
Twelve recommendations following a discussion about the 'Mississippi baby'

Implications for public health programmes to eliminate new
HIV infections among children

GLOSSARY OF TERMS

ANC	Antenatal care
ART	Antiretroviral treatment
AZT	Zidovudine
CAPRISA	Centre for the AIDS Programme of Research in South Africa
CHER	Children with HIV early antiretroviral therapy
DBS	Dried blood spot
EID	Early infant diagnosis
FTC	Emtricitabine
IMPAACT	International Maternal Pediatric Adolescent AIDS Clinical Trials Group
IRD	Institut de Recherche pour le Developpement
LPV/r	Lopinavir/ritonavir
NHLS	National Health Laboratory Services
NIH	National Institutes for Health
NVP	Nevirapine
PCR	Polymerase chain reaction
PHPT	Program for HIV Prevention and Treatment (Thailand)
PK	Pharmacokinetics
PMTCT	Prevention of mother-to-child transmission
POC	Point-of-care
RAL	Raltegravir
TB	Tuberculosis
TDF	Tenofovir
3TC	Lamivudine
WHO	World Health Organization

UNAIDS / JC2531/1/E

This paper was commissioned by the Joint United Nations Programme on HIV/AIDS (UNAIDS). However the views expressed in the paper/report are the authors and do not necessarily represent the view of UNAIDS or its Cosponsors.

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RECOMMENDATIONS

RECOMMENDATIONS

At the meeting on Scientific Advances from the 'Mississippi baby': Implications for public health programmes to eliminate new HIV infections among children, hosted at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) in Durban, participants agreed on 12 recommendations to help reach the goal of eliminating new HIV infections among children. The recommendations follow:

1

Global Plan

The case of the 'Mississippi baby' emphasizes the need to reinforce the existing elements of the *Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive*¹.

2

Paediatric treatment

Outside of a clinical trial setting, children who are taking antiretroviral treatment (ART) should not stop treatment, even if their virus has been well controlled for years and even if they no longer have HIV antibodies.

3

Research protocols

Research agencies should accelerate protocol finalization, approval and funding to facilitate observational studies of similar infants who have stopped HIV treatment against medical advice, and controlled clinical trials that include planned cessation of HIV treatment in specific, well-defined situations in which intensive virological follow-up can be provided. Such research studies should be designed to address questions appropriate to African settings, where most HIV infections among children occur, and whenever possible should involve partnership with African researchers and institutions.

¹ Global Plan towards the elimination of new HIV infections among Children by 2015 and keeping their Mothers alive. 2011-2015. Joint United Nations Programme on HIV/AIDS (UNAIDS), 2011.

4

Breast-feeding

Prospective cohort studies and modelling studies are needed to determine the potential value of adding longer infant prophylaxis to maternal HIV treatment for infants who are breastfed.

5

HIV testing schedule

Prospective cohort studies, implementation science and programmatic and economic modelling are needed to evaluate strategies for infant diagnosis that include earlier testing (to find HIV-positive infants earlier, and to prevent losses to follow-up) as well as more complete later testing (to find infants who have acquired HIV through breastfeeding).

6

Diagnostic technology

In order to improve the timely, accurate and complete diagnosis of HIV among infants born to HIV-positive mothers, the potential benefits and challenges of different rapid diagnostic systems need to be articulated by health care providers and users and these parameters should be discussed with developers and manufacturers.

7

Treatment 2.0

The Treatment 2.0 agenda, to simplify HIV treatment, needs to be made more relevant to the treatment of children, and particularly infants and young children.

8

Pharmaceutical manufacturers

An urgent priority is to work with pharmaceutical manufacturers to define the most useful formulations and to find innovative ways to create incentives to bring them to market. A specific recommendation is to stimulate manufacturers to provide existing Zidovudine (AZT)/Lamivudine (3TC) dispersible tablets with score marks to allow them to be broken into quadrants of 15/7.5 mg.

9

Pharmacokinetics

Pharmacological researchers and infant treatment centres should push forward to produce pharmacokinetics (PK) and safety data for more antiretroviral drugs during the first few weeks of life, and in particular for therapeutic dosing for Nevirapine (NVP) (the current recommended NVP dosing for neonates is low, to achieve levels sufficient for prophylaxis; higher levels are required for therapeutic dosing).

10

Presumptive treatment

Modelling, pharmacology and prospective clinical cohort studies are needed to weigh up the balance of presumptive HIV treatment rather than prophylaxis for HIV-exposed infants, especially for those with the highest HIV risk, until the diagnosis of HIV is confirmed or refuted.

11

Immediate treatment

Encourage earlier diagnosis and HIV treatment for infants, with quality-assured diagnosis performed as early as possible and HIV treatment started in all infants with HIV. This is in accord with the 2010 World Health Organization (WHO) guidelines that already recommend immediate initiation of ART in all HIV-positive children under the age of two years, regardless of clinical or immune findings. The new 2013 WHO consolidated ARV guidelines² expand on this and recommend treating all children under five years of age, regardless of other criteria.

12

Neonatal HIV testing

Earlier HIV testing of infants, including testing in the first few days of life, should be considered where capacity exists or can be developed, in addition to existing testing programmes that test at the age of six weeks and after the breastfeeding risk has ceased.

² Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach. World Health Organization (WHO), June 2013.



SUMMARY OF THE DISCUSSION

The first meeting organized by the Office of the Joint United Nations Programme on HIV/AIDS (UNAIDS) Scientific Expert Panel discussed the implications of the case report of the 'Mississippi baby', which had first been presented in March 2013 at the 20th Conference on Retroviruses and Opportunistic Infections held in Atlanta, Georgia. The 'Mississippi baby' is the first report of a functional cure being achieved in an infant. Despite being infected at birth, the infant is no longer taking ART, remains well and has negative routine tests for HIV.

The case of the 'Mississippi baby' represents a paradox. On the one hand, it represents a failure of well-understood interventions and systems to prevent infants from becoming infected with HIV and a failure of systems to maintain HIV-positive mothers and their exposed infants in care. On the other hand, the meticulous clinical care, the bold decision to start antiretroviral treatment (ART) prior to confirmation of the infant's HIV status, early DNA and RNA polymerase chain reaction (PCR) testing to diagnose HIV infection, accurate recording and early follow-up with regular blood tests to monitor viral load, and the collaboration with a network of specialized laboratory scientists allowed the Mississippi case to be reported as the first example of a functional cure in an infant.

