicines than for those intended for adults.[31] In addition, despite modelling by UNAIDS and WHO that confirm the existence of a substantial market for paediatric HIV treatment well into the future, some companies appear to be sceptical that a robust market will be available for new antiretroviral medicines, highlighting the need for focused advocacy targeting the private sector.[3] Paediatric medicines account for a mere 7% of the global antiretroviral market, with virtually no demand for paediatric antiretrovirals in high-income countries.[32]

[28] UNITAID, HIV medicines technology and market landscape, 2014.
[29] UNITAID, HIV medicines technology and market landscape, 2014.
[30] UNITAID, HIV medicines technology and market landscape, 2014.
[31] UNITAID, HIV medicines technology and market landscape, 2014.
[32] UNITAID, HIV medicines technology and market landscape, 2014.

25. Prices available in low- and middle-income for paediatric antiretrovirals (US$ 230 per patient per year) remain higher than those for adults (US$ 177), and while paediatric prices have declined, the fall has been much more modest than for adult medicines.[33] Efforts to lower the costs of paediatric HIV treatment regimens will need to be combined with additional funding to support expedited treatment scale-up for children. Many low- and middle-income countries have shown important leadership in increasing domestic outlays for HIV activities[34] but ensuring the long-term sustainability of treatment programmes for children may require exploration of innovative financing models, such as advance market commitments or innovative use of equity markets.[35]

26. While the number of child-friendly treatment options remains inadequate, the array of options has increased. Progress has also been made in streamlining and simplifying global WHO guidance on recommended regimens and treatment approaches for children.[8] In 2013, the IATT updated lists of optimal and limited-use products to include both preferred and alternative medicines recommended in the WHO's 2013 Consolidated Guidelines. A total of 10 optimal formulations for paediatric treatment were selected as recommended products for implementing partners and procurement and supply chain managers to consider in order to deliver optimal care and to stabilize the market sector by consolidating procurements around a small number of key products.

27. At least 10 paediatric HIV medicines from multiple antiretroviral classes are currently in development.[36] All but one are granules, dispersible tablets or powders, which may aid in overcoming some of the difficulties currently associated with administration of HIV treatment in children.[37] The Paediatric ARV Drug Optimization (PADO-1), convened by WHO in 2013, has established a list of key medicines and formulations that should be prioritized by manufacturers in the mid- and long-term. Among others, dolutegravir and TAF have generated significant interest due to their potential for constructing an antiretroviral regimen that can be used from childhood through adulthood.[25] As a result of this consultation, WHO has also outlined key characteristics for the target product profiles (TPPs) and designed a roadmap of actions to be taken to increase access and uptake of paediatric medicines and formulations.[2]

28. As efforts to optimize paediatric HIV treatment bear fruit, countries will need to move swiftly to implement changes in international treatment recommendations. Experience to date suggests considerable room for improvement in this regard, as there is often a considerable lag between the issuance of global recommendations and their uptake at country level. As of July 2014, only nine countries had aligned their national treatment guidelines with WHO's 2013 recommendation for immediate treatment initiation, regardless of CD4 count or clinical staging, for children under five, compared to 41 countries for pregnant women living with HIV, 30 for HIV-

[33] UNITAID, HIV medicines technology and market landscape, 2014.
[34] UNAIDS, Global report on the AIDS epidemic, Geneva: UNAIDS, 2013.
[35] WHO, March 2014 Supplement to the 2013 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. Geneva: WHO, 2014.
[36] UNITAID, HIV medicines technology and market landscape, 2014.
[37] UNITAID, HIV medicines technology and market landscape, 2014.

positive partners in serodiscordant couples, and more than 50 for people with HIV-related tuberculosis or hepatitis B.[38] In addition, an increasing number of countries are moving beyond the WHO treatment guidelines and offer immediate treatment upon diagnosis (test and treat) for all children below 10 years of age such as in Kenya and for all children below 15 years such as in Namibia, Uganda and Zambia.[39]

29. The shortage of age-disaggregated data, also contributes to less-than-optimal service delivery for children. Improving data collection and ensuring data quality is critical to inform medicine forecasting and programme planning. Rapid scale-up of recently revised monitoring and evaluation tools will be needed to enable collection of age-disaggregated data.

