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Perinatal Transmission [1]

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DOCUMENT NO. AND TYPE	SUBJECT/TITLE	DATE	RESTRICTION
001. list	Participants, Mother-To-Child Transmission Discussion (partial) (2 pages)	07/21/2000	b(6)

COLLECTION:

Clinton Presidential Records
National AIDS Policy Office

OA/Box Number: 21075

FOLDER TITLE:

Perinatal Transmission [1]

2007-1550-F

kc1317

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P1 National Security Classified Information [(a)(1) of the PRA]
P2 Relating to the appointment to Federal office [(a)(2) of the PRA]
P3 Release would violate a Federal statute [(a)(3) of the PRA]
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b(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
b(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
b(9) Release would disclose geological or geophysical information concerning wells [(b)(9) of the FOIA]

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ALEX ROSS
219-0507

[001]

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July 21, 2000**

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USAID ACTIVITIES TO PREVENT PERINATAL TRANSMISSION OF HIV

April, 2000

USAID's goals are to compliment the advances made in simple drug regimens with the research necessary to implement actual programs in the field. Recent clinical trials using short course AZT, Combivir, and Nevirapine have paved the way to less costly interventions. However to realize the promise of these findings, additional work is needed to overcome the service delivery barriers, address the critical issues surrounding breastfeeding and replacement feeding, and to understand the impact these interventions will have on the communities they are intended to serve. Our goal is to link prevention of mother to child transmission of HIV (PMTCT) to our overall child survival, HIV prevention, safe motherhood, and reproductive health services. Currently we have activities in Kenya, Zambia, and Zimbabwe. In addition to these current activities, our missions are in discussion with a number of other governments to initiate PMTCT programs. It is likely that we will assist with the provision of VCT services, improvements in antenatal care, as well as monitoring and evaluation.

KENYA/ZAMBIA

This multi-site study in Kenya and Zambia assesses the effectiveness, acceptability, operational barriers, costs, and impact on child morbidity and mortality of a package of services in antenatal clinics. Among other things, the research examines voluntary HIV counseling and testing, the provision of antiretroviral drugs and breast milk substitutes to HIV-infected mothers and the overall efficacy of this package of interventions to prevent HIV infection. Milestones to date include the development of a research protocol, needs assessments in clinics and communities, training materials for health care workers, and development of a monitoring and evaluation plan in line with international guidelines. This research is being carried out with a wide array of local partners including government, academic and community stakeholders.

Objective and Methodological Approach: This study aims to develop a best practice in the prevention of mother to child transmission of HIV in resource constrained settings. The intervention addresses operational issues of access, acceptability, resources, and cost and will assess whether the project activities have resulted in a best practice on measures of availability of services, utilization, effectiveness, absence of adverse outcomes for the baby, and cost. The intervention package includes advocacy, strengthening of antenatal, delivery, and child health services, counseling, voluntary HIV testing, drug therapy, supporting women to make choices regarding infant feeding, and links to care and support.

The research component will:

1. Evaluate the implementation of a package of antenatal services for the prevention of mother to child transmission of HIV.
2. Systematically examine relevant service delivery variables including acceptability of the intervention by health staff and patients; direct and indirect costs; and use of these findings to enhance the potential for replication and sustainability.
3. Measure the effect of the interventions on the well being of the infant.
4. Measure the effect of the interventions on mother to child transmission of HIV.
5. Assess the effect of the interventions on the choices women make to reduce MTCT.

6. Assess the effect of VCT in the antenatal setting on assisting HIV negative women to protect themselves from infection.

Target Population: Pregnant women, their children, and their partners

Monitoring and Evaluation Plan: During FY00 the implementation of this activity will be monitored through periodic Horizons staff site visits, regular substantive progress reports, financial progress reports, meetings with the implementing organization(s) and principal investigator and research coordinator, and review of the activity work plan time table. This activity will be evaluated at the end of the activity period by Horizons staff together with the staff of the implementing organization(s). The principal evaluation criteria will be to compare the outcome of the activity against the objective(s) of the activity as listed in the activity proposal.

ZIMBABWE/ZVITAMBO

This is a study jointly funded by CIDA and USAID, of postpartum Vitamin A supplementation to newborns and postpartum mothers, whose purpose is to learn if this intervention will reduce infant mortality, reduce transmission of HIV via breastfeeding and reduce postpartum HIV infections of mothers.

The study is a double blind placebo controlled trial of 14000 mother infant pairs. Major outcomes for the study are infant mortality, the rate and timing of vertical HIV transmission, and post partum infection of mothers.

The study is designed to address the following key questions:

1. Does vitamin A supplementation of infants at birth reduce infant mortality?
2. Does vitamin A supplementation of infants at birth reduce the incidence of HIV infection via breastmilk?
3. Does vitamin A supplementation of mothers postpartum reduce the incidence of postpartum HIV infection?
4. What is the best way to inform HIV infected mothers about the risks of breastfeeding to their infants and the options that are available to them?

This study is being carried out in partnership with the University of Zimbabwe and the Harare City Health Department.

HIV/AIDS UPDATE ON NEVIRAPINE

April 13, 2000

In July 1999 the results of an NIH sponsored study of Nevirapine were announced. This study conducted in Uganda demonstrated that a single dose of Nevirapine given to HIV infected women in labor and to their infants after birth, could greatly reduce the transmission of HIV from mother to infant. Since that time many questions have arisen about the use of this drug. Below are responses to the most frequently asked questions regarding the drug Nevirapine.

Background: Since 1994 antiretroviral drugs have been shown to reduce the transmission of HIV to infants. AZT is the most studied drug but other antiretroviral drugs including Combivir (a combination of Lamivudine and AZT) and Nevirapine have shown efficacy in preventing peri-natal transmission in regimens that are realistic for developing country settings. These are not new drugs, simply new uses for existing drugs. They are very similar; they are oral drugs; they suppress HIV in the same way; and in the cases of AZT and Nevirapine, the U.S. price of both is about the same (roughly \$4 per pill). Combivir costs about \$9 per pill.

What is the difference between Nevirapine and other drugs for preventing MTCT?

The table below outlines the difference between the two drugs when used for prevention of MTCT.

	Short Course AZT	Nevirapine	Combivir
Dose	One pill twice a day for the last month of pregnancy.	One pill at the onset of labor, then some drops to newborn	Similar to Short Course AZT Plus one week to infant.
Number of pills	About 70	One + pediatric Syrup	Over 70
Cost	About \$50 in developing countries ¹	About \$5	Over \$100
Efficacy	Effectiveness appears to be similar ²		

Nevirapine clearly has the advantage in cost and ease of use. As this table shows, Nevirapine is currently the only drug that is effective as a single dose for mother and infant. This not only lowers the costs associated with preventing MTCT; it also allows for more discrete treatment of the mother and is only drug regimen that allows for intervention late in pregnancy. In settings where women often do not receive antenatal care this is a significant issue.

Are antiretroviral drugs safe for pregnant women and infants?

AZT has been used by pregnant women and infants for many years now with no evidence of birth defects or tumors. However AZT has produced tumors in the offspring of mice that were given near lethal doses. We have far less experience with Nevirapine in humans but in animal testing, no birth defects or tumors have been reported, even with very high doses. Since this drug is given in labor, after the critical periods of fetal development have passed, it is unlikely to have developmental effects on the infant. The U.S. Centers for Disease Control is maintaining a registry of children exposed to antiretroviral drugs to aid in identifying effects that might not appear until later in life.

Recent news from South Africa has raised new safety issues for Nevirapine. Five deaths have been reported in a trial of combination therapy for people with AIDS. Nevirapine was one of four drugs under study including a new experimental drug. While these results are tragic, it should be pointed out that (1) This trial did not involve pregnant women; (2) This was a trial of continuous treatment rather than a single dose of Nevirapine; and (3) It is not known what role Nevirapine played in these deaths. These results probably have no bearing on the use of Nevirapine for prevention of mother to child transmission.

¹ This price is lower than the \$4/pill cost would suggest because of a major price reduction for developing countries offered by the manufacturer.

² The two regimens have not been directly compared but based on the results of AZT studies in west Africa and one Nevirapine study in Uganda the two appear to have similar efficacy.

To: s
From: David Stanton@G.PHN.HN@AIDW
Cc:
Subject: urgent update on recent AIDS related news stories
Attachment: BEYOND.RTF
Date: 04/13/2000 8:22 AM

Colleagues,

This email responds to two recent news stories regarding AIDS. The first is the report regarding deaths in South Africa of participants in an AIDS treatment trial. The second is the announcement by WHO and UNAIDS regarding the use of Cotrimoxazole to prevent opportunistic infections.

South Africa: Last week a Reuters article out of South Africa reported that the government had halted a clinical trial of Nevirapine due to the deaths of 5 of the participants. The story gave some false impressions which must be clarified.

There have been no deaths to pregnant women taking single dose Nevirapine to prevent mother to child transmission. The reported deaths were among participants in a treatment trial of combination therapy (of which Nevirapine was one of four drugs under study). To our knowledge no pregnant women were in the study, and without further information it impossible to say which (if any) of the four drugs is considered responsible for these deaths. In her press conference the Minister of Health did state that the South African government wants to see further safety data on Nevirapine before using it to prevent mother to child transmission (MTCT). She cited a recent statement by WHO (attached) stating that it was too soon to move to wide-scale use of Nevirapine for MTCT. This statement did OK continued use in pilot studies.

Cotrimoxazole: Some good news. On April 5th a joint statement by WHO and UNAIDS endorsed (cautiously) the use of the antibiotic Cotrimoxazole for the prevention of opportunistic infections for persons with HIV AIDS in Sub-Saharan Africa. Cotrimoxazole is known by many names: Bactrim, Septra, Septrim, and Trimethoprim-Sulfamethoxazole. Cotrimoxazole is an antibiotic which since the late 1980's has been used in developed countries to prevent a number of life threatening opportunistic infections in persons with AIDS and other forms of immune suppression. The recent decision by UNAIDS and WHO to endorse the similar use of Cotrimoxazole in Africa is welcome news to USAID. The prevention and treatment of opportunistic infections is one of the major aims of the LIFE initiative and this decision paves the way for our programs to provide a significant, realistic, and cost effective intervention to prolong and improve the quality of life of people living with HIV-AIDS. This announcement could also enhance efforts to encourage people to seek voluntary testing and counseling. UNAIDS estimates the annual cost of prophylaxis to run between \$7 and \$18. This is a generic drug (no patents or license issues) and is on probably every essential drug list already.

There are some outstanding issues raised by this announcement. The first of which is the acknowledgment by WHO and UNAIDS that the wide spread use of Cotrimoxazole could lead to increased microbial resistance. This will require monitoring systems currently not in place. Second, even though Cotrimoxazole is safe and well tolerated, some persons will not be able to use it due to allergies and stomach upset. For these persons there is no inexpensive alternative available.

I have attached documents related to these two stories:

- 1 WHO NVP March 2000.doc
- 2 hiv aids update-nevirapine.doc
- 3 MTCT guidance to missions.doc
- 3 cotrimoxazol press release 4_4_00.doc
- 4 UNAIDS guidance on use of Cotrimoxazole.doc

David Stanton M.P.H.
USAID HIV-AIDS Division



HIV/AIDS Care and Support for Persons Living in Developing Countries

Discussion Paper on *Mother to Child Transmission of HIV*

Sub-Saharan Africa is suffering tremendously from the HIV/AIDS epidemic. Since the beginning of the epidemic, about 35 million Africans have been infected. As of 1998, there were about 22 million Africans living with HIV, including about 1 million children. In 1998 alone, about 4 million Africans became infected with HIV. This means that every *day* about 10,000 men, women, and children are contracting the virus.

Although the vast majority of people with HIV are adults who have contracted the virus from an infected partner, the problem of mother-to-child transmission has become increasingly important, and is estimated to be the cause of about 10 percent of all *new* infections and nearly 100 percent of all cases of pediatric HIV. In other words, about a half-a-million African babies become infected with HIV every *year*. Mother-to child infections are likely to increase because of the growing epidemic among women, particularly women less than 25 years of age. Data suggest that about 55 percent of all new infections in Africa occur among women. A startling 70 percent of these occur in women between 15 and 24 years of age - these are new infections among women who are beginning their reproductive lives.

Mother-to-child transmission of HIV can occur during pregnancy, at the time of delivery, and after birth through breastfeeding. In Africa, of 10 children born to HIV infected mothers, it is estimated that 2 will be infected during pregnancy or delivery, 1 will be infected through breastfeeding, and 7 will remain uninfected, even with continued breastfeeding. There are several conditions that make a mother more likely to transmit HIV to her baby. These include:

- high viral load (amount of virus in the body) due to recent HIV infection or advanced disease (AIDS);
- untreated sexually transmitted infections;
- prolonged rupture of membranes during labor;
- invasive delivery procedures that increase the likelihood of blood interchange between mother and baby;
- non-exclusive breastfeeding during the first months of life (i.e., breastfeeding with additional milk, formula, water, solid foods, etc.); and
- breastfeeding while experiencing breast infections, such as mastitis and abscesses.