The meeting mirrors this paradox. The *Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive* has facilitated acceleration of action in many countries and considerable progress has been reported since 2009. Nonetheless, in the 22 priority countries³ that report almost 90% of new HIV infections in infants, there were still estimated to be 210 000 new infections in 2012. ([Recommendation 1](#))

Furthermore, children have not benefited as much as adults from the current scale-up of ART. Current estimates (from 2011 figures) are that only 28% of HIV-positive children who are eligible for treatment are receiving it, whereas the equivalent figure for adults is around 58%.

The case of the 'Mississippi baby' is an interesting success story; while it provides hope, the details of this single case remain to be fully reviewed and published. Laboratory studies have shown that the virus isolated from the mother is capable of replication and behaves like other wild-type or laboratory isolates and that the mother and baby do not have genetic markers typical of elite controllers. However, until the findings are replicated in other infants, the Mississippi case does not provide grounds for stopping HIV treatment in infants or children currently in HIV treatment programmes throughout the world. Research agencies are already developing a range of studies investigating potential strategies for an infant cure and the Mississippi case has accelerated discussions and should speed up the development of protocols within the National Institutes for Health (NIH) and other research agencies. ([Recommendation 2, 3](#))

³ Angola, Botswana, Burundi, Cameroon, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Ghana, India, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia and Zimbabwe

The HIV clinician who treated the 'Mississippi baby' used her clinical judgement and, realizing that the risk of transmission was high, started the baby on therapeutic dosing of ART at the age of about 30 hours. The tests confirming HIV infection in the baby were not available until a few days later. Even in a well-resourced country like the United States of America, the diagnosis of HIV infection among infants is not always straightforward. PCR-based diagnostic testing is recommended at the ages of 14 to 21 days, one to two months, and four to six months; diagnostic testing at birth is recommended for infants at elevated risk of in utero HIV infection, such as infants born to mothers who did not receive ART during pregnancy, as in the Mississippi case. Some experts confirm the absence of HIV infection in infants with prior negative virologic tests by performing an antibody test to document loss of maternal HIV antibodies at 12 to 18 months of age. The Mississippi samples were transported to Clinical Laboratory Improvement Amendments (CLIA)-certified laboratories and results returned some days later.

In resource-limited countries, the logistics of diagnostic testing, the timeline for test result availability, the opportunity for follow-up testing and transmission risk during breastfeeding creates a very different situation to that in the USA. In these countries, typical guidelines suggest sending a dried blood spot (DBS) to a centralized laboratory facility for testing; this is usually a single sample taken at six weeks of age, with the time for obtaining test results usually several weeks. If the test is negative, this is followed by an HIV antibody test after breastfeeding has stopped.

The positive DNA PCR test taken at 30 hours of life in the 'Mississippi baby' suggests that the baby was most likely infected in utero rather than intrapartum. Conversely, the relatively low viral RNA load on a separate sample taken at 31 hours implies that infection probably occurred extremely late in pregnancy or potentially through maternal to foetal blood transfusion occurring during uterine contractions in labour.

In the absence of ART and breastfeeding, approximately 25–30% of transmissions occur in utero, and 65–70% intrapartum; in a breastfeeding population, as much as 35–40% of infections may occur postnatally, with 10–25% in utero and 35–40% intrapartum. However, the proportion of infections occurring during each risk period may be modified by maternal and infant ART. For example, while the number of infections is decreased, it may be that the proportion of infections occurring in utero or postpartum will be higher in the presence of a highly effective intervention in later pregnancy and intrapartum.

As soon as an infant is known to be HIV-positive, treatment with ART is recommended. However, current practice is often to test the infant at six weeks of age. The rationale for this is to "catch" those infections that occurred both in utero and intrapartum, and to have early infant testing occur in conjunction with the first scheduled immunization visit, when most infants re-enter the health system after birth. By six weeks, it is possible to reassure a mother that initial interventions to prevent mother-to-child transmission have worked, although the risk of transmission during breastfeeding continues. Breastfeeding remains a cornerstone for infant survival and well-being in resource-

limited countries. Treatment for the HIV-positive mother or antiretroviral prophylaxis for the HIV-exposed breastfeeding baby have both been shown to reduce the risk of postnatal transmission of HIV significantly, but the insufficient delivery of ART during this period now makes breastfeeding a greater contributor to the proportion of HIV transmission events. [\(Recommendation 4\)](#)

Early infant diagnosis (EID) strategies are often aimed at demonstrating the efficacy of HIV prevention programmes and detecting all infants infected during pregnancy and labour rather than trying to initiate infants early on ART. However, many infants born to HIV-positive mothers are either lost to postpartum follow-up, including during the breastfeeding period, resulting in many undetected HIV-positive infants until they return to the health system with HIV-related symptoms. Unknown HIV exposure status also contributes to this late HIV detection in infants. [\(Recommendation 5\)](#)

A diagnosis of HIV in infants could be made easier with the aid of modern technology. Rapid technological advances have created a range of new devices for detecting HIV RNA and HIV DNA. Several options currently in the pipeline do not require sophisticated laboratories and could be used close to or at the point-of-care (POC) for the infant. However, before these new technologies can be widely adopted, they should be carefully evaluated. The rapid roll out of the GeneXpert® system for detecting tuberculosis (TB) and drug-resistant TB in South Africa means that many district laboratories can now do sophisticated nucleic acid amplification but they have never been equipped or trained to perform mycobacterial culture. Such “leap-frogging” technology (similar to mobile phones overtaking terrestrial telephone services) has been called “disruptive technology”, because many systems will have to be changed to incorporate the benefits of the new platform. Nonetheless, the number of confirmed cases of TB and the number of diagnosed cases of drug-resistant TB has risen rapidly with the new machines. The GeneXpert® system already has modules for several other bacterial pathogens, and an HIV viral load assay is under development. HIV viral load assays are increasingly being recognized as an important part of the programmatic management of HIV treatment services. Incorporating DNA assays into a joint platform or combining multiple assays into a single format would enhance simplicity and should reduce capital costs. The WHO currently plans to hold a meeting later this year to provide guidance on POC technologies that are already available. [\(Recommendation 6\)](#)

The ‘Mississippi baby’ started HIV treatment at approximately 30 hours of age, before HIV infection was confirmed and very early in the course of the HIV infection. In the USA, standard infant prophylaxis for HIV-exposed infants is administration of six weeks of AZT alone; however, in high-risk situations, a dual prophylaxis regimen is recommended (six weeks of AZT plus three doses of NVP in the first week of life). In the case of the ‘Mississippi baby’, therapeutic dosing of three antiretroviral drugs (AZT, 3TC and NVP) were administered. WHO guidelines recommend infant prophylaxis with a single drug, NVP, at prophylaxis dosing for six weeks, with maternal use of a fully suppressive ART regimen during pregnancy and breastfeeding. If maternal ART was not

received during pregnancy, extension of the infant NVP to 12 weeks can be considered. With effective programmes to eliminate new HIV infections among children, the risk of HIV transmission at the time of birth is already low, so that more than 95% of infants will not acquire HIV. The hazards of giving more antiretroviral drugs at therapeutic doses to HIV-exposed infants, whose infection status is still unknown, needs to be weighed against the low risks of transmission.