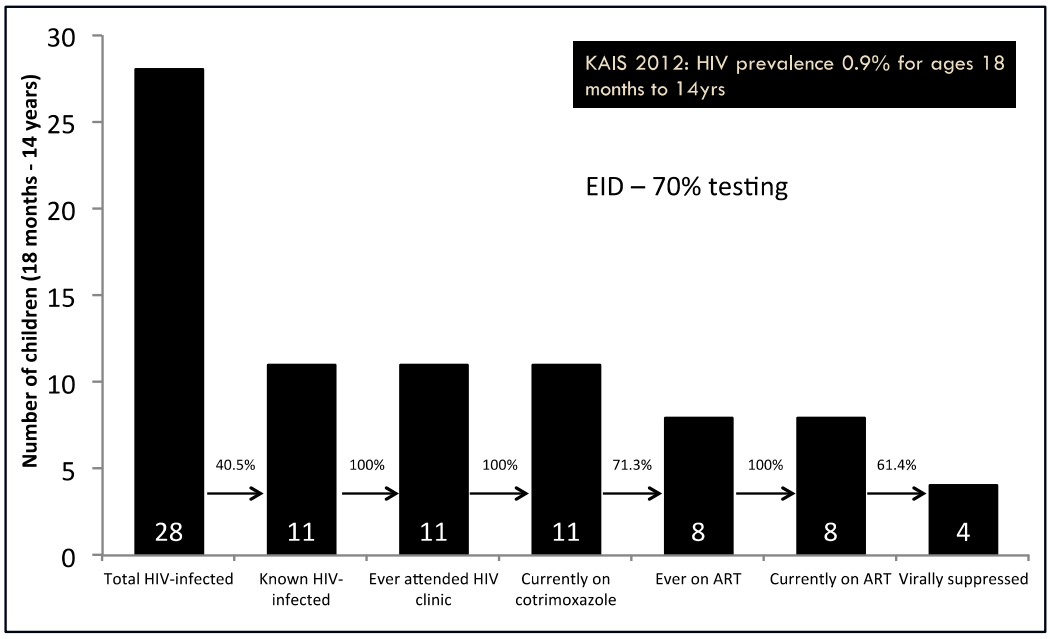
Discontinuity of care for children living with HIV

30. In a pooled analysis of results from 16 paediatric HIV treatment programmes in sub-Saharan Africa, substantial loss to follow-up was found.[40] According to a study involving 17 000 children receiving antiretroviral therapy in four African countries, 51% of children who were enrolled in HIV treatment before their first birthday were lost to follow-up within 24 months.[41]

31. Losses across the paediatric HIV treatment continuum greatly worsen health outcomes for children living with HIV. Kenya, for example, estimates that only 14% of children living with HIV are virally suppressed as a result of gaps in the continuum of care.[42] In particular, substantial loss to follow-up appears to occur for children who are not referred for care at the centre where they received their positive test result.[43] Among individuals receiving antiretroviral therapy in Kenya, rates of viral suppression are notably lower for children (60-70%) than for adults (90%).[44]

[38] UNAIDS analysis, unpublished.
[39] Somya Gupta, Brian Williams & Julio Montaner, Realizing the Potential of Treatment as Prevention: Global ART Policy and Treatment Coverage, 2014
[40] Leroy V et al. Outcomes of antiretroviral therapy in children in Asia and Africa: A comparative analysis of the IeDEA Pediatric Multiregional Collaboration. J Acquir Immune Defic Sydr, 2013, 62:208-219.
[41] McNairy ML et al. Identifying optimal models of HIV care and treatment in Sub-Saharan Africa Consortium. Retention of HIV-infected children on antiretroviral treatment in HIV care and treatment programs in Kenya, Mozambique, Rwanda, and Tanzania. J Acquir Immune Defic Syndr, 2013, 62:e70-e81.
[42] Mukui I, Presentation at Global Paediatric HIV Treatment Consultation, Geneva, 10 July 2014.
[43] Mukui I, 2014.
[44] Mukui I, 2014.