A combination of interventions are needed to reduce mother-to-child transmission of HIV:

- Primary prevention of HIV among women, including behavior change interventions; decision making and negotiation skills; early diagnosis and treatment of sexually transmitted infections; and increased condom use are important strategies for preventing HIV infections in mothers.
- HIV voluntary and confidential counseling and testing services must be available and accessible to pregnant women and their partners so that families can make informed choices about their reproductive lives.
- Health workers and other care givers need to be skilled in counseling HIV-negative women and their partners about how to avoid risky behaviors, and in counseling HIV-positives on how to discuss their situation with their families and to live positively with the disease.
- Health workers need to understand the risk factors and practices that increase the likelihood of mother-to-child transmission of HIV; they must be able to follow safe birthing practices; and they must be able to counsel women about infant feeding options, including safe breastfeeding and appropriate replacement feeding during the first two years of life.
- A package of antenatal interventions, including essential drugs, must be available for all women without discrimination.
- Antiretroviral drugs, if available, should also be given according to locally agreed upon protocols.

Key Issues Regarding the Use of Anti-retroviral Drugs To Prevent Mother to Child Transmission of HIV (MTCT)

Recently released scientific study results show that a short course of oral antiviral medications (Zidovudine or Nevirapine) can significantly reduce HIV transmission from mother to infant during gestation and birth. However these interventions still have significant safety, cost, capacity, social, and ethical implications, and their ability to provide true public health impact remains in doubt. USAID is now devoting approximately \$6 million to answering key questions surrounding MTCT interventions. The following issues need to be addressed:

Potential for increased deaths from the use of breast milk substitutes: Breast feeding by HIV positive mothers accounts for about one third of all MTCT. In Sub Saharan Africa, where diarrhea is the leading cause of death for children under 5, more children could die from the misuse of breast milk substitutes than would die from AIDS. Also, not breastfeeding carries other health risks, including from 2 to 20 times the risk of infant and child mortality, as well as significantly increased fertility among the mothers.

High costs in addition to the cost of antiretroviral drugs: *Drug prices are only a small fraction of the cost of MTCT interventions.* The actual cost of preventing one HIV infection ranges from \$800 to \$5000 depending on the cost of breastmilk substitutes, the proportion of pregnant women who are infected, and the capacity of existing antenatal services to implement MTCT interventions.

Lack of HIV testing in most of the world: More than 90% of all persons infected with HIV have never been tested. MTCT programs will need to include a substantial investment in voluntary counseling and testing programs in order to have a true impact.

Marginal health systems: Antenatal care programs are often overburdened. MTCT interventions need to be carried out in ways that do not threaten the quality of antenatal care for all women. Health planners need to budget for the cost of maintaining (or bringing antenatal services up to) basic standards of antenatal care.

High risk for discrimination: Women who are infected with HIV are at great risk for discrimination, rejection, and violence by their families and communities. MTCT interventions have the potential to disclose a woman's HIV status. This could happen in the health care setting but also could result from other components of MTCT interventions. For instance taking anti retroviral drugs during labor essentially discloses one's HIV status to those present. In many communities breastfeeding is the norm. To be seen giving breastmilk substitutes also discloses one's HIV status.

Need for additional research: There are many unanswered questions regarding MTCT interventions. The programs involving drugs are largely untested. Some of the issues include: how antenatal clinics can best absorb new, technically complicated tests and service delivery; how best to safely inform or advise women about infant feeding and the risk of HIV infection; how to safeguard confidentiality of women; and how MTCT interventions can be made affordable and sustainable. In addition, policy guidance is needed regarding care of the HIV infected mother after birth.

Realizing opportunities: Despite the current questions and concerns, carefully implemented MTCT programs have the potential not only to save the lives of infants, but also to serve as a catalyst for improving and expanding HIV and antenatal services. MTCT programs highlight the need for expanded voluntary counseling and testing, for high quality prevention programs for women who test negative for HIV, and for expanded programs to care for those infected with HIV. The provision of MTCT services instead of being a burden on antenatal services could bring the resources needed to provide quality services for pregnant women.

5

MOTHER TO CHILD TRANSMISSION (MTCT) OF HIV

Mother to child transmission (MTCT) accounts for about 10% of new HIV infections. Interest in measures to reduce MTCT in developing countries has increased following a number of studies showing relatively inexpensive doses of antiretroviral medications such as Zidovudine or Nevirapine combined with replacement of breastfeeding reduced pre- and peri-natal transmission of HIV up to 50%.

The current approach to preventing MTCT combines three core elements: voluntary counseling and testing (VCT), antiretroviral drugs (ARV), and replacement feeding (RF). This approach, however, has not been examined outside of research settings and carries risks for the women and children it is intended to help. In addition, this approach may exceed service capacity and has significant cost, behavioral and ethical implications.

This document provides a brief technical discussion of these issues and offers advice, developed by representatives of Global and Regional Bureaus and their cooperating agencies, for USAID missions addressing the question of MTCT of HIV/AIDS.

- **MTCT causes approximately 600,000* of the 6 million new HIV infections annually.** Of 10 children born to HIV infected mothers, about 2 will be infected during pregnancy or delivery, 1 will be infected through breastfeeding, and 7 will remain uninfected, even with continued breastfeeding. The impact of this level of transmission is likely to increase due to the growing epidemic among young women.

- There are many interventions that may reduce MTCT. Recently, much attention has been given to the provision of voluntary counseling and testing (VCT), along with short-term antiretroviral drugs, and replacement feeding (ARV and RF).

- **VCT:** It is estimated that no more than 10% of HIV-infected persons in developing countries have ever been tested. Therefore, voluntary counseling and testing, which is central to many treatment and prevention activities, is a critical component of this approach to prevent MTCT.

- **ARV:** Antiretroviral drugs given during the last weeks of pregnancy, during labor, and to infants, can greatly reduce the transmission of HIV from mother to child.

- **RF:** Children who escape HIV infection during pregnancy and delivery are still at risk for

infection through breastfeeding. The use of breastmilk substitutes, or RF, is a consideration in MTCT interventions. However, not breastfeeding carries other health risks, including 2 to 20 times the risk of infant and child mortality, as well as significantly increased fertility among the mothers.

- UNICEF, funded by the Turner Foundation and in collaboration with the UNAIDS Secretariat, has started to pilot interventions to prevent MTCT in about 11 sites, mostly in Africa.

- USAID has devoted approximately \$5 million in 1999, out of our HIV/AIDS budget of \$125 million, and close to \$1 million in PHN core child survival funds, to address some of the key questions surrounding these and other MTCT approaches.

RECOMMENDATIONS:

- **Continue support for primary prevention of HIV infection.**

- **Continue to support primary health care interventions: breastfeeding, the Code of Marketing of Breastmilk Substitutes, and maternal and child survival efforts.**

- **If a mission chooses to support a prevention of MTCT pilot study, we recommend that process, outcome, and long term monitoring and evaluation of the impact on overall health and mortality be among the first priorities.**

* There are about 12-15 million child deaths annually from all causes combined.

MTCT ISSUES AND CONCERNS

MTCT interventions may have an adverse impact on other health services.

MTCT interventions add a complicated set of tasks to clinical settings, which are often already overburdened. Program managers need to know whether antenatal clinics are able to handle the added burdens of MTCT interventions. While HIV/AIDS is a growing and deadly threat to individuals and to societies, we must be sure that we do not harm active health services currently in place and saving lives in order to more fully address HIV/AIDS. At highest risk are the new maternal health initiatives and preventive child health services. The interventions may divert funding from these critical services. On the other hand, it has been suggested that concerns about HIV/AIDS might serve as catalysts to increase attention to maternal and infant mortality, thus increasing resources.

We have limited experience with implementing programs to inform the general public and counsel HIV+ women about safe breastfeeding and replacement feeding practices

In developing countries, infectious diseases, such as diarrhea and pneumonias, continue to be the leading cause of death among children under 5 years of age. Breastfeeding, through immune activity and nutrition, protects against the morbidity and the mortality of these diseases. Therefore, replacement feeding can be life threatening. RF also leads to significantly increased fertility for the woman. In Africa, where the average duration of breastfeeding approaches 2 years, RF preparation is difficult and costly for the family. Misunderstanding or misuse also could erode community breastfeeding norms. Research is needed to guide the implementation of programs that counsel and support HIV+ women who have been tested and know their status on the risk and options for feeding their infants.

Safeguarding confidentiality of participants is critical and very difficult.

Women who are known, or believed, to be infected with HIV are at great risk of discrimination and rejection by their families and communities. The issues of anonymity begin with the provision of VCT in health care settings and extend to every aspect of MTCT interventions. Childbirth is a social event in some societies with many family members in attendance; taking ARV during labor discloses one's HIV status to those present. In addition, breastfeeding is the norm in many communities, so to be seen using breastmilk substitutes discloses one's HIV status in these settings. Reports from some of the pilot sites confirm that cultural norms and fear of stigma prevent women from using RF even when it is made available at low or no cost.

We do not know the full cost of these interventions.

Drug prices are only a small portion of the overall price tag for MTCT interventions. Other costs include VCT for all women, social and personal costs, costs of training healthcare workers, costs of improvements in healthcare infrastructure, costs of breastmilk substitutes, and the cost of the support services needed to make breastmilk substitutes as safe as possible.

USAID estimates that the total costs per HIV infection prevented by an MTCT program including VCT, ARV, and RF can range from as low as \$800 to as high as \$5000. This amount depends on the proportion of women who are infected, the use and cost of the replacement feeding, and the excess health services that such feeding demands.

WHAT USAID MISSIONS CAN DO TO ADDRESS MTCT

1. **DO support primary prevention for women and for the general population, especially youth, and among pregnant and lactating women.**

Certainly, the best way to prevent mother-to-child transmission is through primary prevention of HIV/AIDS, especially among women of reproductive age or younger. Prevention efforts include behavior change interventions; STI diagnosis, treatment and prevention; and social marketing of condoms. Prevention efforts work and inevitably reduce MTCT. Continued and expanded support of prevention efforts focusing on reduction of HIV/AIDS in the general population, especially among youth and those who are currently of reproductive age, is likely to have the greatest impact on MTCT.

HIV infection during pregnancy and breastfeeding is associated with a higher level of transmission to the infant than occurs if the mother was already infected before pregnancy. This emphasizes the importance of not only testing pregnant women but also investing in prevention before, during and after pregnancy.

The risk of HIV infection to women during the pre- and post-partum period may be higher than at other times for a number of reasons:

- Most new mothers are in the high-risk age group;
- Pregnant women have clearly had unprotected sex;
- In some countries, women are more likely to abstain from sex with husbands or partners during this time. The men may seek sexual relations elsewhere, exposing themselves and, eventually, their partner and her children, to increased risk of HIV;
- Many women in these groups are nutritionally and immunologically compromised.

Data from Uganda show that the percent of pregnant women found to be HIV+ in 12 sentinel sites was significantly decreased following HIV/AIDS education, voluntary counseling and testing, condom promotion, and political leadership. Preventing HIV infection among

women during their pregnancy and during the years of breastfeeding would significantly reduce mother-to-child transmission of HIV/AIDS.

2. **DO continue to support breastfeeding for all mothers and infants UNLESS the mother has been tested and found to be HIV positive. Continue to support the principles of the Code of Marketing of Breastmilk Substitutes.**

Even in countries with the highest levels of HIV infection, the majority of pregnant women remain uninfected. And, even among the HIV+ women, the majority of their infants remain uninfected.

Current guidance suggests that breastfeeding, exclusive for the first six months, and sustained for 2 years or more, is by far the best source of nutrition and the most cost-effective disease fighter in areas with a high burden of infectious disease. In areas of high infant mortality rates, any reduction in breastfeeding will increase fertility rates and can have dire consequences on infant and child survival.

Although current advice in the United States is that women who test positive should not breastfeed, breastfeeding still should be considered in many situations worldwide. Why? Even if a woman is HIV positive, chances are nearly 2 out of 3 or better that her infant will not become infected. Those children who are denied the benefits of being breastfed may suffer 2-20 times the mortality of their breastfed peers. These risks must be considered in program and policy decisions.

This difficult and complex decision concerning infant feeding choice should be based on adequate counseling, ready availability and affordability of RF, and the judgement as to the adequacy of the health care facilities available to handle the increased incidence of other diseases that will occur when children are not breastfed.

If breastmilk substitutes are available, affordable, and safe, and if adequate health care is available and affordable, then RF should be promoted as being safer than breastfeeding. If HIV-positive mothers are encouraged to use RF, then

breastfeeding should be promoted and protected among the general population.

We know very little about replacement feeding strategies; preliminary studies indicate that current recommendations cannot be implemented in impoverished settings due to complexity and cost. Local options for replacement feeding must be identified and evaluated, as well as counseling methods for imparting that information to mothers. Feasible recommendations must be developed that will maximize the health and well being of mothers, their infants, and their families. This should be accomplished in a manner that is not in violation of the International Code of Marketing of Breastmilk Substitutes.

3. It is in USAID's interest to encourage the rigorous monitoring and evaluation of current MTCT pilot programs.

Missions considering support for the UNICEF or other such pilots should take steps to ensure the quality of evaluation. **The replicability, as well as the generalizability, of findings from the pilot sites are of great significance at this early stage of the development of these interventions. Of special importance is the long-term monitoring of the impact of these interventions on overall health and survival.**

USAID is currently supporting studies that will allow us to assess other interventions and to better understand the risks inherent in alternative MTCT interventions. Perhaps, more importantly, USAID studies are being designed to discover how these risks can be minimized. **If a mission chooses to support a MTCT pilot study, we recommend that process, outcome, and long term monitoring and evaluation of the impact on overall health and mortality be among the first priorities.**

Mission support of the evaluations might include technical input into development of plans and policies for pilot activities, including support for monitoring and evaluation. The greatest concern is that the outcomes of these costly and specially selected "pilots" will be misinterpreted and/or over generalized, and then replicated in areas or circumstances where the findings do not apply.