However, in situations where a known HIV-positive mother has not been able to benefit from an effective programme preventing mother-to-child transmission and has had little or no access to ART, then the risk of transmission to the infant is much higher and may outweigh the potential risks of adverse events from the use of high doses of multiple drugs. This is also true if there are other predisposing risk factors, such as prematurity, prolonged rupture of membranes, concomitant infections and high maternal viral load. Nevertheless, this is complicated by the lack of data on PK and safety of therapeutic doses of antiretroviral drugs in infants, particularly preterm infants.

Thus, a big challenge for health care workers and their patients is the scarcity of ART regimens with appropriate dosing and safety data that are licensed for their use in infants. Lack of PK and toxicity data and limited pharmaceutical preparations suitable for the administration to newborn infants all limit the choices for a health care worker who wishes to start HIV treatment in the first weeks of life. The market for paediatric HIV preparations is much smaller than that for adults and as children grow, different dosages or formulations are needed. Health care providers may feel less confident providing HIV treatment, given the range of options recommended for children.

[\(Recommendation 7, 8, 9, 10\)](#)

The 'Mississippi baby' was continued on the empiric treatment regimen because it is increasingly clear that early treatment of HIV-positive infants is life-saving. Several studies have demonstrated reduced early mortality, but also better virological and immunological outcomes with less viral diversity and possibly smaller reservoirs of infection.

The possibility of easier and earlier diagnostic approaches, particularly ones that can be used close to the POC, converges with the benefits to infants from earlier HIV treatment. The 'Mississippi baby' also raises the question of when (or whether) to stop HIV treatment in the setting of immediate therapy to assess for functional cure rather than when to start HIV treatment since there is a universal agreement that HIV-positive infants should start ART as soon as possible based on data from well-designed, randomized clinical trials demonstrating benefit.

Over the coming years, it is possible that research will demonstrate that more infants who start HIV treatment promptly are indeed functionally cured. The benefits of starting ART earlier could therefore be immeasurably greater, with the possibility of generating a functional cure in a proportion of such infants, and thus avoiding the enormous social, financial and clinical challenges of HIV treatment that continue through childhood and adolescence and into adulthood. This is a goal that is well worth striving for.

[\(Recommendation 11, 12\)](#)

Report of the meeting

The Centre for the AIDS Programme of Research in South Africa (CAPRISA), a UNAIDS collaborating centre for HIV research and policy, hosted the first scientific symposium under the umbrella of the new UNAIDS Scientific Expert Panel.

Salim Abdool Karim (Co-Chair of the symposium) welcomed all participants to the meeting and everyone had an opportunity to introduce themselves. Michel Sidibé, Executive Director of UNAIDS, summarized the goals of the symposium, which was to get guidance on and translate the discussions on the case of the 'Mississippi baby' and related studies into recommendations for the elimination of new HIV infections in infants, and to obtain expert guidance on how to proceed in the future. He also took the opportunity to announce that Professor Abdool Karim will be chairing the newly established UNAIDS Scientific Expert Panel.

The aim of this panel is to help UNAIDS to reflect on and use scientific developments. UNAIDS has recognized the need to seek advice from international experts, and tapping into the existing global knowledge through a Scientific Expert Panel. UNAIDS works to ensure that scientific knowledge is not hindered by bureaucratic hurdles, thus allowing for a quicker pace of action.

Day one, session one: an update on the achievements and challenges of global elimination of new HIV infections among children

Session one focused on the achievements and challenges in the field of mother-to-child transmission. Karusa Kiragu from UNAIDS provided an update on the *Global Plan towards the elimination of new HIV infections among children by 2015 and keeping their mothers alive*. This plan focuses on four strategic areas: (1) preventing HIV among women of reproductive age; (2) filling the unmet needs of women living with HIV for family planning and birth spacing, optimizing health outcomes for these women and their children; (3) preventing HIV transmission through antiretroviral drugs during pregnancy and breastfeeding; and (4) provision of HIV treatment, care and support for women and children living with HIV and their families. Dr Kiragu presented a preliminary analysis of data from 2012, which suggests that there has been significant progress towards the elimination of new HIV infections among children in the 22 priority countries. However, although the mean coverage is now 65% in these countries, there are some emerging signs of a slowdown. Dr Kiragu's presentation highlighted that there is a need to strengthen provider-offered family planning as well as primary HIV prevention in health care settings. HIV transmission through breastfeeding is also becoming a greater contributor to mother-to-child transmission, so ART provision is vital to make breastfeeding safe. In addition, there is a need to greatly strengthen access to HIV treatment, particularly for children, and to accelerate efforts to secure domestic funding to make programmes for the elimination of new HIV infections among children more sustainable.

Discussions focused on the timing of infant HIV diagnosis and the ability to test infants earlier than six weeks will be central to earlier HIV treatment initiation in infants. At a global level it is hard to determine when early testing is done. The six-week target for testing stems from the WHO guidelines that recommends infant diagnosis at six weeks and is based on scientific evidence indicating near 100% sensitivity and specificity for diagnosis of in utero and intrapartum infection at that age as well as programmatic considerations. In contrast, testing at birth only identifies infants infected in utero, and without repeat testing at four to six weeks will miss intrapartum infant infections, thus, while highly specific, earlier testing is less sensitive.

One of the key challenges in programmes for the elimination of new HIV infections among children is the high rate of loss to follow-up. This situation can be remedied by earlier initiation of ART in infected women during pregnancy. However, repeat testing for HIV-negative women, particularly during the breastfeeding period to detect acute maternal infection, which puts the infant at high risk of postnatal HIV acquisition, is more challenging. In general, good progress has been made with respect to reducing new HIV infections among children but there is still much to be done – more than 300 000 children globally are still getting HIV each year. The epidemiology of mother-to-child transmission is changing with the proportion of infections in utero and during breastfeeding increasing compared to peri-partum transmission.