Cascade of the Care of HIV infected Children in Kenya



Poorly run clinics also contribute to loss to follow-up, with sub-optimal retention of children living with HIV associated with various clinic characteristics, including long wait times, understaffing and loss of early infant diagnostic tests results.[45] The lack of standardized, well-developed patient information systems – compounded by the fact that mothers and their infants may commonly be followed through separate register systems, rather than as a mother-baby pair – also contributes to high rates of loss to follow-up among HIV-exposed children.

The persistence of stigma and discrimination:
An overarching barrier to favourable health outcomes for children living with HIV

The persistent stigma associated with HIV deters timely and robust utilization of paediatric HIV treatment services. In one study of children living with HIV who were lost to follow-up, 30% of caregivers cited fear of disapproval among families or communities as the reason their children were no longer engaged in care.[46] In addition, stigmatizing attitudes among health care providers may deter mothers from enrolling their children in HIV treatment programmes.[47]

[45] Phelps BR et al., 2013.
[46] Cohen D et al. HIV testing coverage family members of adult antiretroviral therapy patients in Malawi. AIDS Care, 2010, 22:1346-1349.
[47] Tolle MA et al. Delivering paediatric HIV care in resource-limited settings: cost considerations in an expanded response. AIDS, 2013, 27(Supp. 2):S179-S186.

Experience indicates that adherence rates for children are strongly related to the motivation and attitudes of their adult caretakers. A mother who hides her own HIV status due to fear of discrimination is less likely to enrol her child in HIV treatment services. Efforts to mitigate HIV-related stigma among adults have an important role to play in improving treatment outcomes for children living with HIV.

Older children and adolescents face similar types of discrimination, compounded by elements of self-stigma and peer pressure.[48] Caregivers of adolescents living with HIV may perpetuate and reinforce stigma as a result of their own attitudes or their perception of what others think.[49]

Programmatic responses to close the paediatric treatment gap

32. The persistence and severity of the treatment gap for children living with HIV have prompted increased programmatic attention on strategies to close the gap and improve paediatric treatment outcomes.

Initiatives to improve health outcomes for children living with HIV

33. There are signs that the historic under-prioritization of children's HIV treatment needs may be ending, as a number of high-profile initiatives have emerged to close treatment gaps for children. As previously noted, WHO is leading global efforts to develop treatment recommendations and to optimize treatment options through the PADO work as well as the Paediatric ARV working Group (PAWG). CHAI, DNDi and MPP are collaborating with UNITAID to accelerate the development of paediatric antiretroviral formulations, while the Global Fund has assumed leadership of collaborative procurement efforts for paediatric antiretroviral medicines. In 2013, 66 countries order paediatric antiretroviral medicines through the Paediatric ARV Procurement Working Group.

34. In addition, in 2014, the US President's Emergency Plan for AIDS Relief (PEPFAR) partnered with the Children's Investment Fund Foundation (CIFF) to launch the *Accelerating Children's HIV/AIDS Treatment (ACT)* initiative. ACT is a US$200 million initiative that aims to double the number of children receiving antiretroviral therapy over two years in African countries. The new initiative represents an important shot of new energy into efforts to accelerate scale-up of paediatric HIV treatment.

35. Jointly launched by UNICEF, WHO and EGPAF, the Double Dividend initiative aims to better align paediatric HIV treatment with maternal, neonatal and child health (MNCH). Through an evidence-based approach, the Double Dividend seeks to encourage 'smart' joint investments that generate synergies and improve child survival.