Another important area for study is how to reduce transmission through breastfeeding. Informed women choose to breastfeed for a variety of social, cultural, and economic reasons, as well as for infant and child survival, and economic reasons. There are conditions, including mastitis, cracked nipples, and damage to the infant's mouth or gut caused by infections or by use of other milks, that may enhance passage of the virus.

4. Do continue other activities in Mission portfolios that might contribute to increasing infant survival and reducing HIV transmission, with concomitant reduction of MTCT, such as:

HIV/AIDS Programs –

- "Beyond awareness" campaigns
- Condom promotion
- Policy dialogue
- VCT for all

Other Health Programs –

- Reproductive health/FP/STI centers
- Breastfeeding support networks
- Child and Youth initiatives
- Maternal health initiatives
- Malaria prevention/treatment programs
- Health communications, education and counseling programs

QUESTIONS?

Detailed documents and technical assistance on these issues are available. For further information, please contact:

David Stanton or Linda Sussman
G/PHN/HN/HIV-AIDS
Kristen Marsh or Miriam Labbok
G/PHN/HN/NMH

employees are treated like any other employee with a chronic life threatening condition," declared Fantan.

An AIDS activist Helen Ditsebe-Mhone who has also gone public about her positive HIV status, said she supports the Debswana move. "If you send people for training you would expect those people to work.

I think they are right," said Mhone, approving the Debswana stand. She does not feel that testing people for HIV and rejecting those who are positive is discriminatory.

However, Mhone suggested that those candidates who are found to be HIV positive should be counselled and empowered. She suggests that maybe Debswana should sponsor them for short-term courses.

"I do not want to see a situation where they are just telling people that you have tested HIV positive so we cannot give you a scholarship. They should not just dump them," she said.

If the candidates who are HIV positive were neglected, she said they would suffer two blows. Firstly they would lose the scholarship and then face the stigma of being HIV positive.

Mhone stressed that Debswana should come up with a comprehensive programme to address the problem. When contacted for comment, officials of Ditshwanelo - the Botswana Centre for Human Rights said they have arranged a meeting to discuss the matter with Debswana.

Candidates who are given scholarships by the government do not undergo an HIV test. Government policy on AIDS/HIV discourages discrimination against people who are HIV positive.

>>>>Reuters 11 April 00

AIDS KILLING MORE PEOPLE THAN FAMINE IN ETHIOPIA.

ADDIS ABABA, April 11 (Reuters) - Food shortages may be threatening the lives of up to eight million people in Ethiopia but certain death awaits at least three million people infected with HIV in the next eight years, health experts say.

Last year, nearly 300,000 people in Ethiopia died of AIDS-related illness - a rate of over 800 per day - and a further three million are believed to be infected with the HIV virus that will eventually lead to the deadly disease.

The toll is far higher than any figures relating to the food shortages in the Horn of Africa country and also threatens the most economically productive part of the population.

"AIDS is a far greater crisis facing Ethiopia than famine," one health expert told Reuters on Tuesday.

"At risk of sounding cynical, I am amazed at the reaction of the Ethiopian government and the West to the food shortages compared to their reaction to the AIDS crisis."

Last week, latest figures on Ethiopia's AIDS crisis showed that nearly 10 percent of the sexually active population - those aged between 15 and 49 - were infected with HIV.

Some 27 million of Ethiopia's 61 million people fall in that age group and those infected are projected not only to pass on the virus to tens of thousands of others, but also produce thousands of HIV-positive babies who will become orphans before probably falling to the disease themselves.

These figures are conservative estimates and based on testing at pregnancy clinics in mainly urban areas, experts say. The Ethiopian government has introduced public awareness campaigns, but health experts say privately that these are half-hearted and have had little impact.

"Perhaps the government feels vulnerable to blame if there is a national food shortage whereas contracting HIV is considered the fault of the individual," one said.

>>>>Reuters 11 April 00

SOUTH AFRICA FAILING TO TACKLE AIDS, WARNS BANK.

By Steven Swindells

JOHANNESBURG, April 10 (Reuters) - South Africa, with one of the world's highest HIV infection rates, is failing to act quickly enough to keep AIDS from ravaging the country, a leading investment bank warned on Monday.

The criticism by bankers ING Barings was the latest assault on Pretoria, which has been criticised for questioning the causal link between the Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS).

"The government really needs to formulate an AIDS strategy. It doesn't help when the government debates whether HIV causes AIDS. We can't waste any time," Kristina Quatteck, chief economist at bankers ING Barings told Reuters after the bank presented a study of the future economic impact of AIDS.

South Africa's government has incensed the scientific world by inviting AIDS dissidents - scientists who question the link between HIV and AIDS - to an international AIDS conference in July and allowing them on a panel of international experts.

Pretoria also attracted controversy by refusing to give the AIDS-retardant drug AZT to HIV-infected pregnant women or rape victims, citing conflicting scientific reports and its cost.

President Thabo Mbeki, who succeeded Nelson Mandela last June, questioned the efficacy of AZT in preventing infection and reducing the likelihood of transmission in the womb.

The country's health minister has also fanned the flames by accusing the scientific community of using South Africa as a dumping ground where drugs could be tried but most people would never benefit from them because they were unaffordable.

The need for a clear policy was made all the more pressing by the estimated 1,700 South Africans who become infected each day with HIV.

According to government statistics, about 12 percent of the country's 40 million people are HIV positive.

ING Barings' report, a year in the making, forecast that HIV infection rates would peak at almost 17 percent by 2006 and AIDS related deaths top off five years later at 256 AIDS deaths per 100 normal deaths.

AZT treatment could significantly change the future growth of HIV-AIDS, the bank said.

"The fact that there is a lack of policy response means that the AIDS epidemic is a dark cloud on the horizon," said Quattek.

The ING-Barings study showed that the population growth rate would stagnate by 2010, by which time 2.5 times as many South Africans would die of AIDS than any other causes.

>>>>Associated Press 11 April 00

AIDS to slash South Africa's economic growth, reports find

JOHANNESBURG, South Africa (AP) _ The AIDS crisis will cut South Africa's economic growth, increase inflation and exacerbate the country's shortage of highly skilled labor, according to newspaper reports Tuesday.

A new report from ING Barings concluded that the epidemic will cut South Africa's annual growth rate by .3 to .4 percentage points over the next 15 years, the Business Day daily reported.

Though the infection rate among highly skilled labor is only a third of that among less skilled, it is still enough to cause a shortage of highly skilled people, the Star newspaper said, citing the Barings report. That shortage is likely to increase inflation.

A third of South Africans are unemployed, but most of the jobless lack skills.

Barings criticized public and private policy for not presenting a clear strategy to combat the epidemic. It noted that uncertainty about the epidemic's effects deterred foreign investors.

A paper prepared by the World Bank to be discussed at a meeting next week of the International Monetary Fund and the World Bank in Washington, said "the epidemic poses the foremost challenge to development in sub-Saharan Africa."

Inaction by governments has played a crucial role in the disease's spread, the paper said.

Once the prevalence of AIDS in a population reaches 8 percent, the per capita growth is reduced by .4 percent a year, the paper said. According to the Actuarial Society of South Africa, 12 percent of South Africans are infected with HIV. The society predicts the infection rate will peak at 17 percent in 2006 and AIDS-related deaths will begin to decline about five years later.

In countries such as Zimbabwe, where the infection rate exceeds 25 percent, the annual per capita growth is slashed by at least a full percentage point, the World Bank paper said.

>>>>Associated Press 11 April 2000

UNESCO sponsors world education conference in Senegal in late April

PARIS (AP) -- A UNESCO-sponsored summit later this month on worldwide education will look at ways to improve learning amid debilitating crises such as widespread AIDS in Africa and gender discrimination, the group's director said Tuesday.

The World Education Forum, to be held in the Senegalese capital of Dakar from April 26 to 28, is expected to draw leaders including U.N. Secretary-General Kofi Annan and the presidents of Egypt, Nigeria, Senegal and Uganda.

Legislation prevents mandatory screening for HIV/AIDS on recruits or personnel of the SANDF.

Defence force spokesman Maj Fanie Pretorius said recently 254 SANDF members had committed suicide between 1994 and the end of January this year. Afusa secretary-general Nare Makgakga said: "We are opposed to compulsory tests for HIV/AIDS because they are illegal and will lead to many more soldiers committing suicide."

Makgakga quoted soldiers from the Seventh Battalion of the medical contingent saying they had been put under pressure to take the tests in February. Members of the battalion said authorities demanded everybody be tested, saying these were the orders of defence force chief Gen Sphiwe Nyanda.

Defence Minister Mosiuoa Lekota's spokesman, Sam Mkhwanazi, said it was not government policy to test troops unless they were part of a contingent that was to be deployed on a United Nations mission outside SA.

The union, which is on a recruitment drive, told a meeting in Johannesburg last week that it was concerned blacks had had to contend with more obstacles than any other grouping since integration. Makgakga called for an investigation of the "nature of the causes of suicide in the defence force", saying the problems seemed to afflict blacks more than others. He said it was disconcerting that 98% of cases of people going absent without leave, most dismissals and most cases of disciplinary action involved African soldiers.

The union said in light of a court martial moratorium passed last year by former defence minister Joe Modise, it was calling on all cases of soldiers court marshalled since 1994 to be reviewed.

The union again expressed disappointment with the low percentage of black, "particularly African soldiers", in positions of influence within the SANDF.

It also alleged that several soldiers from the former liberation forces occupied the same positions they had three years ago. "In terms of defence force regulations, a soldier must be considered for promotion after three years; or at the least, if there are no posts available, have a salary increment," Makgakga said.

He said: "We are working to end discrimination within the defence force. We want a person to be promoted on merit and nothing else. If the minister wants us to be a pressure group in that sense, then we are prepared to do that."

Referring to poor salaries, Makgakga said one of the problems was that soldiers working on a stand-by basis were "paid only R16,50 a day".

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>>>> Boehringer Ingelheim, 10 April, 2000 Boehringer Ingelheim Clarifies AIDS Drug reports

Ingelheim, Germany (Boehringer Ingelheim, April 10, 2000) - Media reports have focused on a triple combination study of AIDS drugs in HIV-infected adults in South Africa (FTC 302) conducted by Triangle Pharmaceuticals (located in Durham, North Carolina) to assess their investigational drug FTC (emtricitabine). Boehringer Ingelheim's AIDS drug nevirapine (VIRAMUNE) is one of the products involved in this trial.

News reports implied that nevirapine may have been associated with five deaths in the study. According to investigator reports, of the 470 patients enrolled in the trial (394 receiving nevirapine in combination with other antiretroviral treatments), two hepatic deaths were possibly related to nevirapine.

However, in a clinical trial in which patients are taking multiple drugs, it is not possible to determine with certainty, which drug, if any, may have caused the two deaths. The other three deaths were due to other specifically identified causes. According to news reports, there was also a higher than expected incidence of liver toxicity in the study. In fact, the incidence of liver toxicity seen in the study is in line with what is commonly seen in similar studies of triple combination antiretroviral therapies in HIV-infected individuals.

As with all potent antiretroviral treatments, there are known side effects of nevirapine as described in the product labeling. Boehringer Ingelheim takes all adverse events seriously and reports events to the health authorities internationally, and the company is further evaluating the study and intends to meet with the South African authorities to address questions.

Nevirapine has been studied extensively and has been approved in over 60 countries including Australia, Canada, South Africa, United States and in European countries. Large, multi-center international trials have shown that nevirapine, when used in combination therapy, can durably suppress the amount of HIV in the blood to undetectable levels (Atlantic, INCAS).

While not currently a labeled indication, nevirapine has also been shown to reduce mother-to-child transmission (MTCT) of HIV in a trial in Uganda (The Lancet, Sept 4, 1999). It has recently been added to the World Health Organization essential drug list as an option for the prevention of MTCT of HIV in the developing world. Contact: Ulrich Bock Corporate Public Relations Division
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>>>> All Africa News Agency, 10 April, 2000

AIDS: Rising Infection Rate Worries Prison Authorities

Blantyre (All Africa News Agency, April 10, 2000) - The first study of its kind in Africa initiated by the Penal Reform International PRI in 1998 to critically analyse the HIV/AIDS situation in Malawi's prisons has revealed that the spread of the epidemic has reached dangerous proportions in the country's gallows.

The findings of the study, which was initiated after the 1998 conference on HIV/AIDS in African prisons held in Dakar, Senegal, are published in a report called HIV/AIDS In Malawi Prisons.

The report says that over 50 prisoners die everyday in the country's prisons. Of the 8,400 cases treated at Zomba Central Prison Clinic during 1997, 25 percent



HIV/AIDS Care and Support for Persons Living in Developing Countries

Discussion Paper on *Mother to Child Transmission of HIV*

Sub-Saharan Africa is suffering tremendously from the HIV/AIDS epidemic. Since the beginning of the epidemic, about 35 million Africans have been infected. As of 1998, there were about 22 million Africans living with HIV, including about 1 million children. In 1998 alone, about 4 million Africans became infected with HIV. This means that every *day* about 10,000 men, women, and children are contracting the virus.