Antiretroviral drugs are highly effective when taken and the failure of ART to prevent new infections is mainly due to a lack of adherence or inadequate access. It is important to ensure that the best regimens and the best coverage are provided.

In summary, programmes to eliminate new HIV infections among children and keeping their mothers alive are complex and multifaceted. Four main issues arising from the discussions that stand out are:

- progress in reducing HIV transmission is heterogeneous, with a particularly high incidence in young women in many communities;
- identification of HIV-positive pregnant and breastfeeding women remains suboptimal, as does provision of effective ART for eliminating new HIV infections among children;
- despite all the progress in programmes to eliminate new HIV infections among children, additional efforts are needed to make breastfeeding safe by improving ART during the breastfeeding period; and
- the need to do better in treating children with HIV in general.

Countries that are lagging are the ones with a high HIV burden, and by focusing on these countries, it may be possible to have a bigger impact.

The 2013 WHO Consolidated ARV guidelines

Nathan Shaffer from WHO provided a summary of the 2013 WHO consolidated ARV guidelines to be released at the International AIDS Society (IAS) Conference in Kuala Lumpur, Malaysia in July 2013. His presentation summarized the major changes in the new guidelines and specifically focused on the recommendations directly related to pregnant women and children. New recommendations include earlier initiation of ART for adults (CD4 <500) with prioritization of those with CD4 <350, and immediate treatment of all HIV-positive children below the age of five years. All HIV-positive pregnant and breastfeeding women should be initiated on ART, and this should be continued throughout the risk period for mother-to-child transmission or continued lifelong. Lifelong ART for pregnant women, regardless of CD4 count, or the offer of "Option B+", is now recommended to ensure that women in need of treatment receive ART. Recommendations also include fixed-dose tenofovir (TDF)-based combinations as the preferred first-line choice, improved patient monitoring (including viral load monitoring) and task shifting. One of the major issues now is not "when to start" but "when to stop" or "whether to stop".

Discussions focussed on the fact that paediatric HIV treatment and care has lagged in contrast to adult care and much more needs to be done to scale up treatment for infants. Guidelines recommend a four- to six-week visit for EID and to initiate ART based on the outcome. Although there has been a scale-up in EID with DBS DNA PCR, there is still limited access and limited early HIV treatment, even in settings where positive PCR tests are obtained. There is also a need to address stigma and discrimination. It is important to recognize that it may take countries a few years to adopt the guidelines and support is needed to accelerate transition.

Obstacles to the global elimination of new HIV infections among children

The final presentation in Session one focused on the scientific and operational obstacles to the global elimination of mother-to-child transmission and was delivered by Chewee Luo from UNICEF. Dr Luo's presentation highlighted the heavy burden of HIV among young women in Africa and the three-fold higher risk of HIV transmission in infants of mothers with acute infection during pregnancy or lactation compared to mothers with chronic HIV. Her presentation also highlighted the need to increase male involvement in maternal and child clinics and gave an overview of the status of implementing lifelong ART regardless of CD4 count throughout sub-Saharan Africa. A current challenge in programmes to eliminate new HIV infections among children is the scaling up of HIV treatment to infants and children and a summary of the laboratory capacity for EID was provided. The experiences from Swaziland, Uganda and the United Republic of Tanzania with respect to EID were summarized. The six-week testing cut-off for EID seems to be too late and some consideration should be given to POC testing, and newer technologies may make this possible. Another important obstacle



highlighted is the disconnect between investments in programmes to eliminate new HIV infections among children and reaching those in need of ART – even if infants are identified they are often not successfully linked to care. The attrition rates between EID and starting on active ART reach levels as high as 70%. Another important consideration is that almost 50% of mother-to-child transmission occurs when the HIV status is not known; indicating the importance of HIV testing during the entire cascade where mother-to-child transmission is likely to occur. Future activities in programmes to eliminate new HIV infections among children should consider: expanding HIV testing into delivery units and vaccination points; decentralizing and task shifting delivery of ART in pregnancy and to children; and tracking of risk factors of HIV in children.

Session two: the evidence from the ‘Mississippi baby’ and related studies

Session two focused on the scientific evidence from the ‘Mississippi baby’ studies. Hannah Gay, paediatrician at the University of Mississippi, provided a detailed summary of the case history and described the rationale for choosing the treatment regimen that was administered to the child. The infant was referred to her shortly after delivery because of a detectable viral load in the mother and the infant at birth. She decided to commence prophylaxis using therapeutic doses of three antiretroviral drugs immediately, 31 hours after delivery, and before receiving HIV DNA confirmation of the diagnosis. Even in the US setting this test can take up to 10 days to be processed and reported. Dr Gay commenced three active drugs: AZT, 3TC and NVP, and switched NVP to Lopinavir/ritonavir (LPV/r) after confirmation of HIV infection status was received at seven days old. Over the next three weeks the infant showed a biphasic decline in the viral load PCR until reaching undetectable levels. Safety blood monitoring, including mean corpuscular volume, indicated that the infant took medication until 15 months. The mother then stopped attending the clinic with her baby and ART was not administered. On retesting several months later, results indicated that the infant had no detectable viral load.

Deborah Persaud, paediatrician and virologist from Johns Hopkins University, presented the laboratory studies of the ‘Mississippi baby’ and specifically focused on providing evidence that the infant was indeed HIV-positive, whether the maternal infection was with HIV-1 and if so, which subtype, and that there was no laboratory mix-up of specimen. These studies also determined if the maternal infection was attenuated due to multidrug-resistant HIV, and whether this was really a case of HIV “cure”.

The definition of “cure” was summarized as follows:

- cure is the permanent remission of disease in the absence of ART;
- functional cure is when HIV-infected cells persist but HIV-specific immune responses confer lifelong control of the virus in the absence of ART; and
- sterilizing cure is the elimination of all HIV-infected cells to permit ART discontinuation.

One of the interesting findings from the Mississippi case was the relatively low viral load levels at birth ($\pm 20\,000$ c/ml). However, in one study of 18 children with in utero infection, the median viral load was 26 940 c/ml; other studies have suggested higher RNA levels of 80 000 to 100 000 when testing infants with in utero infection at birth. A functional cure is biologically plausible as other studies have suggested that infants treated early have significantly lower viral reservoirs than those treated later in life.

Dr Persaud's presentation also summarized the Washington International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) meeting on the next steps in research. Specifically, a proof-of-concept study (P1115) of very early intensive treatment of HIV-positive infants to achieve functional cure is planned. Dr Persaud emphasized that, although the 'Mississippi baby' was a single case, it has provided hope that a functional cure is possible and the top priority now is to replicate a functional cure in perinatal HIV infection to gain insight into the mechanisms of cure with very early ART.