[48] UNAIDS. Coalition for action: No adolescent living with HIV left behind, 2014.
[49] Washington CH, Oberdorfer P. Perceived and experienced stigma and discrimination among caregivers of perinatally HIV-infected adolescents in Thailand. J Therapy and Management of HIV Infection, 2013, 1:63-68.

36. In July 2014, the UNAIDS Secretariat joined with CHAI, WHO, the African Society of Laboratory Medicine, UNICEF and PEPFAR to launch the global Diagnostics Access Initiative. A key focus of the initiative is to support the development of new, affordable diagnostic tools for infants and to galvanize more effective use of existing diagnostic tools. The initiative will advocate for greater funding for laboratory services, the development of new diagnostic tools and well-coordinated partnerships to close diagnostics access gaps.

37. UNITAID continues to play a pivotal role in expanding diagnostic and treatment access for children living with HIV. In 2006-2014, UNITAID supported efforts by the Clinton Health Access Initiative to provide more than 2 million early infant diagnostic tests and antiretroviral treatment for 467 319 children living with HIV. In May 2014, the UNITAID Board considered a number of paediatric-focused recommendations from participants at the first-ever UNITAID HIV Market Forum, including focused financial support to nest pharmacokinetic and acceptability data for children in clinical trials in order to accelerate availability to breakthrough medicines for use in children.

38. In 2010, DNDi entered the paediatric HIV treatment field. DNDi aims to develop two solid fixed dose combinations based on ritonavir-boosted lopinavir, as well as a granule for ritonavir to be used in the treatment of children who are also receiving TB treatment.[50] DNDi has developed a target product profile for first-line antiretroviral therapy for young children, aiming to generate a product that has no taste, is simple to use, combines four products in a single granule formulation, requires no cold chain and is affordable.[51]

39. WHO is leading global efforts to optimize antiretroviral therapy for children, particularly by setting mid-term and long-term priorities for key products to be developed, including more potent second-line regimens for young children.[28] The treatment optimization strategies being promoted also aim to improve medicine sequencing for children, prioritizing optimally potent and tolerable regimens to prolong the duration of first-line treatment .[28] The increasing prominence of patent-sharing arrangements (such as the voluntary licenses of the Medicines Patents Pool) is cause for optimism that improved medicines that are developed in future years will be affordable and accessible for resource-limited settings. For this reason, WHO is also working closely with the MPP to develop antiretroviral forecasts for the emerging markets of potential new adult and paediatric treatment regimens through 2020. In this regards, WHO and the UNAIDS Reference Group are actively collaborating in revising the Spectrum model and produce more accurate estimates for the future burden of HIV among children, in order to characterise the need for paediatric antiretroviral medicines and contribute to establishing the market size for paediatric products.

40. DNDi, MPP, CHAI and UNITAID are also joining together under the umbrella of the Paediatric HIV Treatment Initiative (PHTI) to implement WHO recommendations for priority products and to address the factors that impede development of paediatric antiretroviral medicines and slow uptake of new products that emerge. In particular, the four organizations are working to identify interventions relevant to overcome intellectual property barriers and to shape a robust, sustainable market for paediatric

[50] http://www.dndi.org/diseases-projects/portfolio.html.
[51] http://www.dndi.org/diseases-projects/diseases/paediatric-hiv/target-product-profile.html.

HIV medicines.[52] This initiative will follow up on dosing recommendations identified by the PAWG, an expert advisory group convened by WHO to assist in discussing pharmacokinetics and dosing issues, and has developed a pathway to ensure access to affordable paediatric medicines, identifying key roles and synergies between multiple actors. Addressing part of this pathway, MPP has already concluded licensing agreements with ViiV Healthcare, Bristol-Myers Squibb and Gilead to facilitate access to affordable paediatric HIV medicines in low- and middle-income countries, and as of June 2014 was in negotiations with Merck and AbbVie.[53]

41. The Global Steering Group of the *Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive* provides umbrella leadership and coordination to efforts to implement the Global Plan by 2015, greatly reducing the number of new pediatric HIV infections. Co-chaired by UNAIDS Executive Director Michel Sidibé and United States Global AIDS Coordinator Ambassador Deborah Birx, the Global Plan covers the 22 countries with the highest burden of pediatric AIDS[54]. In addition to its focus on actions to eliminate new HIV infections in children, the Global Plan has a core target of ensuring that 100% of children under the age of five receive treatment and that mothers are provided treatment for their own health and that of their children.