Although the vast majority of people with HIV are adults who have contracted the virus from an infected partner, the problem of mother-to-child transmission has become increasingly important, and is estimated to be the cause of about 10 percent of all *new* infections and nearly 100 percent of all cases of pediatric HIV. In other words, about a half-a-million African babies become infected with HIV every *year*. Mother-to child infections are likely to increase because of the growing epidemic among women, particularly women less than 25 years of age. Data suggest that about 55 percent of all new infections in Africa occur among women. A startling 70 percent of these occur in women between 15 and 24 years of age - these are new infections among women who are beginning their reproductive lives.

Mother-to-child transmission of HIV can occur during pregnancy, at the time of delivery, and after birth through breastfeeding. In Africa, of 10 children born to HIV infected mothers, it is estimated that 2 will be infected during pregnancy or delivery, 1 will be infected through breastfeeding, and 7 will remain uninfected, even with continued breastfeeding. There are several conditions that make a mother more likely to transmit HIV to her baby. These include:

- high viral load (amount of virus in the body) due to recent HIV infection or advanced disease (AIDS);
- untreated sexually transmitted infections;
- prolonged rupture of membranes during labor;
- invasive delivery procedures that increase the likelihood of blood interchange between mother and baby;
- non-exclusive breastfeeding during the first months of life (i.e., breastfeeding with additional milk, formula, water, solid foods, etc.); and
- breastfeeding while experiencing breast infections, such as mastitis and abscesses.

A combination of interventions are needed to reduce mother-to-child transmission of HIV:

- Primary prevention of HIV among women, including behavior change interventions; decision making and negotiation skills; early diagnosis and treatment of sexually transmitted infections; and increased condom use are important strategies for preventing HIV infections in mothers.
- HIV voluntary and confidential counseling and testing services must be available and accessible to pregnant women and their partners so that families can make informed choices about their reproductive lives.
- Health workers and other care givers need to be skilled in counseling HIV-negative women and their partners about how to avoid risky behaviors, and in counseling HIV-positives on how to discuss their situation with their families and to live positively with the disease.
- Health workers need to understand the risk factors and practices that increase the likelihood of mother-to-child transmission of HIV; they must be able to follow safe birthing practices; and they must be able to counsel women about infant feeding options, including safe breastfeeding and appropriate replacement feeding during the first two years of life.
- A package of antenatal interventions, including essential drugs, must be available for all women without discrimination.
- Antiretroviral drugs, if available, should also be given according to locally agreed upon protocols.

Key Issues Regarding the Use of Anti-retroviral Drugs To Prevent Mother to Child Transmission of HIV (MTCT)

Recently released scientific study results show that a short course of oral antiviral medications (Zidovudine or Nevirapine) can significantly reduce HIV transmission from mother to infant during gestation and birth. However these interventions still have significant safety, cost, capacity, social, and ethical implications, and their ability to provide true public health impact remains in doubt. USAID is now devoting approximately \$6 million to answering key questions surrounding MTCT interventions. The following issues need to be addressed:

Potential for increased deaths from the use of breast milk substitutes: Breast feeding by HIV positive mothers accounts for about one third of all MTCT. In Sub Saharan Africa, where diarrhea is the leading cause of death for children under 5, more children could die from the misuse of breast milk substitutes than would die from AIDS. Also, not breastfeeding carries other health risks, including from 2 to 20 times the risk of infant and child mortality, as well as significantly increased fertility among the mothers.

High costs in addition to the cost of antiretroviral drugs: *Drug prices are only a small fraction of the cost of MTCT interventions.* The actual cost of preventing one HIV infection ranges from \$800 to \$5000 depending on the cost of breastmilk substitutes, the proportion of pregnant women who are infected, and the capacity of existing antenatal services to implement MTCT interventions.

Lack of HIV testing in most of the world: More than 90% of all persons infected with HIV have never been tested. MTCT programs will need to include a substantial investment in voluntary counseling and testing programs in order to have a true impact.

Marginal health systems: Antenatal care programs are often overburdened. MTCT interventions need to be carried out in ways that do not threaten the quality of antenatal care for all women. Health planners need to budget for the cost of maintaining (or bringing antenatal services up to) basic standards of antenatal care.

High risk for discrimination: Women who are infected with HIV are at great risk for discrimination, rejection, and violence by their families and communities. MTCT interventions have the potential to disclose a woman's HIV status. This could happen in the health care setting but also could result from other components of MTCT interventions. For instance taking anti retroviral drugs during labor essentially discloses one's HIV status to those present. In many communities breastfeeding is the norm. To be seen giving breastmilk substitutes also discloses one's HIV status.

Need for additional research: There are many unanswered questions regarding MTCT interventions. The programs involving drugs are largely untested. Some of the issues include: how antenatal clinics can best absorb new, technically complicated tests and service delivery; how best to safely inform or advise women about infant feeding and the risk of HIV infection; how to safeguard confidentiality of women; and how MTCT interventions can be made affordable and sustainable. In addition, policy guidance is needed regarding care of the HIV infected mother after birth.

Realizing opportunities: Despite the current questions and concerns, carefully implemented MTCT programs have the potential not only to save the lives of infants, but also to serve as a catalyst for improving and expanding HIV and antenatal services. MTCT programs highlight the need for expanded voluntary counseling and testing, for high quality prevention programs for women who test negative for HIV, and for expanded programs to care for those infected with HIV. The provision of MTCT services instead of being a burden on antenatal services could bring the resources needed to provide quality services for pregnant women.

Summary of UV Waterworks Demonstrations Around the World

General Background

In economically deprived areas, waterborne diseases lead to illnesses and sometimes even death, especially in children. The unavailability or excessive cost of fuel prevents many families from boiling their water for disinfection before drinking it. A device for water disinfection was developed by DOE at the Lawrence Berkeley National Laboratory which allows water to be disinfected for much less energy than it would take to boil it.

This device, called Ultra-Violet Waterworks (UVWw) uses ultraviolet light to disable viruses, bacteria, and protozoa. It requires only 40 watts of electricity to disinfect the daily needs of 1000 people and was specifically designed to be inexpensive and low maintenance for rural village applications in the developing world. The device does not require a pressurized water source (it can work with a hand held pump and a surge tank) and can operate powered by photovoltaics, without access to grid electricity.

In 1996, researchers at Lawrence Berkeley National Laboratory licensed the system to Water Health International (WHI) in Napa, California. Water Health international holds an exclusive world wide license for the device (except for in India) and pays a 3.5% royalty on all sales, except those to the Federal Government, to the Lawrence Berkeley National Laboratory. The latest model can provide 10 liters of clean water daily to 1000 people at 10 cents per year per person. An individual device sells for about \$620. Larger devices are available.

South Africa

Under the Gore-Mbeki Binational Commission, the Department of Energy's Lawrence Berkeley National Laboratory worked with the South African Center for Essential Community Services to conduct a field test of UVWw at the "Lily of the Valley" AIDS clinic outside of Durban. This clinic is a hospice for abandoned infants with the HIV antibody. For infants infected with the antibody, clean water can mean the difference between life and death. At the hospice, the untreated water was contaminated with 4000 microorganisms such as E.coli per deciliter, while none were detectable after passing the water through the device.

A solar-powered UV Waterworks demonstration system was installed in 1998 at the Greenock Clinic, a rural health clinic located near Dundee, KwaZulu-Natal. The clinic sees approximately 40 patients per day, most of them children complaining of diarrhea caused by contaminated water. The clinic's own groundwater supply has been contaminated by nearby pit latrines but requires no pre-filtration before UV treatment.

This installation was made possible under a grant from the U.S. Department of Energy to the Lawrence Berkeley National Laboratory, using UV Waterworks units donated by WaterHealth International.

Philippines

WHI's Philippines distributor has established 37 "Aqua Sure" water stations in urban areas and 30 community water centers in rural areas of the Philippines. At these installations, people without access to reliable drinking water can buy water (which is treated by UV Waterworks™ plus pre-filters) for one-third the cost they are paying for bottled water.

Approximately 50,000 people are now being served daily by UV Waterworks™-treated water in the Philippines. In addition, the Rotary Club has allotted funds for nine Philippine public schools to be outfitted with community water centers.

Mexico

WHI installed its first integrated community water system near Acapulco in Zihuatenejo (Guerrero State), Mexico in late 1998. The system can provide clean water for 2,000 people daily. It includes sand and roughing filters to remove turbidity and cysts, solar panels for its electrical requirements, and UV Waterworks for treatment of bacterial and viral contamination. WHI recently installed 60 smaller-scale systems in rural clinics throughout Guerrero. An additional 40 systems will be installed in early 2000. Two non-profit organizations - A Cup of Water and the Clearwater Project - will install a community water disinfection system at Tunzingo, Guerrero, Mexico, in early 2000.

Bangladesh

In areas throughout Bangladesh where boreholes are heavily contaminated with arsenic, WHI's water disinfection systems provide an immediate alternative of switching to surface water as a source of clean drinking water. WHI installed its first Bangladesh demonstration unit in May 1999 with the support of Energy, which made a gift of WHI's equipment to the people of Bangladesh. The initial demonstration unit is a compact water station that includes four mechanical pre-filters to remove large particles, fine turbidity and cysts, a carbon filter to remove dissolved chemical contaminants, and a UV Waterworks unit to treat bacterial and viral contamination. The station can provide water for approximately 2,000 people daily.

WHI hopes to install additional community water systems in rural areas throughout Bangladesh in 2000. In doing so, WHI will work closely with the Bangladesh government, international agencies and respected Bangladeshi NGOs. In urban areas, Golden Fair Trading Company (WHI's agent in Bangladesh) is commercially marketing WHI's products.

Nigeria

In Nigeria, USDOE installed one unit outside of Abuja that Secretary Richardson dedicated, and DOE (with USAID) had hoped to deploy thousands of similar units in villages around the country. The whole program was dependent on USAID's efforts at organizing communities on the local level to be able to manage the operation and maintenance of simple community projects, like the UV waterworks. USAID's efforts at creating community level political entities have not met with the success they had hoped for, in spite of a major effort over the past two years, so they never felt it would be a good investment to provide communities with the waterworks, as they would be vandalized, stolen, or broken for lack of maintenance in a very short time. Unfortunately, this is what happened to the one unit installed in what is really a suburb of Abuja. The local chief took it over for his own use, some small parts broke, and the system was kaput in a very short time.

India

UV Waterworks technology was field tested in India and in 1996, Lawrence Berkeley Laboratory granted a license for its manufacture and sale in India to Urminus Industries in Bombay, which manufactures the outer shell of aluminum (as opposed to thermoplastics used by Waterworks International elsewhere in the world).

Possible Talking Points for
USG Meeting on AIDS
Vice President's Ceremonial Office
Friday, July 21, 2000
1:15 p.m.

- The Department of Energy was asked to come to this meeting today to discuss UV waterworks technology and its potential to be mixed with infant formula to combat AIDs transmission through mother's milk. We believe the technology has excellent potential but the Department of Energy does not have the funds to implement the technology.
- As you know, millions of South Africans do not have access to safe drinking water. In economically deprived areas, waterborne diseases lead to illnesses and sometimes even death, especially in children. The unavailability or excessive cost of fuel prevents many families from boiling their water for disinfection before drinking it.
- A device for water disinfection was developed by DOE at the Lawrence Berkeley National Laboratory which allows water to be disinfected for much less energy than it would take to boil it.
- This device, called Ultra-Violet Waterworks (UVWw) uses ultraviolet light to disable viruses, bacteria, and protozoa. It requires only 40 watts of electricity to disinfect the daily needs of 1000 people and was specifically designed to be inexpensive and low maintenance for rural village applications in the developing world.
- The device does not require a pressurized water source (it can work with a hand held pump and a surge tank) and can operate powered by photovoltaics, without access to grid electricity. The latest model can provide 10 liters of clean water daily to 1000 people at 10 cents per year per person. An individual device sells for about \$620.
- Under the Gore-Mbeki Binational Commission, the Department of Energy's Lawrence Berkeley National Laboratory worked with the South African Center for Essential Community Services to organize a field test of UVWw at the "Lily of the Valley" AIDS clinic outside of Durban. This clinic is a hospice for abandoned infants with the HIV antibody. For infants infected with the antibody, clean water can mean the difference between life and death. The biweekly monitoring of the unit indicated adequate performance with no detectable coliform bacteria in the water, reduced from 4000 microorganisms per deciliter.
- A solar-powered UV Waterworks demonstration system was installed in 1998 at the Greenock Clinic, a rural health clinic located near Dundee, KwaZulu-Natal. The clinic sees approximately 40 patients per day, most of them children complaining of diarrhea caused by contaminated water. The site test is ongoing. We have been struggling a bit with the second site, as we have encountered vandalism of some outdoor components of the PV-powered system, and some problems with the

reporting of the bacterial tests of the water quality. Researchers at LBNL visited the site in February, 200 and report that they believe that these problems have been now solved.