The discussions focused on the limitation of EID, because only infants infected in utero are likely to have HIV detected within the first 24 hours. The window of opportunity for treating infants who become infected in utero needs to be defined. In reality, few countries perform PCR testing at delivery. Current guidelines are to provide prophylaxis to the baby but use of a triple ART regimen at therapeutic doses is not standard practice. The Children with HIV Early Antiretroviral Therapy (CHER) study, a randomized controlled study that was conducted in 2005 showed that early HIV treatment at six to 12 weeks of life was beneficial, but also showed that children experienced virological rebound once HIV treatment was stopped. It is therefore possible that therapy started by six to 12 weeks is too late to achieve a possible "cure" because a viral reservoir would have already been established. Treatment interruptions should not occur on the basis of current evidence. However, treating as early as possible seems to be important. If ART is started early enough, then the viral reservoir could potentially be controlled. Future research may show that the size of the reservoir may predict whether a functional cure and stopping therapy may be possible.

Implications of the 'Mississippi baby' and related studies

The final presentation in Session two was delivered via video link by Lynne Mofenson from the National Institute of Child Health and Human Development, NIH, who presented on questions and implications of the 'Mississippi baby' for research plans and priorities. Dr Mofenson described how mother-to-child transmission provides a unique opportunity to assess if early therapy can prevent HIV reservoir development because the timing of infection is relatively known. The use of combination antiretroviral regimens at therapeutic doses to the infant may outweigh the risks if the mother has not received ART. However, this would not be the case if the mother has already received ART and the risk of infant infection is extremely low. She further stressed that, while there is excitement about the Mississippi case, questions remain, including the very unusual low viral loads in both the mother and baby. The relevance to the general population of HIV-exposed infants also remains unclear. Before there are widespread

changes in policy guidance regarding antiretroviral prophylaxis in HIV-exposed infants, more data are required, including knowing safe and appropriate neonatal antiretroviral therapeutic dosages, particularly for preterm infants in whom there are significant differences in drug metabolism compared to term infants. Except for AZT and 3TC, there is a lack of PK and safety data for therapeutic dosing of antiretroviral medication in neonates. In preterm infants, the evidence on appropriate dosing is even more limited with data only available for AZT. This information will be critical to be able to move forward with the planned studies of functional cure in infants.

Dr Mofenson reiterated that the requirement for EID remains a challenge, particularly in low resource settings. POC virological diagnosis is crucial to be able to determine which infants should receive and continue intensive ART. There are a number of research questions that need to be answered including more information about basic neonatal and preterm infant developmental immunology, including whether the immunologic immaturity of the neonatal immune system and lack of memory T cells diminish the ability to establish a reservoir, what the “window of opportunity” is for interventions following birth, and the need for biomarkers of persistence to guide decisions on the optimal timing for ART interruption to determine “cure”.

A robust research agenda for infant cure is already underway and the IMPAACT Cure Committee and Cure Neuro Sub-Committee have been established⁴. Once again, retrospective evaluation of children from existing paediatric cohorts and early HIV treatment studies are planned. This is to characterize latent reservoir, and host and viral processes; and the proof-of-concept early treatment study (P1115) will also be implemented soon. A new Request for Application on latent reservoir in children has been published, with a due date of August 2013, with funding of well-scoring grants planned in early 2014. Dr Mofenson noted that it is already known that early ART in infected neonates is lifesaving from the CHER study, thus an emphasis on early diagnosis and ART is needed regardless of the cure debate.

The discussions focused on how the increasing proportion of transmission during breastfeeding complicates the issue of achieving a functional cure. While the meeting scope was limited to approaches that are ready or almost ready for implementation, in particular neonatal ART provision, experimental approaches beyond ART were briefly mentioned, such as passive immunization with broadly neutralizing HIV antibodies, such as VRC01.

The clinical work of Dr Gay, which has led to the discussion of a “cure”, was acknowledged. There is convincing evidence that there was established infection in the Mississippi case and that the early initiation of ART resulted in an undetectable viral load, but it is unknown whether the reservoirs have been totally eradicated from the baby. More research is required before acting on this finding as this may have been a unique situation resulting in the perfect conditions for this baby to be cured.

⁴ <https://impaactgroup.org/research-areas>

Clearly there are large numbers of infants not getting HIV treatment and the Mississippi case also highlights the need to get more infants onto treatment earlier. Good care is crucial. In the USA there may be the resources to start HIV treatment early but similar resources may not be available in resource constrained settings.

To be able to capitalize on the 'Mississippi baby' approach, mechanisms for very early infant diagnosis need to be in place – with repeated testing to detect later intrapartum and postnatal infections – with improved and safe antiretroviral regimens for neonates. The approach of initiating therapeutic ART from birth as prophylaxis in high-risk infants until the infection status is known could be an approach when mothers have not received antenatal ART. However, this should not diminish the critical need for adequate and optimal implementation of proven interventions to eliminate new HIV infections among children. Additionally, having different interventions for different groups may not be consistent with the "public health approach" by simplifying and harmonizing guidelines, which differs from an "individualized patient approach" to care.

To summarize, there have been tremendous advances towards the elimination of new HIV infections among children, and there may be progress towards meeting the global targets by 2015; but there are still more than 300 000 infants becoming infected globally each year. There are many parallels between the story of the 'Mississippi baby' and the global effort to eliminate new HIV infections among children – poor access to health care, complicated social circumstances and poverty. The health system in the USA sprang into action in response to one vigilant health professional. Providing good clinical care in this case may have contributed to achieving a possible cure. How much good health care is a prerequisite for allowing a cure of infants at a global level remains to be seen, but most likely these two terms, "care" and "cure", are inextricably linked. Beyond that, it is well worth investing in preventing new neonatal infections. Guidelines already exist, but further action is required to accelerate the implementation of the guidelines. Finding a cure is another agenda – it is a research agenda, which needs to be pushed by stakeholders such as IMPAACT and the NIH. One of the important issues will be the earlier diagnosis of HIV infection, which could be a major step forward in implementing the existing guidelines. Many uncertainties still exist around dosing and safety of neonatal HIV treatment.