42. As a partner in the Global Plan, the Inter-Agency Task Team (IATT) on the Prevention and Treatment of HIV Infection in Pregnant Women, Mothers and Children has played an important role in harmonizing and improving treatment for children living with HIV, taking steps in 2013 to reduce the paediatric HIV medicine formulary to focus on the 10 most effective regimens. In addition, the IATT has disseminated strategic information through a special supplement on *AIDS* devoted to paediatric HIV treatment issues and has developed toolkits for the adaptation and implementation of WHO paediatric treatment guidelines.[55] The IATT develops guidance and advances advocacy towards ending new HIV infections among children and promoting treatment for those who acquire HIV. Working collectively as a group makes the IATT more effective than any one partner alone. With member presence at both global and country levels, joint technical missions are undertaken at the request of countries, and additionally, the IATT has focal points in each of the priority countries for in-country technical support.

Programmatic innovation to improve health outcomes for children living with HIV

43. Although the global picture for children living with HIV is dire, political leadership and programmatic innovation are helping to close paediatric treatment gaps in a number of countries.

[52] http://unitaid.org/en/resources/press-centre/releases/1356-paediatric-hiv-treatment-initiative-phti-to-spur-innovation-and-access-to-improve-the-lives-of-children-living-with-hiv.
[53] http://www.medicinespatentpool.org/current-licences/
[54] Angola, Botswana, Burundi, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, India, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Uganda, United Republic of Tanzania, Swaziland, Zambia and Zimbabwe.
[55] http://www.emtct-iatt.org/toolkit/.

44. Among the 21 priority countries of the Global Plan, Botswana strongly emphasizes the pivotal importance of political leadership. Among the first countries in the world to commit to bring HIV treatment to all who need it, Botswana was one of the first countries to implement early infant diagnosis through dried blood spots.[56] In 2013, 84% of all children living with HIV in Botswana received HIV treatment, the highest paediatric coverage of any priority country.[1] (As previously described, some programmes in Botswana struggle with timely initiation of HIV treatment for children diagnosed with HIV[15], underscoring that even countries with robust political support experience service delivery challenges that will need to be addressed to achieve the new treatment targets and goals.) Namibia and Swaziland, while reaching slightly less than half of all children living with HIV with antiretroviral treatment (45% and 46%, respectively), are both approaching parity in coverage between adults and children, while in South Africa HIV treatment coverage among children (44%) actually exceeded treatment coverage for adults (42%) in 2013.[57] South Africa's Strategic Plan for 2012-2016 established a national target of ensuring that 90% of all children living with HIV receive sustained antiretroviral therapy.[58]

45. Countries are innovating to improve case-finding among HIV-exposed children. Using a district by district approach, South Africa is ramping up efforts to implement provider-initiated testing and counseling at all points where children encounter the health system.[59]

46. Countries are also using innovative approaches to strengthen linkage to care and reduce loss to follow-up among children living with HIV. In Kenya, health facilities are incorporating mothers living with HIV, providing a monthly stipend to support their efforts to increase retention in care and treatment adherence.[60] To improve linkage to care, Kenya has strengthened integration of early infant diagnosis and maternal, newborn and child care and moved child services to places where HIV testing occurs.[61] Increased emphasis is being placed on caregiver education and support and on decentralization of paediatric treatment services. Kenya is also exploring steps to improve tracking systems, using such strategies as electronic medical records and use of mobile communications technology.[62]

47. Recognizing the need to expedite scale-up of paediatric HIV treatment, Mildmay, a non-governmental organization in Uganda, implemented a family-centred model of comprehensive, multi-disciplinary care in 10 health facilities and 10 community clinics.