- In 1996, researchers at LBNL licensed their UV Waterworks disinfection system to WaterHealth International in Napa, California. WaterHealth International holds an exclusive worldwide license for the device and pays the government a 3.5% royalty. A U.S. government entity purchasing UV waterworks devices pays no royalty charge.

Potential for Distribution

- We examined three ideas for broad implementation of the UV Waterworks system in Africa.
 1. **USAID / Private Foundation funding:** UV waterworks system could be funded through grants to rural organizations. This costly on a broad scale but could be used to demonstrate the benefits of the technology and as a public relations effort to gain rural population buy-in.
 2. **Micro credit/Franchise sales:** With a micro-credit loan program, local water sales entrepreneurs could sell purified water and recover the cost to the equipment as well as enhance economic growth in the community.
 3. **Private Industry sponsorship.** The Department of Energy has been approached by the pharmaceutical industry regarding cooperation between UV Waterworks technology and drugs for combating AIDS. We plan to follow up with them to discuss this idea further.

Closing

- We are eager to work with other interested agencies to bring UV waterworks technology to bear on meeting this need.
- I have copies of our initial memo for Leon Fuerth (with a technology brochure) and a summary of world wide demonstrations of the device.

U.S. DEPARTMENT OF ENERGY
OFFICE OF INTERNATIONAL AFFAIRS

OFFICE OF AFRICAN AND AMERICAN
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FAX COVER SHEET

TO: Jim Babbitt	FROM: Andrea Lockwood
COMPANY:	DATE: 7/14
FAX NUMBER: 456-9500	TOTAL NO. OF PAGES INCLUDING COVER: 7
PHONE NUMBER:	SENDER'S PHONE NUMBER: 586-2518
RE: Request for information on UVWaterworks for Leon Fuerth	



Department of Energy

Washington, DC 20585

MEMORANDUM FOR

Leon Fuerth, Senior Foreign Policy Advisor to the Vice President

FROM:

David Goldwyn, Assistant Secretary
Office of International Affairs

A handwritten signature in black ink, likely of David Goldwyn, is written over the typed name and title.

SUBJECT:

UV Waterworks Technology: Gore-Mbeki Binational
Commission Experience and Potential Applications in
AIDS battle

Issue

You requested a brief backgrounder on the UV Waterworks technology that had been field tested in South Africa under the auspices of the Gore-Mbeki Binational Commission and the potential for its use in combining clean water with powdered infant formula to prevent the transmission of AIDS to infants through mother's milk.

We believe the technology has excellent potential and will examine some proposals for funding in this paper.

Background

Millions of South Africans do not have access to safe drinking water. In economically deprived areas, waterborne diseases lead to illnesses and sometimes even death, especially in children. The unavailability or excessive cost of fuel prevents many families from boiling their water for disinfection before drinking it. A device for water disinfection was developed by DOE at the Lawrence Berkeley National Laboratory which allows water to be disinfected for much less energy than it would take to boil it.

This device, called Ultra-Violet Waterworks (UVWw) uses ultraviolet light to disable viruses, bacteria, and protozoa. It requires only 40 watts of electricity to disinfect the daily needs of 1000 people and was specifically designed to be inexpensive and low maintenance for rural village applications in the developing world. The device does not require a pressurized water source (it can work with a hand held pump and a surge tank) and can operate powered by photovoltaics, without access to grid electricity. The latest model can provide 10 liters of clean water daily to 1000 people at 10 cents per year per person. An individual device sells for about \$620.

Under the Gore-Mbeki Binational Commission, the Department of Energy's Lawrence Berkeley National Laboratory worked with the South African Center for Essential Community Services to organize a field test of UVWw at the "Lily of the Valley" AIDS clinic outside of Durban. This clinic is a hospice for abandoned infants with the HIV



antibody. For infants infected with the antibody, clean water can mean the difference between life and death. A team from LBNL was in South Africa from July 19 to August 7, 1997, to set up and begin monitoring the performance of the UVWw system. The biweekly monitoring of the unit indicated adequate performance with no detectable coliform bacteria in the water.

Following this field test and field tests in India in 1996, researchers at LBNL licensed their UV Waterworks disinfection system to WaterHealth International in Napa, California. WaterHealth International holds an exclusive worldwide license for the device.

Potential for Distribution

We examined three ideas for broad implementation of the UV Waterworks system in Africa.

1. **USAID / Private Foundation funding:** UV waterworks system could be funded through grants to rural organizations. This is costly on a broad scale but could be used to demonstrate the benefits of the technology. This could also drive a public relations effort to gain rural population buy-in.
2. **Micro credit/Franchise sales:** With a micro-credit loan program, local water salesmen/entrepreneurs could sell purified water and recover the cost to the equipment as well as enhance economic growth in the community.
3. **Private Industry sponsorship.** The Department of Energy has been approached by the pharmaceutical industry regarding cooperation between proponents of UV Waterworks technology and drug manufacturers interested in combating AIDS. We plan to follow up with them to discuss this idea further.



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UV WATERWORKS™

UV WATERWORKS™ IS A TRADEMARK OF WATERHEALTH INTERNATIONAL, INC.

**RELIABLE,
AFFORDABLE
WATER
DISINFECTION**

WATER QUALITY
ASSOCIATION

MEMBER

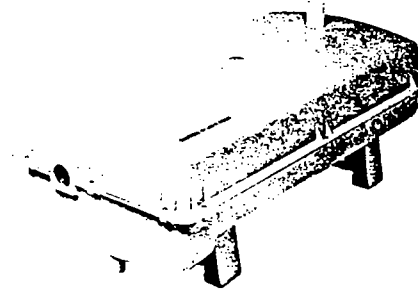


WaterHealth International, Inc. holds the worldwide patent rights (except India) for UV Waterworks. UV Waterworks was developed by and patent rights were obtained from the Lawrence Berkeley National Laboratory, Berkeley, California.

UV WATERWORKS

SAFE DRINKING WATER FOR SINGLE HOMES OR ENTIRE COMMUNITIES

UV Waterworks is an efficient, affordable water disinfection device that uses ultraviolet light to quickly and reliably disable bacteria and viruses in drinking water, making it safe to drink. Low purchase price, simple operation and low operating cost make UV Waterworks practical and affordable for a wide range of uses, from rural communities in developing nations to individual residences in developed countries that lack access to centralized water disinfection.



RELIABLY DISINFECTS 1,000 LITERS OF WATER FOR LESS THAN 5 CENTS

With no moving parts and requiring only 40 watts of power, UV Waterworks reliably disinfects 4 gallons of water (15 liters) per minute. That's enough to serve 500-1,500 people if used for drinking water and cooking at low usage rates, or up to 150 homes at higher usage rates.

PROVEN GERMICIDAL EFFECTIVENESS

UV Waterworks contains a germicidal ultraviolet (UV) lamp positioned over a shallow water pan. Water flows through the unit by gravity, staying in the chamber 12 seconds to ensure adequate disinfection. Delivering a UV dosage of over 80,000 microwatt-seconds per cm^2 , UV Waterworks disables 99.995% of water-borne bacteria and viruses.

* More often if the water contains chemicals that create a film on the water pan or a lot of solid matter.

** In the Ultra model the UV meter and solenoid valve must be replaced periodically.

EASY SET UP, LOW MAINTENANCE

UV Waterworks' small size, light weight and simple gravity-feed operation mean that it can be installed virtually anywhere there is a water supply and electricity. Maintenance consists only of cleaning the water pan with a damp cloth once every six months*, replacing the UV lamp once a year, and replacing the ballast at least every ten years.**

OTHER BENEFITS INCLUDE:

- UV Waterworks uses no chemicals. Imparts no taste or odor to water; has no risk of overdose.
- Does not require pressurized water to work.
- Costs less than comparable systems.
- Eliminates the need to purchase fuel or gather wood to boil and purify water.
- Suitable for a wide range of uses, including: rural communities, single residences with wells, farms, hospitals, and more.
- Easily powered by a car battery, a bicycle generator, wind, solar cells or a small hydroelectric source.



Discover Magazine's
Award for
Technological
Innovation
(Environment Category)



Popular Science Magazine's
Best of What's New Award

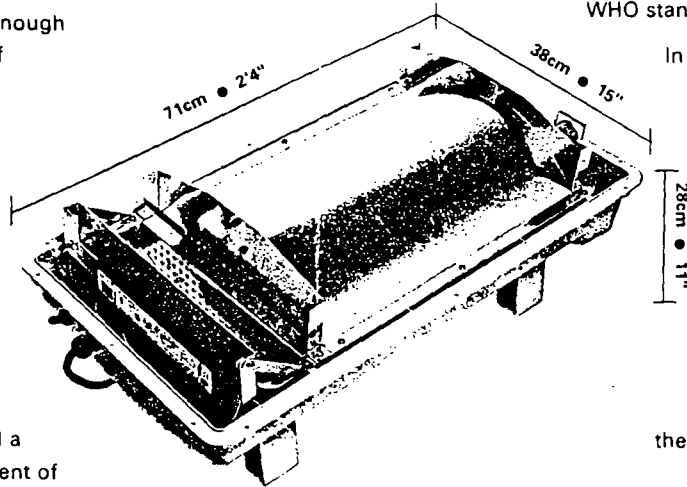
ANSWERS TO YOUR QUESTIONS ABOUT UV WATERWORKS

Q. HOW SAFE IS ULTRAVIOLET DISINFECTION?

A. EXTREMELY SAFE.

Rapid and inexpensive, UV light is a World Health Organization-approved method of disinfecting drinking water.¹ A UV dosage of 38,000 microwatt-seconds per square centimeter (cm²) disables the most virulent bacteria. Typical UV systems provide a dosage of 25,000-35,000 microwatt-seconds per cm².

UV Waterworks, however, delivers a minimum dosage of 80,000 microwatt-seconds per cm², more than enough to disable 99.995% of waterborne bacteria and viruses. UV disinfection is not generally recommended for long-term storage of water. UV Waterworks effectively disinfects water with up to 20 NTUs of turbidity and a UV extinction coefficient of .25/cm or lower. Turbidity can be reduced with a settling tank, sand filter or other type of filter.



Q. HAS UV WATERWORKS BEEN PROVEN UNDER CONTROLLED CONDITIONS?

A. YES.

Tests were conducted by the Lawrence Berkeley National Laboratory using World Health Organization (WHO) protocols. These demonstrated that when concentrations of colony-forming units of *E. coli* per 100 ml of water were more than 100,000 at the inlet of UV Waterworks, the concentration at the outlet was less than one, thus meeting the WHO standard for drinking water.

In separate tests, tap water with no residual chlorine was spiked with high concentrations of the infectious waterborne pathogens listed below. UV Waterworks effectively disabled all of the pathogens.

¹Guidelines for Drinking Water Quality, vol. 1, World Health Organization, Geneva, Switzerland, 1993, p. 135.

Q. HAVE FIELD TESTS PROVEN EFFECTIVE?

A. AGAIN, YES.

Weekly tests of UV Waterworks conducted over five months in several Philippine communities demonstrated that highly polluted water (run through a two-micron filter to remove solid matter) contained no measurable trace of bacteria or viruses after being treated by UV Waterworks.

UV Waterworks successfully treated contaminated ground water from a borehole at a children's clinic near Durban, South Africa. The water contains "wild" (as opposed to "laboratory") strains of bacteria, which are more resistant to UV treatment than clean water dosed with pure cultures of the same organisms.

Results: Before entering the UV Waterworks unit, the South African water contained an average of 3,000 colony-forming units per 100 ml of water, including 200 fecal coliforms per 100 ml. Water leaving the UV Waterworks unit contained no detectable coliforms (including *E. coli*) or other Enterobacteriaceae.

In addition, extensive tests by the National Water Commission of Mexico confirmed UV Waterworks' effectiveness.

SPECIFICATIONS

- **Maximum Flow Rate:** 15 liters (4 gallons) per minute
- **People Served:** 500-1,500 per unit (if used primarily for drinking water and cooking at low usage rates), or up to 150 homes (at typical U.S. water usage rates)
- **Cost per 1000 liters (one ton of water):** 4 cents U.S.
- **UV Dosage:** Exceeds 80,000 microwatt-seconds per cm² (more than enough to disable 99.995% of waterborne bacteria and viruses)
- **Power Consumption:** 40 watts (UVW Standard), 60 watts (UVW Ultra)

- **Voltage:** 120V AC, 220V AC or 12V DC
- **Length:** 71 centimeters (2 feet, 4 inches)
- **Width:** 38 centimeters (15 inches)
- **Height:** 28 centimeters (11 inches)
- **Weight:** 7 kilograms (15 pounds)

Note: UV Waterworks under standard operation does not treat parasites or micro-organism cysts with protective coverings such as *Cryptosporidium* and *Giardia*. Such organisms are effectively removed by a flocculating agent, settling tank or sand filter.