Session three: novel diagnostics and pharmacological challenges in infants

Session three focused on the pharmacology and diagnostic issues. Pravi Moodley (Department of Virology, National Health Laboratory Services [NHLS]) and the University of KwaZulu-Natal, South Africa) presented the work of Susan Fiscus from the University of North Carolina on the laboratory techniques for earlier diagnosis in infants. The presentation highlighted the benefits of EID and available technology for determining HIV infection during the first week of life. Diagnostic laboratory tests such as POC

p24 antigen rapid test, the Liat™ HIV Quant assay, IQuum Liat™ WB HIV assay, Simple Amplification Based Assay (SAMBA) system for HIV diagnosis and Alere® POC NAT were reviewed. The presentation provided evidence that diagnosis within 48 hours is possible even in resource constrained settings. There are compelling reasons for testing at birth in addition to four to six weeks of age and there are several POC nucleic acid assays in the pipeline, which look promising but still need to be evaluated in newborns.

Discussions focused on how other countries, such as Mozambique, have approached the introduction of POC testing. A matrix for implementing POC testing has been established and some of the lessons learned are that introducing new technologies into health facilities can ensure that high-risk groups are getting their results in real time, thereby improving care provision and reducing the need for repeat visits.

In South Africa, the experience of implementing the GeneXpert® for rapid TB diagnosis was shared. GeneXpert® was widely introduced with the aim to revolutionize testing and to speed up the diagnosis of TB patients. Before it was implemented, the South African government worked closely with the NHLS and assessed which facilities would benefit from high-volume testing. However, despite the widespread implementation of GeneXpert® in many facilities, a reduction in the time between diagnosis and treatment has not yet been realized. A key issue is how quickly one can put individuals on HIV treatment. The availability of rapid and high throughput platforms can also substantially reduce operating costs.

There are a number of studies in progress which assess the performance of POC diagnostics and pilots are underway to establish effective use of these technologies. Several are already available for POC EID, but field experience is required to establish whether and how to align POC testing with the guidelines. WHO already has a process to systematically evaluate these new technologies, but beyond that, it is now crucial to look at these in the context of health system changes, implementation strategies, and community engagement. Furthermore, more discussion is required to address the timing of testing. If the goal is to identify in utero infections, then testing at birth or within 48 hours may be valid but testing at six weeks must still be done to detect intrapartum infections. The purpose of testing will determine the timing of testing. Some studies have shown that if testing is performed at birth, then 50–75% of all those who are currently HIV-positive at six weeks could be detected. Testing at birth could decrease early perinatal morbidity and mortality. Guidelines already exist for when birth testing should be undertaken. Additionally, sometimes the only opportunity for testing is at birth because mothers and their infants are lost to follow-up. However, testing must be accompanied by care and appropriate HIV treatment, and it would be essential to ensure that this group of infants tested at birth continues to be linked to care. A test result by itself is not the answer – the result must be linked with appropriate HIV treatment.

PK and choice of regimen for infants

The second presentation in Session three focused on the PK and the choice of regimens for infants by Timothy Cressey from Harvard and the School of Public Health & PHPT-IRD Chiang Mai universities. Dr Cressey highlighted the unique challenges for neonates and infant ART including immaturity of gastrointestinal, hepatic and renal system, toxicities, tolerability and the limited antiretroviral drug PK data before 14 days of age. In the Mississippi case, the baby received triple therapy from birth. During the first seven days of life, PK data for therapeutic dosing for ZDV/3TC is known, but optimal dosing to achieve therapeutic (as opposed to prophylactic) levels of NVP in the neonate is still unclear. The 'Mississippi baby' was switched to an AZT/3TC/LPV/r regimen from seven days to 18 months.

The problem with the LPV/r liquid formulation is its high alcohol and propylene glycol content, and it is therefore not recommended before 14 days of life. Before scaling up the regimen used in the Mississippi case optimal formulations need to be considered. LPV/r tablets/sprinkles/granules are in development. Limited PK data are available on TDF and emtricitabine (FTC) in neonates, with use as prophylaxis as opposed to therapy, and data on renal and bone safety of therapeutic dosing of TDF in neonates is not available. PK data on raltegravir (RAL), an HIV integrase inhibitor, in neonates are being studied in the IMPAACT P1110 trial.

Thus, the optimal length of time necessary to maintain targeted levels for viral suppression is not entirely evident; PK and safety of NVP administered at therapeutic doses in neonates is also unknown. There is even less antiretroviral drug PK data available for premature babies, and it is not absolutely clear what the ideal ART regimens are for infants.

Discussions focused on the available HIV treatment regimens and their challenges. Paediatric drug formulations are faced with challenges on dosing, toxicity, and licensing. Further, available antiretroviral drugs are often not licensed for use in older children, let alone neonates. It is clear that current choices are limited for neonates and this highlights the need for studies on the safety of current and potential drugs in neonates. A number of studies are planned or underway to address this question. There is also a need to look at simpler regimens for treating children. With the number of infants found positive for HIV declining, it is important to ensure that the interest in finding solutions for neonates is sustained as the elimination of new HIV infections among children draws near. Pharmaceutical companies need to stay involved and UN agencies need to engage with these companies. Even if there is a diminishing paediatric market, meaningful guidance should be provided.

Beyond neonates, there are still many children in need of HIV treatment; the more HIV positive children are on HIV treatment, the more sustainable the market will become. From the perspective of HIV treatment, work towards aligning paediatric and adult treatment, simplifying regimens and harmonising drugs and diagnostics is required.

Adherence in children is also a challenge. The question arises, therefore, whether it would be prudent to invest in drugs with a higher threshold to resistance.

Key points on day one

At the end of day one, each symposium participant had the opportunity to summarize the most important issues discussed during the day. The following broad themes were considered to be most important.

- There have been massive changes in preventing mother-to-child transmission and the move is now to look beyond prevention to potential elimination. ART could potentially be used as a pathway towards elimination and cure.
- Early ART saves lives and if focus is given to getting infants on HIV treatment very early, it may result in a cure further down the line.
- Effective solutions for preventing mother-to-child transmission already exist and, if implemented optimally, these can prevent many infections. Early diagnosis and HIV treatment in children is already known, but it is not being implemented well. The number of children on HIV treatment is quite low and part of the challenge is that nurses may be hesitant to initiate children on HIV treatment, so simpler guidelines would be welcomed.
- Delivery of POC viral testing for adults and paediatrics would be a great advance, when it becomes available. However, the rapid development of new technologies should be carefully considered – it is important to understand what would realistically be available and the role key agencies could play.
- There remain many unknowns with regards to drugs that can be used in neonates. However, antiretroviral regimens and formulations for paediatrics have always been challenging, thus, more work is required on how to deliver paediatric ART more effectively and to strengthen paediatric programmes.
- The issues also need to be discussed at community level to ensure that the community is aware and accesses the services that are already available.
- HIV transmission through breastfeeding remains a big issue and improving the uptake of existing services and to increase early antenatal care (ANC) appointments is vital. Continued breastfeeding transmission should be linked to the broader agenda of improving childhood survival.
- In the current recommendations a single drug prophylaxis is given to infants. This raises the concern about potential emergence of early drug resistance in infants who are found HIV positive despite prophylaxis. If the mother is receiving fully suppressive ART, then the risk of HIV infection in the infant is extremely low and a single-drug prophylaxis is reasonable. However, in higher-risk situations, combination regimens may be more optimal – as has already been shown in the NICHD/HPTN 040 trial, where dual and triple antiretroviral prophylaxis was superior in efficacy in reducing intrapartum transmission when the mother had not received antepartum drugs.