48. In the 84 months after roll-out of the family-centred model, there was a 50-fold rise in family enrolment in care, a 40-fold increase in enrolment in paediatric HIV treatment,

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[56] Creek T et al. Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission. Pediat Infect Dis, 2008, 27:22-26.
[57] UNAIDS 2013 estimates.
[58] Abdullah F, Presentation at Global Paediatric HIV Treatment Consultation, Geneva, 10 July 2014.
[59] Abdullah F, 2014.
[60] Mukui I, 2014.
[61] Mukui I, 2014.
[62] Mukui I, 2014.

and universal access to paediatric cotrimoxazole prophylaxis.[63] Key programme attributes that appear to have contributed to its success include provision of incentives for care-seeking, integrated service delivery, task-shifting to enhance the use of nurses, creation of child-friendly service environments, and minimizing missed paediatric testing opportunities by mainstreaming early infant diagnosis and provider-initiated testing and counselling.

49. In an effort to expand the array of facilities where children may receive HIV treatment, a number of priority countries have worked to decentralize paediatric treatment delivery. In, concerted efforts to decentralize paediatric HIV treatment to primary health facilities have been undertaken. In 2008-2010, the number of primary health facilities delivering paediatric HIV treatment more than trebled. Experience in five such countries (Kenya, Lesotho, Mozambique, Rwanda and the United Republic of Tanzania) indicates that loss of HIV-infected children to follow-up was found to be 45% lower in these primary health facilities than at secondary and tertiary facilities. Children living with HIV treated at primary health facilities were 34% less likely to die than HIV-infected children treated at secondary and tertiary facilities.[64]

A NEW TREATMENT TARGET TO HELP END THE PAEDIATRIC HIV EPIDEMIC

50. Powerful momentum is now building towards a new narrative on HIV treatment and the ambitious target of providing:

- By 2020, 90% of all people living with HIV know their HIV status.
- By 2020, 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy.
- By 2020, 90% of all people receiving antiretroviral therapy will have viral suppression.

51. With unanimous support provided by attendees at the global paediatric treatment consultation, UNAIDS has embraced the above three-part target for all children living with HIV (0-14 years of age). This target also encompasses and reaffirms the goal of the *Global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive* (Global Plan) to reach 100% of all HIV-exposed children with HIV testing and treatment, with intensified testing recommended for older children who may be missed through services for the prevention of mother-to-child transmission.[65] *Every* child born to a woman living with HIV has the right to timely diagnostic testing and, if infected, immediate HIV treatment, in accordance with the WHO 2013 consolidated antiretroviral guidelines, which recommend immediate initiation of HIV treatment for all children under five years who are living with HIV.

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[63] Luyirika E et al. Scaling up paediatric HIV care with an integrated, family-centred approach: an observational case study from Uganda. PLoS ONE, 2013, 8:e69548.
[64] Fayorsey RN et al. Decentralization of paediatric HIV care and treatment in five sub-Saharan African countries. J Acquir Immune Defic Syndr. 2013, 62:e124-e130.
[65] UNAIDS, Global plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive. Geneva: UNAIDS, 2011.

TREATMENT STRATEGY TO HELP END THE PAEDIATRIC AIDS EPIDEMIC

52. Launch of the new 90-90-90 target for children reflects new global commitment and resolve to close treatment access gaps for all children living with HIV. However, achieving these targets will require intensified action to close access gaps, innovation to improve diagnostic and treatment programmes and the rapid scale-up of transformative new tools as they emerge.

Build leadership for children living with HIV

53. Advocacy for children's HIV treatment needs should build on existing mechanisms and coordinating bodies. With specific focus on priority countries, the Joint Programme will work with key decision-makers to generate broad political support for prioritized efforts to close children's treatment access gap. Towards the goal of ending the paediatric AIDS epidemic, UNAIDS will work to maximize coordination among partners and stakeholders working on HIV treatment issues for children.