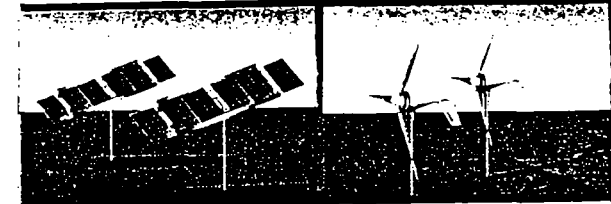
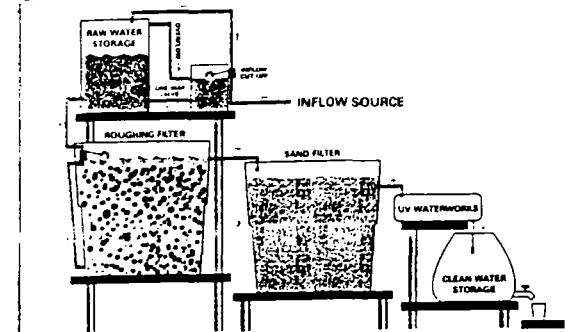
PATHOGENS TESTED AGAINST

- *Escherichia coli* (ATCC-10148)
- *Salmonella typhi* (NCTC-786)
- *Vibrio cholerae* (569 Inaba)
- *Streptococcus faecalis* (water isolate)
- *Clostridium welchii* (water isolate)
- *Shigella dysenteriae* (clinical isolate)
- *Proteus vulgaris* (clinical isolate)
- *Klebsiella aerogenes* (water isolate)
- *Enterobacter cloacae* (clinical isolate)
- *Pseudomonas aeruginosa* (Immunotype IV)

ADDITIONAL EQUIPMENT & SERVICES

WaterHealth International, Inc. offers the following equipment and services at additional cost. See product literature for more information.

- **Spare parts:**
UV lamp and 120V AC, 220V AC or 12V DC ballast.
- **Pressure control and water shutoff system:**
adjusts water flow from pressure source and controls water level in clean water storage tank.
- **Sand and roughing filters:**
filter out turbidity and larger pathogens not effectively treated by UV Waterworks (e.g., Giardia, Cryptosporidium, amoebae and worms).



- **Wind, solar or small hydroelectric power packages:**
wind turbines, solar panels and small hydroelectric power packages to operate UV Waterworks.
- **Installation and maintenance services:**
engineering information for installation of units and associated equipment.
- **Community education materials to assist communities to use the system properly.**

TECHNOLOGY SOLUTIONS

UV light brings cheap, clean water to HIV babies

Near Durban, South Africa, an inexpensive ultraviolet disinfection system is providing very clean drinking water for abandoned infants with the HIV antibody. Not all of these babies are infected with the virus, but for the fraction that are, disinfected water can mean the difference between life and death.

The system takes advantage of the germicidal property of UV light, which only recently has been harnessed effectively enough to work in a community with a low level of technology. Following field tests in rural Indian villages (see *Biophotonics International*, March/April 1996, p. 30), researchers at Lawrence Berkeley National Laboratory in Calif., licensed their redesigned UV Waterworks disinfection system to WaterHealth International in Napa, Calif. With an exclusive worldwide license (except in India, where it is sold by Urminus Industries Ltd. of Bombay), WaterHealth is selling production models in developing countries including Mexico, Haiti, the Philippines, Uruguay, Brazil, Nepal and Bangladesh.

Berkeley physicist Ashok Gadgil and his group invented the system in response to a 1993 Indian outbreak of cholera. Based on the initial field tests and with new support, the Berkeley researchers re-engineered the system to be less costly and more compact, said Gadgil. A field test of the new design is in progress at the Lily of the Valley HIV Hospice in South Africa.

Other methods impractical

The two most common water disinfection methods are boiling and chlorination. Chlorine treats a broader range of organisms than UV and offers residual protection until it evaporates, but chlorination can be expensive and requires skilled maintenance as well as a supply of potentially hazardous chlorine. Boiling provides no residual protection against recontamination, such as from

dipping a soiled hand or pot into the cistern. Typically done over a biomass cookstove, boiling is the most effective treatment but is slow and labor-intensive, and can use as much as 20,000 times more energy than efficient UV treatment.

The simplicity, low cost and speed of UV disinfection justifies its use in less technological communities, despite the following limitations: UV light cannot treat nonbiological pollution nor the parasites *Giardia* and *Cryptosporidium*, and its disinfectant action offers no residual effect, leaving it susceptible to recontamination. However, simple mechanical devices such as a 10,000-lb sand-based roughing filter

can remove the larger parasites and other floating particles from the water, said Elwyn Ewald, president and CEO of WaterHealth. Collecting the disinfected water in closed containers can minimize the risk of recontamination.

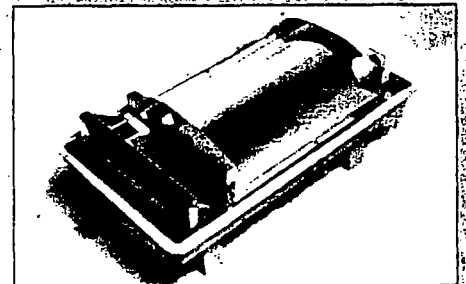
Other UV-based systems were impractical in the developing world because they require a pressurized water source. (These communities tend to use surface or hand-pumped water that is not pressurized.) In addition, because other systems submerge the UV bulb in the water, biological and chemical deposits accumulate on the bulb's protective sleeve and necessitate frequent cleaning by trained personnel.



With the UV disinfection system on the outside kitchen wall, clean water becomes available at the sink inside. Durban Metro Water plumbers and a Berkeley lab researcher installed a manufacturing prototype at an HIV hospice for a 1-year field test starting in August 1997. Courtesy of A. Gadgil.



Researchers hope to improve the water quality in developing communities permanently. Therefore, in addition to sampling the water, field tests address social factors such as community acceptance, education about sanitary practices, and local maintenance and management. Courtesy of A. Gadgil.



The plastic exterior of the production model protects it from the environment in hot as well as cold climates. WaterHealth is looking into field testing the unit in native communities in Alaska where clean unsalted water is scarce. Courtesy of WaterHealth International.

SPECIAL DOUBLE ISSUE

U.S. News & WORLD REPORT

DEC. 30, 1996-JAN. 6, 1997/\$3.50

Outlook '97

20 WAYS TO SAVE THE WORLD

ALSO
Toxic Fame,
Failed Predictions,
Buzzwords and
the Year
in Pictures,
1996



KEEP ON SALE UNTIL JAN. 31, 1997

■ EDITORIAL

A test for market forces: Clean water and UV light

BY PAULA DiPERNA

Recently, at a resort hotel on a water-short island, few people seemed concerned about water. The hotel went only so far as to discreetly place a small card near the sink that said, "Help us by keeping water use in mind." Meanwhile, in the restaurant, eager waiters kept topping up large glasses of iced drinking water almost the moment after a diner had taken a sip. Water shortages don't seem to mean a thing anywhere the affluent gather.

Yet severe water scarcities are among the most worrying trends for the future. The United Nations Industrial Organization (UNIDO) suggests that 1995's industrial water use could double by the year 2025, causing a four-fold increase in the pollution load on the world's fresh water.

At the same time, water-use inefficiencies persist, despite trends toward privatizing water services, and the world's poor people still cannot imagine the day when



clean water will be readily available to them, let alone to be taken for granted.

An encouraging sign is emerging currently on the water front, as a new technology developed over three years by a research team headed by innovative physicist, Ashok J. Gadgil of the Lawrence Berkeley National Laboratory, moves toward mass commercial application and, one hopes, closer to the people who need it most.

Gadgil held audiences rapt in June 1996, at the Habitat II conference in Istanbul, with his description of a gravity-driven water purification unit that uses ultra-violet (UV) light to remove bacteria and viruses from water to make it safe to use and drink. The costs were below negligible—roughly two cents per metric ton or about seven cents a year to disinfect one year's drinking supply for one adult.

• • •

Gadgil's apparatus seemed to hold out a promising solution so accessible and affordable, one would expect to soon find the UV units in every community lacking potable water around the world. Customers would hardly seem to be lacking. But, in a world focused on private sector forces as the solution for development, commercial viability of such new technologies has to be established, and customers must have enough money to buy.

A small group of investors who had heard of Gadgil's work have formed a for-profit company, WaterHealth International, with an initial capitalization of US\$300,000, and successfully negotiated a licensing and royalty agreement with the Livermore Laboratory for the rights to manufacture and market the UV water units worldwide, except in India, where a different firm was granted the rights. According to WaterHealth, a unit can purify water to meet the daily drinking and other potable water needs of 500 to 1,500 people in developing countries.



The unit requires only 40 watts of electricity to light the needed UV bulb, which means the water unit can run on a car battery or bicycle-pump generator. Where even such rudimentary power sources are lacking, separate power packs can be added to the water unit to harness solar or wind power, for \$600 to \$1,200 additional cost per unit, depending on local conditions. The power packs even generate surplus power that could be put to other uses.

This all means that about 1,000 people can have their daily water needs met, plus pick up some extra electrical power, for not more than \$2,000 in initial investment, with very low maintenance thereafter for the 15-year life of the unit. This is a cost roughly equivalent to a 10-day stay for one person in the hotel where water conservation seemed a mere footnote.

WaterHealth says the first UV units will be ready to ship this fall, and it has begun to establish networks of local retail distributors around the world, including micro-enterprises using micro-credit loans. But what can insure that the units will be priced at the retail level cheaply enough to be accessible to the rural poor, yet high enough to return a profit to permit continued mass production? Will governments be sufficiently motivated to meet their people's water health needs to buy and install the units if a community is too poor itself to do so? Or will governments shun this too as "subsidy"?

In short, will such an apparently appropriate and affordable technology get into the hands that need it most, especially since Gadgil himself is acutely mindful of the development needs of the poor.

The UV technology involved has gone from concept to practice, production and international outreach in just a few years—nearly record time—presumably because its viability seems a given. Thus, this relatively simple and inexpensive device offers a true chance for profitability demands and human needs to be met together. The test will be as clear as water.

THE EARTH TIMES

PUBLISHED BY THE EARTH TIMES FOUNDATION
A not-for-profit foundation duly certified as tax-exempt
under Section 501 (c) (3) of the US Internal Revenue Code
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Ranjit Sahni, Treasurer; Auditors: Rosenzweig & Maffei, Inc. (New York)
NEW YORK ADDRESS: 305 East 42nd Street, Suite 1316, New York, NY 10017
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DAILY INTERNET EDITIONS: <http://www.earthtimes.org>

contents

Seeking solutions

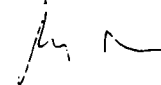
The work of the South African Centre for Essential Services (SACECS) has rapidly developed since the Centre's foundation in 1996 under a collaborative agreement between ESKOM and US-based EPRI.

SACECS endeavours to develop, demonstrate and utilise appropriate technologies to support the needs of communities in meeting their environmental challenges by creating opportunities for economic growth, development and social well-being.

This is the first issue of a quarterly newsletter planned by SACECS. Our objective is to continue to promote and market SACECS' activities and projects, and explore management strategies that will strengthen the synergy between ourselves, water utilities and the health care industries.

We are particularly proud of the solid relationships we have established with the MRC, WRC, FRD, CSIR, Umgeni Water, Rand Water and the Department of Water Affairs and Forestry in addressing issues of mutual concern.

By continuing with the strengthening of collaboration with critical stakeholders, we hope to be able to more efficiently and effectively influence national and regional government on social change and upliftment of communities.