Day two, session four: discussion on the wider health systems implications of changes under consideration for programmes to eliminate new HIV infections among children

Day two started with a summary of the previous day and was followed by a discussion on the wider health systems implications of the Mississippi case.

Michael Eliya (Department of Health, Malawi) summarized the programme to eliminate new HIV infections among children in Malawi, where lifelong ART for all pregnant women had recently been introduced. He reported that the attendance at ANC at first visit was 95%. The majority (85%) of the Malawian population lives in rural areas. The advantages of Malawi's programme are: integrated ART and prevention of mother-to-child transmission guidelines, training and supervision, and decentralized provision of ART at primary care level in maternal and child health clinics. However, the programme faces a few challenges related to the supply of HIV care commodities, EID sample transportation to the three public reference laboratories, linking of HIV-positive children to care and retention of women in care. Retention rates of pregnant women are currently at 78%, but only 14% of exposed children are getting their six-week PCR result. Current transmission rates based on these samples are 6% (PCR positive). Early HIV treatment could improve linkages between programmes to eliminate new HIV infections among children and ART programmes for children. POC testing could be the solution to address the EID issue, if the supply chain could be guaranteed.

The cost of transporting blood samples can be reduced using DBS but reagents are still costly. Higher volumes could be processed at centralized laboratories with well-trained staff who ensure high quality work in other programmes in the sub-Saharan African region. A text messaging-based system with results being available online could reduce turnaround time to two weeks, and allows real-time data collection for surveillance to inform governments at country level.

An example would be the Department of Virology, NHLS-UKZN at Inkosi Albert Luthuli Central Hospital that conducts all the public sector EID in the KwaZulu-Natal province in South Africa. The average proportion of HIV PCR (using Cobas® Ampliprep Taqman, Roche Diagnostics) positive tests at six weeks of age is approximately 2%. The Department processes about 90 000 HIV PCRs per annum with about 90% coverage in KwaZulu-Natal. The Roche and Abbott platforms are two of the most widely used tests for infant diagnosis worldwide, with a combined volume of more than one million tests per year. Around 30% of the estimated 1.4 million HIV exposed infants born each year have access to EID testing. The DBS system has allowed this scale-up of testing and has revolutionized care in HIV and programme services for the elimination of new HIV infections among children.

The need to send out a clearer message to the community about the risks and benefits of breastfeeding were highlighted. Community engagement and empowerment are instrumental for the success of implementation. For most settings, the advantages of breastfeeding continue to outweigh the risks of HIV transmission, but these risks can be reduced even further by better approaches of addressing inequities in health care access, better community engagement and addressing stigma.

Simple ways to engage are:

- giving ownership of ANC services to communities;
- sharing guidelines;
- addressing transport concerns (how to travel longer distances when pregnant? why attend ANC if one is well and not due to deliver for several months?);
- ensure supply lines and prevent stock-outs, especially in rural settings; and
- involve men in ANC and in programmes to eliminate new HIV infections among children.

Even within countries there is a great variation in the success of programmes. In South Africa, for example, the Eastern Cape Province is currently performing poorly with regards to the elimination of new HIV infections among children, while other provinces are doing better. Fortunately, the Eastern Cape does not represent the whole of South Africa. Access to services for high-risk mothers needs to be improved. In Africa, high-risk mothers are predominantly teenage girls who have never had an ANC visit.

It will be important for UNAIDS, WHO and others to communicate what the results of the Mississippi case means to the public. The messaging should be that it was a single case and is unlikely to change policy, but it could be used as a motivation for early diagnosis and treatment and specifically for HIV treatment of children. The issue of increasing treatment for children is not only about ART – we need to invest in delivery systems and specifically in delivery of interventions that work. The elimination of new HIV infections among children needs to be linked to the bigger agenda of maternal-child survival. The ‘Mississippi baby’ makes a strong case for POC diagnostic testing, provided it is used strategically.

Discussions included examples from Mozambique and how the government had tried to impact on some of its challenges. Specifically, in increasing retention of women and children and capturing more children. The community HIV treatment programme has shown improved retention for clients who have proven adherence for six months, significantly reducing the number of visits to, and the burden on, the clinic. The Mozambique government is also looking at integrating immunization and HIV services, a “one stop shop” for HIV, TB, malnutrition and immunization services. Streamlining HIV treatment regimens will reduce the fear of initiating children on HIV treatment and simplifying the care of children living with HIV. With regard to procurement and supply management, Mozambique has been using private companies for the distribution of medications, which has resulted in cost savings. However, this has not resolved stock issues.

On the other hand, the necessities of political leadership, policy implementation and advocacy to be able to make an impact on the elimination of new HIV infections among children are some of the relevant lessons learned in South Africa. Eliminating new HIV infections among children and keeping their mothers alive should be situated in a continuum of care for the family including fathers, mothers and children.

Session five: priorities for implementation

At the final session, participants provided a brief summary of the most important issues they felt emanated from the symposium and a list of draft recommendations was drawn up. Some of the most important messages included the following.