54. Strategic action is needed to enhance public-private and community partnerships to support the scale-up of high-quality HIV treatment programmes for children. Participants in the global consultation recommended that children be considered a key population in the AIDS response. Particular attention is required to fully integrate paediatric HIV treatment within global and country-level maternal, newborn and child health programmes and initiatives, including inclusion of paediatric HIV in professional training mechanisms.

55. To implement this vision, one or more focused meetings will be held to develop public-private and community partnerships to support treatment scale-up for children. The Joint Programme and partners will encourage countries to adopt the 2013 WHO recommendations regarding HIV treatment for children.

Urge national target setting

56. UNAIDS will intensify its work with countries to develop clear, ambitious targets for paediatric treatment scale-up. Globally and in priority countries, UNAIDS will assist efforts to develop annual scale-up targets that address outcomes across the paediatric HIV treatment continuum.

57. The Joint Programme has already made a concerted effort to encourage the routine collection and analysis of age-disaggregated data on HIV treatment. Since 2014, the Global AIDS Response Progress Reporting system compiles data by five-year age groups to monitor coverage and outcomes for different age groups. National, Regional and Global mechanisms will be used to track progress towards the 90-90-90 targets for children and to hold stakeholders accountable for results. Surveillance mechanisms are being strengthened to track children living with HIV as they move from paediatric to adolescent services and from adolescent services to adult services. Adolescent-specific treatment targets are also being developed in the *All In* agenda promoted by UNICEF and UNAIDS Secretariat.

Mobilize sufficient resources

58. Recognizing that a sure sign of political commitment is the allocation of sufficient resources, UNAIDS will collaborate with partners to mobilize the resources needed to achieve the 90-90-90 target for children. In particular, UNAIDS will emphasize the importance of budgeting specifically for paediatric testing and treatment services in order to overcome the longstanding neglect of paediatric HIV treatment issues. In addition focus will be maintained on efforts to eliminate new HIV infections among children and thereby reduce the number of new children requiring antiretroviral therapy.

59. As in the broader response, principles of global solidarity and shared responsibility will need to prevail if sufficient resources for paediatric treatment services are to be mobilized. Including through the PEPFAR/CIFF ACT initiative, UNAIDS will work with key donors to encourage ramped-up investments in paediatric HIV treatment services. Advocacy and technical support will focus on ensuring inclusion of robust paediatric treatment components in country concept notes for the Global Fund, as well as increases in domestic public sector spending allocated to diagnostic and treatment services for children. Specific efforts will focus on aiding countries in exploring innovative financing mechanisms to ensure sustainable funding for paediatric HIV treatment services.

Promote effective service delivery

60. The Joint Programme will collaborate with partners to support the development of global operational guidance for paediatric HIV treatment. This guidance will summarize best and promising practices from successful paediatric treatment programmes. Information sharing between countries regarding best and promising practices for paediatric HIV treatment will be encouraged. Using existing coordination mechanisms, partner coordination in the paediatric HIV treatment field will be intensified, with the aim of effectively leveraging the core competencies and comparative advantages of key actors.

61. The Joint Programme will actively encourage decentralization of paediatric treatment services, task-shifting, community involvement and other strategies to expand the range and accessibility of paediatric testing and treatment services. The Joint Programme will continue to support procurement pooling for paediatric treatment commodities and will assist countries in strengthening supply management and monitoring systems to prevent commodity stockouts.

62. Building robust demand for treatment will require a range of actions. Intensified efforts to eliminate stigma – both generally, and specifically with respect to the diagnosis and treatment of children – will be critical to expediting treatment uptake for children. Demand creation efforts will need to prioritize community education and sensitization, and involve community in the promotion and delivery of services.