Cynthia Motau, National Director



mechanical engineering

VOL. 119/NO. 7 JULY 1997

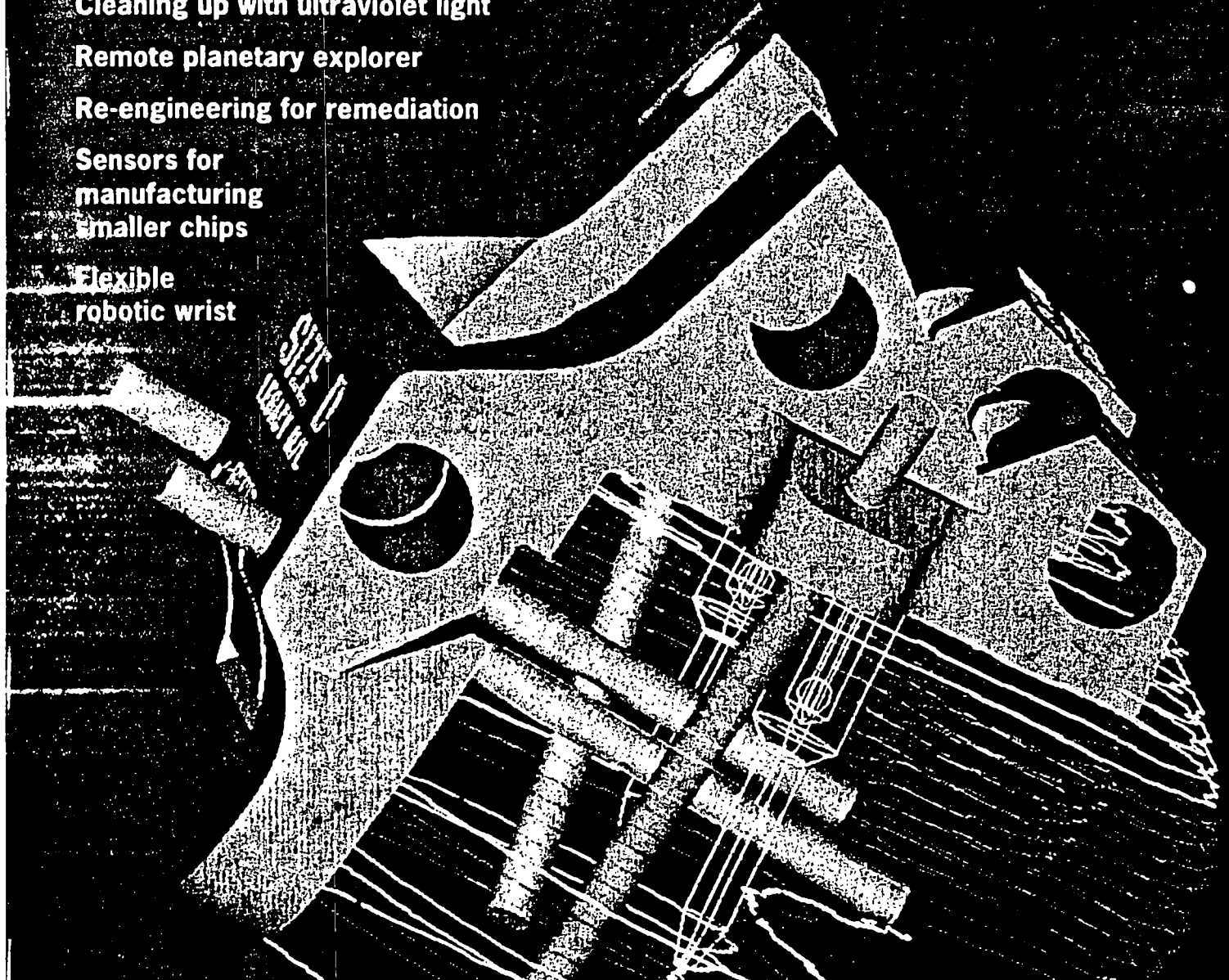
Cleaning up with ultraviolet light

Remote planetary explorer

Re-engineering for remediation

**Sensors for
manufacturing
smaller chips**

**Flexible
robotic wrist**



**Customizing
Biomechanical Parts**

ULTRAVIOLET LIGHT HAS a proven track record of killing bacteria and viruses found in municipal wastewater. In addition, environmental concerns over the use of chemical disinfectants, coupled with improvements in ultraviolet-lighting technology, have led to the development of UV systems that treat spent metalworking fluids in the industrialized world; disinfect drinking water in developing countries; and clean aquaculture water, ballast water, and hospital air everywhere.

Typically, chlorine gas or liquid is injected by a high-speed inductor directly into wastewater to kill bacteria before the water is discharged. "The main advantage UV has over standard disinfection techniques is that the light-based system eliminates the transport and use of chlorine," said George Tchobanoglous, professor emeritus of civil and environmental engineering at the University of California, Davis. "Even though the water is dechlorinated by the addition of other chemical compounds such as sulfur dioxide, residues of these toxic compounds remain in the water, which is a matter of increasing concern." Tchobanoglous chaired a committee of academic, industrial, and environmental consultants who drafted guidelines on UV disinfection for California in 1994.

Another factor leading municipalities to reconsider chlorination is its increased cost due to the national *Uniform Fire Code* adopted in 1993. This specifies double containment of stored chlorine and chemical scrubbers in case of leaks—both of which are expensive propositions.

"There are no residuals left by UV-light systems, whose effectiveness has been improved with the development of more-intense ultraviolet lamps. Now, one lamp can do the work of 20," Tchobanoglous said.

REPLACING CHLORINATION

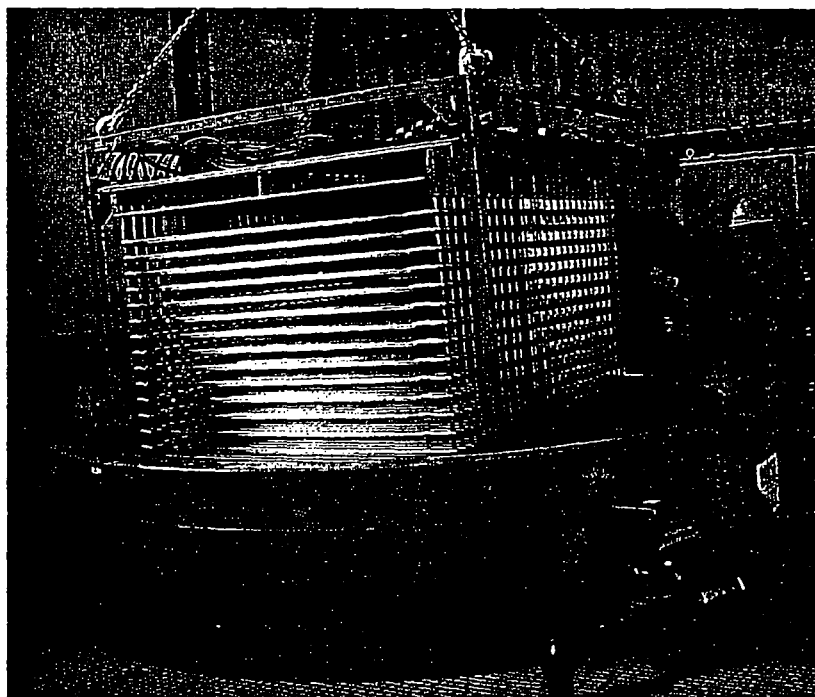
Only about 5 percent of American wastewater is currently treated by UV before being discharged, but the Electric Power Research Institute (EPRI) in Palo Alto, Calif., expects that figure to grow to 25 percent within 10 years.

The Central Contra Costa Sanitary District (CCCSD) in Martinez, Calif., is an example of UV's growing acceptance by U.S. municipalities. The district's treatment plant, located 45 miles from San Francisco, treats approximately 40 million gallons of wastewater per day before discharging it into Suisun Bay and San Francisco Bay. The plant's old treatment system, dating from the early 1970s, involved adding 3,500 pounds of chlorine daily,

along with 2,400 pounds of sulfur dioxide per day to neutralize the chlorine.

CCCSD reconsidered its chlorination strategy in 1990, when community groups expressed concern about the possible accidental discharge of chlorine gas into the air. In addition, provisions of the Clear Air Act required limiting worker exposure to chlorine fumes, and provisions of the looming fire code specified the installation of an expensive leak-containment system to prevent such discharges.

In 1991 CCCSD plant management compared the costs of continuing to use chlorine treatment with those of three other disinfection strategies: hypochlorite, ozone, or UV treatment. Hypochlorite cost about twice as much as chlorine on an annualized basis and ozonation



Water authorities are replacing chlorination by using banks of UV lamps, shown here being cleaned of sediment, to disinfect municipal wastewater.

was even more expensive, but three UV systems were comparable to the cost of chlorination and dechlorination. An additional factor favoring UV treatment was an unused concrete denitrification channel in which lamps could be installed.

A large-scale pilot plant capable of treating less than 1 million gallons per day was built on-site by Los Angeles-based Montgomery Watson and CCCSD in 1992. It demonstrated that UV was just as effective as chlorination in killing bacteria and slightly more effective in destroying viruses found in the Martinez plant's wastewater. It also showed the lamps would need to be cleaned of fouling every two to four weeks.

Montgomery Watson designed the UV system, which was installed in October 1996. Water is piped to a treatment channel that is covered by a clear plastic lid to reduce algae growth. Eighteen banks of low-pressure mercury ultraviolet lamps made by Bailey-Fischer & Porter Co. in Warminster, Pa., line the sides of the chan-

Triton Thalassic Technologies designed a specialized ultraviolet geometry, gas combination, and fluid dynamics that enable its UV technology to emit a monochromatic wavelength that kills bacteria in machining fluids without damaging the fatty acids that provide the fluids' performance characteristics.



Beams from these louvered UV lamps draw in tuberculosis germs by air convection, thus preventing the disease's spread in hospitals and homeless shelters.

the ammonia produced by fish breeding. T&I is working closely with the Biotechnology Center at the University of Connecticut in Storrs, anticipating a state-funded project to adapt its UV technology to treating aquaculture water. Ressler said his company will be field-testing FASTAC in tilapia, flounder, and salmon aquaculture facilities this fall.

T&I originally aimed its UV technology at dealing with industrial-plant zebra mussel fouling and treating contaminated ballast water discharged by cargo ships and tankers, and it has continued to develop these applications. Discharged ballast water has introduced nonindigenous species into countries, including the United States, where they have no natural enemies. As a result, these foreign creatures often proliferate to the point where they pose an environmental and economic problem. The best-known example is the zebra mussels that have clogged industrial and power-plant intakes along the Great Lakes (see "Power Plant Pest," Input/Output, March 1991).

T&I was first approached by its automotive client when it presented its UV technology as an alternative to using chemical biocides to kill the zebra mussel at the Zebra Mussel Conference in February 1995, according to Ressler. Since that time, a congressional task force supporting the National Invasive Species Act and the United Nations' International Maritime Organization have become interested in using FASTAC in conjunction with prefiltration to kill virtually all the microorganisms in ballast water without using chemical biocides.

Ressler's company is in the design phase, and is lab-testing a FASTAC system to serve the typical commercial freighter plying the Pacific Ocean between the United States and the Far East. "The prototype system can treat the required 4,000-gallon-per-minute loading and discharge flow rates through a 12-inch-diameter

pipe, and we can easily scale up the system for larger vessels," Ressler said.

SAVING LIVES IN DEVELOPING COUNTRIES

In developing nations, 400 children under five years old die every hour from diarrheal diseases, including cholera and typhoid, that are transmitted by contaminated drinking water. Although UV treatment can kill these water-borne pathogens, such systems are often too expensive for third-world villages. Scientists at the Lawrence Berkeley National Laboratory in Berkeley, Calif., developed UV Waterworks, an inexpensive, low-maintenance UV treatment system specifically geared for developing nations (see "Cleaning Water with Light," News & Notes, August 1996).

The Berkeley design team was led by Ashok Gadgil, an ASME member and a physicist at Berkeley. "There was a lot of mechanical engineering involved in designing the UV Waterworks system," Gadgil said. "For example, we performed radiometrics calculations to ensure that the proper light intensity is maintained. We also analyzed the hydrodynamics of the flow to prevent a wide distribution of residence time for water flowing under the lamp. This ensures high efficiency."

UV Waterworks can be connected to the pumps common to most villages in developing countries in two ways. In the case of hand pumps, the unit is connected to a surge tank, typically holding 30 liters, that collects water from the pump. For electrical borehole pumps, the disinfecting unit is connected to a tank mounted on a small pedestal.

Water from either tank enters a stainless-steel chamber, and is bathed by UV light at 254 nanometers—the optimum frequency for killing bacteria—emitted by a single 36-watt standard mercury-vapor lamp positioned above the water without contacting it. This eliminates the need for and expense of the UV-transparent sleeve used on

please copy + mail to attendees -

"For your files - version with correct symbols"

GLOBAL OVERVIEW: PERINATAL INTERVENTION TRIALS [REVISED 04/06/00]

Lynne Mofenson, M.D. {IntnatTr.406}

ANTIRETROVIRAL STUDIES			
PHASE III, ZDV ONLY			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
THAILAND (CDC) □ 2 arm, PLACEBO control □ Non-breastfeeding □ N = 392 <u>** (COMPLETED 2/18/98; 51% EFFICACY OF ZDV)**</u>	Arm 1: 36 wks (300 mg bid) Arm 2: PLACEBO	Oral (300 mg q 3h) PLACEBO	NO DRUG NO DRUG
IVORY COAST (CDC) □ 2 arm, PLACEBO control □ Breastfeeding □ (Planned N = 1,200) <u>** (PLACEBO STOPPED 2/18/98; 37% EFFICACY @ 3 MOS; 24% @ 2 YRS [N = 248])**</u>	Arm 1: 36 wks (300 mg bid) ~~Arm 2: PLACEBO~~	Oral (300 mg q 3h) ~~PLACEBO~~	NO DRUG NO DRUG
IVORY COAST/BURKINA FASO (INSERM/ANRS) □ 2 arm, PLACEBO control □ Breastfeeding □ (Planned N = 780) <u>** (PLACEBO STOPPED 2/18/98; 38% EFFICACY @ 6 MOS; 30% @ 15 MOS [N = 389])**</u>	Arm 1: 36-38 wks (300 mg bid) ~~Arm 2: PLACEBO~~	Oral (600 mg x1) ~~PLACEBO~~	♀ only for 1 wk (300 mg bid) ~~PLACEBO~~

PHASE III, ZDV ONLY (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
NORTH THAILAND/ BANGKOK (Harvard) ☐ Currently enrolling (3/99 enrolled 970, projected enrollment ~ 100/mo) ☐ 4 arm factorial: LL/LS/SL/SS ☐ 076-like control ☐ Non-breastfeeding ☐ N = 1,554 ** (SS ARM STOPPED 3/99, INTERIM REVIEW OF 318 INFANTS, DUE TO SIG HIGHER TX RATE IN SS ARM THAN LL ARM (SS RATE 11%); RANDOMIZATION 1:2:2 CONTINUES IN REMAIN ARMS) **	Arm 1 (LL): 28 wks Arm 2 (LS): 28 wks Arm 3 (SL): 36 wks ~~Arm 4 (SS): 36 wks~~ (300 mg bid)	Oral Oral Oral ~~Oral~~ (300 mg q 3h)	Newborn only: 6 wks 3 days 6 wks ~~3 days~~ (2 mg/kg qid)