- The 'Mississippi baby' has given us hope for the future and an example of what is possible – it is a reminder that what is currently being done can be improved. There is a need to focus on current recommendations and doing the best possible implementation.
- Good programmes towards the elimination of new HIV infections among children and keeping their mothers alive already exist, but more needs to be done for children and preventing transmission during the breastfeeding period. Tools are already available and, if these are applied, the makings for early commencement of HIV treatment are there. There is a real opportunity to do more for children. Treating early now may ultimately result in a cure a few years later.
- The Mississippi case provides a bridge between HIV treatment and a cure. Current guidelines have evolved based on already existing evidence. Early diagnosis and HIV treatment may have enormous benefits, but these cannot be realized just yet, because the findings need to be confirmed before they could be generalized. Several challenges need to be overcome, including early diagnosis and drug dosages and formulations.
- High quality of care is essential.
- Some work needs to be done around clarity of information – health care workers need to know about early diagnosis and early HIV treatment initiation and their possible benefits. Consistent messaging on the recommendations on breastfeeding and formula feeding is required. There is a lot of interest in this issue, yet more work needs to be done. Messaging needs to be well-considered if recommendations are made to apply beyond sub-Saharan Africa. It would be important to ensure that mother and infant issues are seen as part of the same agenda to avoid a dichotomy between HIV prevention and treatment.
- Attention should focus on high-risk populations, but also on fully implementing the recommendations for those that are already accessing services for the prevention of mother-to-child transmission.

- Treatment for HIV-positive infants and children started with a single drug prophylaxis and it has taken a long time to get used to triple combination regimens – some work may need to be done on more aggressive therapy for infants. Possibly looking at combination approaches – perhaps antibody interventions or an extension of the existing prophylaxis.
- Solutions that work in one place may not work in others – different areas, even within the same countries, will need different solutions. Perhaps lessons can be learned from immunization programmes that have achieved high coverage.
- The Mississippi case is about when to start, not when to stop – but there is definitely a need to start very early HIV treatment.
- The guidelines have shifted the emphasis from CD4 to viral load monitoring and it is therefore crucial to incorporate in training what a “detectable viral load” means and what actions may be required.
- The Mississippi case highlights the convergence of preventing mother-to-child transmission, HIV prevention and treatment. There is a need to understand prophylaxis and the benefits of continuation of prophylaxis. It is hard to understand why HIV treatment initiation is so low.
- This is one of the most exciting research prospects but it will take time to get all the answers.
- Healthy mothers = healthy babies. More attention needs to focus on existing frameworks to prevent unwanted pregnancies and ensure mothers get the services they need.





ANNEX 2

List of participants (in alphabetical order):

Quarraisha Abdool Karim (CAPRISA),
Salim Abdool Karim (CAPRISA),
Jerry Coovadia (CAPRISA/MatCH),
Timothy Cressey (Harvard/PHPT-IRD, Chiang Mai University),
Michael Eliya-Phiri (DoH Malawi),
Lise Ellyin (CHAI - Mozambique),
Shaffiq Essajee (CHAI),
Nigel Garrett (CAPRISA),
Hannah Gay (University of Mississippi),
Peter Godfrey-Faussett (UNAIDS),
Vuyokazi Gonyela (TAC),
Karusa Kiragu (UNAIDS),
Chewe Luo (UNICEF),
Mahesh Mahalingam (UNAIDS),
Dorothy Mbori-Ngacha (Kenya/UNICEF),
Zenawit Melesse (UNAIDS),
Pravi Moodley (NHLS),
Mbulawa Mugabe (UNAIDS),
Deborah Persaud (Johns Hopkins University),
Yogan Pillay (DoH South Africa),
Chalone Savant (PEPFAR),
Nathan Shaffer (WHO),
Michel Sidibé (UNAIDS),
Catherine Sozi (UNAIDS).

Participating via video conference:

Lynne Mofenson (NICHD/NIH),
Rohan Hazra (NICHD/NIH)
Celeste Sandoval (UNAIDS)
Various UNAIDS and WHO staff members in Geneva

ANNEX 3

PROGRAMME

Title: Scientific advances from the 'Mississippi baby': implications for public health programmes on mother-to-child-transmission of HIV

Day 1: 3 June 2013

08:30 Welcome and Introductions – Salim S Abdool Karim (CAPRISA)

08:50 Opening Address – Michel Sidibé (UNAIDS)

Session 1: MTCT – achievements and challenges

09:10 Presentation: Update and overview of the global epidemic of HIV among infants and children – Karusa Kiragu (UNAIDS)

09:25 Presentation: The upcoming 2013 WHO HIV treatment guidelines, rationale and recommendations for mothers and children – Nathan Shaffer (WHO)

09:40 Presentation: Scientific and operational obstacles to the global elimination of MTCT – Chewe Luo (UNICEF)

10:00 Q&A

10:30 Tea/Coffee

Session 2: The scientific evidence from the 'Mississippi baby' studies

11:00 Presentation: The 'Mississippi baby', case history, laboratory studies and a summary of the Washington IMPAACT meeting on next steps – Hannah Gay (University of Mississippi) and Deborah Persaud (Johns Hopkins)

12:00 Presentation: What does the 'Mississippi baby' mean? What are the implications for research plans and priorities? – Lynne Mofenson (NIH) (via video-link at 6am ET)

12:20 General Discussion: What have we learned from the scientific findings of the 'Mississippi baby'?

13:00 Lunch

Session 3: Pharmacology and diagnostics

- 14:00 Presentation: Laboratory techniques for earlier diagnosis in infants** – Susan Fiscus (University of North Carolina/CDC), presented by Dr Pravi Moodley (Department of Virology, NHLS and UKZN, South Africa)
- 14:20 Presentation: Pharmacokinetics and choice of regimens for infants** – Timothy Cressey (Harvard/PHPT-IRD, Chiang Mai University)
- 14:40 Discussion: Delivery of ART to infants** – Discussants: Jerry Coovadia (CAPRISA/MatCH), Shaffiq Essajee (CHAI) and Lise Ellyin (CHAI – Mozambique)
- 15:30 Tea/Coffee**

Session 4: Implications for PMTCT programmes

- 16:00 General Discussion: Implications of these scientific advances and the challenges in early diagnosis and ART initiation in babies**
- 17:30 Close for the day**
- 18:15 Dinner:** Speaker: Aaron Motsoaledi (Minister of Health, National Department of Health, South Africa)

Day 2: 4 June 2013

Session 5: Priorities for implementation

- 08:30 Recap of Day 1** – Peter Godfrey-Faussett (UNAIDS)
- 08:45 Panel Discussion: Wider health systems implications of the PMTCT changes under consideration** – Discussants: Vuyokazi Gonyela (TAC), Yogan Pillay (NDoH-SA), Dorothy Mbori-Ngacha (Kenya/UNICEF), Catherine Sozi (UNAIDS), and Michael Eliya (DoH-Malawi)
- 10:00 General discussion**
- 12:00 Presentation: Summary of discussions and draft recommendations** – Peter Godfrey-Faussett (UNAIDS)
- 12:15 Discussion on draft recommendations**
- 12:45 Close**



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