Accelerate development and uptake of new innovations

63. Innovation will be needed to address the gaps in paediatric HIV treatment. Innovation will be required to optimize early infant diagnosis, through application of lessons learned and promising practices (e.g., transport networks, use of SMS printers to

reduce time required to receive test results) and through inclusion of emerging technologies in normative guidance. The Joint Programme will support efforts to develop new infant diagnostic tools, including affordable point-of-care technologies, that need to be expedited, and such tools must be swiftly scaled up as they emerge. The Joint Programme will work with country partners and programme implementers to develop and implement innovative strategies to identify infants and children outside the continuum of prevention of mother-to-child transmission services. Methods will be required to reduce gaps in linkage to, and retention in, care. Working closely with relevant partners, the Joint Programme will support efforts to develop a more comprehensive testing algorithm for newborns and will encourage active exploration of virological testing at birth.

64. The Joint Programme will intensify efforts to identify ways that it can support and strengthen efforts to develop new medicines and formulations that are more palatable, adherence-friendly and optimally durable. In particular, the Joint Programme will work to support efforts to develop four-in-one fixed dose paediatric antiretroviral combinations for children under three years. As innovations emerge, such as pellets to replace unsavoury liquid formulations, UNAIDS country and regional offices will intensify technical support to countries to expedite uptake.

65. WHO has developed an implementation science research agenda with stakeholders and partners to address the gaps in research across the continuum of care. As best or promising practices are identified, the Joint Programme will assist countries in implementing measures to improve treatment uptake and health outcomes for children.

66. Using existing coordination mechanisms and advocacy platforms, the Joint Programme will mobilize resources to support the development and introduction of innovative tools, including new paediatric medicines and formulations and point-of-care diagnostic tests. Through early communication with manufacturers, WHO's Expression of Interest List for new antiretroviral formulations and the PHTI initiative, the Joint Programme and partners will endeavour to encourage greater investment in paediatric treatment research and development and to make timely plans to scale up manufacturing capacity to facilitate early adoption of medical innovations.

67. The Joint Programme will prioritize capacity-building assistance to ensure robust quality assurance for paediatric HIV treatment programmes. Advocacy will aim to harmonize national regulatory processes with WHO prequalification to expedite the availability and uptake of new paediatric diagnostics and medicines. The Joint Programme will also advocate for access-friendly policies, including the elimination of user fees and other out-of-pocket costs that may deter service utilization. Task-shifting, scaled-up provider-initiated testing and counselling and improved data collection will be prioritized in the Joint Programme's advocacy and technical support. UNAIDS will intensify its assistance to countries to reduce intellectual property barriers and effective leverage flexibilities available under the Trade Related Aspects of Intellectual Property (TRIPS) agreement.

Engage and promote community leadership

68. Service systems will need to take a more holistic approach, effectively partnering with the community if we are to achieve paediatric treatment goals. HIV care and

treatment for children not only involves administering antiretroviral therapy but also encompasses medical, psychosocial, legal and community support services that, together, address the broad range of needs of the children, their caregivers and their communities at large. UNAIDS will seek innovative ways to strengthen community leadership with the aim to build the needed partnerships to implement effective programmes.

Maximize coordination of efforts

69. Leveraging existing coordination platforms (such as the IATT) and new paediatric HIV treatment initiatives, UNAIDS will use its coordination function to maximize coordination of efforts to end the paediatric AIDS epidemic. The UNAIDS Secretariat will use its role as coordinator, facilitator and advocate to ensure that the Joint Programme's efforts are optimally effective, efficient and inclusive. Outside the Joint Programme, UNAIDS Secretariat and Cosponsors will prioritize partnerships with strategic stakeholders to accelerate the development of new diagnostic and treatment tools for children, to overcome barriers to scale-up and to strengthen results-based monitoring.

DECISION POINTS

The Programme Coordinating Board is invited to:

70. *Take note* of the report and analysis of gaps in children's access to antiretroviral therapy;

71. *Welcome* the strategic directions outlined by UNAIDS for closing the paediatric treatment gap and encourage the Joint Programme to initiate implementation of the outlined steps.

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