ANTIRETROVIRAL STUDIES

PHASE III, ZDV COMBINED WITH/OR OTHER ANTIRETROVIRALS

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
AFRICA (UNAIDS) – PETRA (Uganda/Tanzania/ S.Africa) COMBO: ZDV & 3TC ☐ 4 arm (AP + IP + PP; IP + PP; IP only; PL) ☐ Breastfeeding ☐ N = 1,792 ☐ Completed <u>** (PL STOPPED 2/98;</u> <u>50% EFFICACY AP + IP + PP</u> <u>37% EFFICACY IP + PP</u> <u>NO EFFICACY IP ALONE</u> <u>@ 6 WKS</u> <u>[N = 1357])**</u>	Arm 1:36 wks Arm 2:PLACEBO Arm 3:PLACEBO ~~Arm 4:PLACEBO~~ (300 mg bid ZDV 150 mg bid 3TC)	Oral Oral Oral ~~PLACEBO~~ (300 mg q 3h ZDV {if no AP, 600 mg ZDV → 300 q 3h} 150 mg q 12h 3TC)	♀ & newborn x 1 wk ♀ & newborn x 1 wk PLACEBO ~~PLACEBO~~ (♀: 300 mg bid ZDV, 150 mg bid 3TC) (infant: 4 mg/kg bid ZDV, 2 mg/kg bid 3TC)
UGANDA (HIVNet012) ZDV vs NVP ☐ 3 arm ☐ Breastfeeding ☐ N = ~ 1,500 <u>** (PL STOPPED 2/98; 7/99</u> <u>INTERIM ANALYSIS:</u> <u>47% EFFICACY OF NVP VS</u> <u>ZDV @ 14-16 WEEKS</u> <u>[N = 626])**</u>	Arm 1: NO DRUG Arm 2:NO DRUG ~~STOPPED 2/98:~~ Arm 3: NO DRUG	Oral ZDV (300 mg bid) Oral NVP (200 mg x1)) ~~PLACEBO~~	Newborn only: ZDV x1 wk (4 mg/kg bid) NVPx1 @72h [or @ discharge] (2 mg/kg) ~~PLACEBO~~

PHASE III, ZDV COMBINED WITH/OR OTHER ANTIRETROVIRALS (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
SOUTH AFRICA (Boehringer-Ingelheim) – SAINT <i>NVP vs ZDV/3TC</i> ☐ 2 arm ☐ No placebo ☐ Breastfeeding ☐ N = > 1,000 Ongoing	Arm 1: NO DRUG Arm 2: NO DRUG	Oral NVP (200 mg x1) Oral ZDV/3TC (600 mg, then 300 mg q 3h ZDV, 150 mg q 12h 3TC)	♀ & newborn: NVP x1 @24-48h (♀ 200 mg; infant 6 mg) ♀ & newborn ZDV/3TC x 1 wk (♀ 300 mg bid ZDV, 150 mg bid 3TC; infant 12 mg bid ZDV, 6 mg bid 3TC)
SOUTH AFRICA (Bristol-Meyers) <i>Ddl ± d4T vs ZDV (Thai)</i> ☐ 4 arm ☐ Phase II ☐ Formula-fed ☐ N = 360 Ongoing	Start @ 36 wks: Arm 1: ddl Arm 2: d4T Arm 3: ddl/d4T Arm 4: ZDV	Oral ddl Oral d4T Oral ddl/d4T Oral ZDV	Infant only: ddl x6 wks d4T x6 wks ddl/d4T x6 wks ZDV x6 wks
ETHIOPIA (Hopkins) <i>NVP vs NVP + 6wk PP</i> ☐ 2 arm ☐ No placebo ☐ Breastfeeding ☐ N = 970 Still in development	Arm 1: NO DRUG Arm 2: NO DRUG	Oral NVP Oral NVP (200 mg x1)	Newborn only: NVPx1 @ 72h (2 mg/kg) NVPx1 @ 72h, then once qwk for 6 wks

PHASE III, ZDV COMBINED WITH/OR OTHER ANTIRETROVIRALS (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
INDIA (Hopkins/NIAID) <i>NVP vs NVP + 6wk PP</i> ☐ 2 arm ☐ No placebo ☐ Breastfeeding ☐ N = 1,200 Still in development (collaboration with Ethiopia)	Arm 1: NO DRUG Arm 2: NO DRUG	Oral NVP Oral NVP (200 mg x1)	Newborn only: NVPx1 @ 72h (2 mg/kg) NVPx1 @ 72h, then once qwk for 6 wks
USA/Europe/Bahamas/Brazil (PACTG 316) COMBO: ZDV & NVP ☐ 2 arm ☐ 076 ZDV control ☐ Non-breastfeeding ☐ N = 1,200 Ongoing	Nonstudy (Nonstudy ARV regimen already receiving)	Arm 1: PLACEBO Arm 2: oral NVP (200 mg x 1) (+ Nonstudy IV ZDV in all ♀)	PLACEBO NVP x 1 @ 72h (2 mg/kg) (+ Infant nonstudy 076 ZDV)
MALAWI (Malawi/Fogarty) ☐ In development ☐ Post-exposure prophylaxis <i>NVP vs NVP + ZDV</i> ☐ In development, targeted for ♀ who did not receive NVP in labor ☐ Breastfeeding ☐ N = 1,780	No drug	No drug	NVP x1 @ 48-72h NVP x1 @ 48-72hr + ZDV 4 mg/kg bid x1wk

PHASE III, ZDV COMBINED WITH/OR OTHER ANTIRETROVIRALS (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
THAILAND (Harvard) ☐ Proposal in development ☐ Non-breastfeeding ☐ Discussion possible study with background standard Thai short-course ZDV ♀ AP/IP/infant PP, whether NVP adds benefit	In development	In development	In development
BOTSWANA (Harvard) ☐ Proposal in development ☐ Discussion possible study with background ♀ short ARV, to evaluate infant breastfeeding + ARV vs formula	In development	In development	In development

ANTIRETROVIRAL STUDIES

INTERNATIONAL PHASE I ZDV COMBINED WITH/OR OTHER ANTIRETROVIRALS

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
S.AFRICA, ZIMBABWE (HIVNET 023) ☐ Phase I, safety, 1 arm ☐ <i>ARV infant prophylaxis</i> ☐ Different infant NVP regimens ☐ Breastfeeding ☐ N = 75 Ongoing	All get: ZDV start @ 36 wks	All get: Oral ZDV 300 mg q 3h NVP 200 mg x1	Infant only for 6 mos: NVP 2 mg/kg (increase to 4 mg/kg @ age $\geq$ 3 wks) daily NVP 4 mg/kg (increase to 8 mg/kg @ age $\geq$ 3 wks) twice weekly NVP 4 mg/kg (increase to 8 mg/kg @ age $\geq$ 3 wks) once weekly
S.AFRICA ☐ Phase I & PK safety ☐ <i>Emtricitabine (FTC, Emivirine)</i> ☐ In combination with either ZDV or ZDV/3TC ☐ <u>COMPLETED</u> (CL ♀ 50% NONPREG; INFANT/♀ 77%) ☐ N = 14	21 day study: (RNA < 20,000) ZDV 300 mg bid OR (RNA > 20,000) ZDV/3TC bid x 21d PLUS Arm 1: FTC 750 mg bid day 15-21 Arm 2: FTC 750 mg bid day 8-21	?	?

INTERNATIONAL PHASE I ZDV COMBINED WITH/OR OTHER ANTIRETROVIRALS (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
THAILAND/BALTIMORE (HIVNET 022) □ Phase I, safety/PK: <i>PMPA</i> □ N = 25 Protocol development on hold due to lack drug availability	Nonstudy (All get Short ZDV [Thai] Standard ARV [U.S.])	Nonstudy (All get Oral ZDV [Thai] IV ZDV [U.S.])	Neonate: PMPA SQ @ birth & @ age 72h (dose TBD) (In U.S., all get Infant 076 ZDV)

ANTIRETROVIRAL STUDIES

U.S. PHASE I/II ANTIRETROVIRAL STUDIES

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
USA (PACTG 250) ☐ Phase I, <i>NVP</i> , N < 20 ☐ COMPLETED single dose ph I NVP/ZDV @ labor/newborn only ☐ *Current study: multiple dose, ♀ start NVP @38 wks	Start NVP @38 wks* & (Nonstudy 076 ZDV)	Oral NVP & (Nonstudy 076 ZDV)	Newborn only NVPx1 @ 72h & (Newborn nonstudy 076 ZDV)
USA (PACTG 321) ☐ Phase I, <i>Abacavir</i> , N < 20 ☐ Is study in neonates only ☐ Ongoing	Nonstudy (Nonstudy 076 ZDV)	Nonstudy (Nonstudy 076 ZDV)	Newborn only: Abacavir & 3TC/ZDV x 6wks
USA (PACTG 324) ☐ Phase I, oral <i>ZDV</i> , N < 20 ☐ Ongoing	Nonstudy (Nonstudy 076 ZDV)	Oral ZDV	Nonstudy (Newborn nonstudy 076 ZDV)
USA (PACTG 331) ☐ Phase I, <i>ZDV</i> in premies ☐ Ongoing	Nonstudy (Nonstudy 076 ZDV)	Nonstudy (Newborn nonstudy 076 ZDV)	Newborn ZDV dose: 1.5 mg/kg q 12hr
USA (PACTG 332) ☐ Phase I, <i>d4T</i> , N < 20 ☐ ♀/nb also get 3TC ☐ Done for data for ♀ health purposes ☐ Ongoing	Start d4T @ 14-34 wks & 3TC	IV d4T & 3TC	Newborn only d4T x 6 wks & 3TC

U.S. PHASE I/II ANTIRETROVIRAL STUDIES (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
USA (PACTG 353) ☐ Phase I, <i>Nelfinavir</i> , N = 10-20 ☐ Combination with ZDV/3TC ☐ Ongoing	Start NEL @ 28-34 wks & 3TC/ZDV	Oral NEL & 3TC/IV ZDV	♀ & newborn Oral NEL & 3TC/ZDV
USA (PACTG 354) ☐ Phase I, <i>Ritonavir</i> , N = 10-20 ☐ Combination with ZDV/3TC ☐ Ongoing	Start RTN @ 28-34 wks & 3TC/ZDV	Oral RTN & 3TC/IV ZDV	♀ & newborn Oral RTN & 3TC/ZDV
USA (PACTG 358) ☐ Phase I, <i>Indinavir</i> , N = 10 ☐ Combination with ZDV/3TC ☐ Ongoing	Start IND @ 14-28 wks & 3TC/ZDV	only 3TC/IV ZDV	♀: Oral IND & 3TC/ZDV Neonate: only 3TC/ZDV x 6wks
USA (PACTG 386) ☐ Phase I, <i>Saquinavir</i> , N = 10 ☐ Combination with ZDV/3TC ☐ Ongoing	Start SAQ @ 14-32 wks & 3TC/ZDV	Oral SAQ & 3TC/IV ZDV	♀: Oral SAQ & 3TC/ZDV Neonate: Only 3TC/ZDV x 6wks
USA (PACTG 357) ☐ Phase I, <i>Abacavir</i> , N = 10 ☐ Combination with ZDV ☐ In development	Start Abacavir @ 28-34 wks & 3TC/ZDV	Oral Abacavir & 3TC/IV ZDV	♀ & newborn Oral Abacavir & 3TC/ZDV

U.S. PHASE I/II ANTIRETROVIRAL STUDIES (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
USA (PACTG 394) ☐ Phase I, <i>bis-POC PMPA</i> , N = 20 ☐ In protocol development, but currently on hold due to lack drug	(Routine ARV)	PMPA x1 @ labor (Routine IV ZDV)	Neonate: Phase I: no PMPA Phase II: PMPA x1 dose (Routine ZDV)
USA (PACTG P1022) ☐ Phase II, PI-Sparing [<i>Nevirapine</i>] vs PI-Including [<i>Nelfinavir</i>] Combination [with <i>Combivir</i>] Initial Treatment Regimens for Pregnant ♀ ☐ Objective is to determine optimal treatment for ♀ as well as safety in pregnancy & for /infant ☐ N = 240 ☐ In protocol development	@10-30 wks Nevirapine vs Nelfinavir + Combivir [ZDV/3TC]	(Routine IV ZDV)	♀: Continues treatment postpartum (can change from nevirapine to efavirenz in non-PI arm) (Neonate: Routine ZDV)

NUTRIENT SUPPLEMENTATION STUDIES

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
MALAWI (Hopkins) □ 2 arm, Phase III □ PLACEBO control □ COMPLETED ENROLLMENT by 2/98, infants in follow-up □ All ♀: Fe/Folate ante □ N = 700 □ Vit A improved preg outcome infant ** (NO EFFICACY TX) **	@ 18-34 wks: Arm 1: Vit A (10,000 IU) Arm 2: PLACEBO	NO DRUG NO DRUG	♀ immediately postpartum: 200,000 IU Vit A 200,000 IU Vit A
TANZANIA (Harvard) □ 4 arm, Phase III □ PLACEBO control □ COMPLETED ENROLLMENT by 2/98, infants in follow-up □ Factorial Design: Vit A ± Micronutrients (MN) □ All ♀ Fe/folate ante & infant VitA @6,12,18 mo □ MN improved preg outcome with & ♀/infant morbid/mortality ↓ □ N = 960 ** (NO EFFICACY TX) **	@ 12-28 wks: Arm 1: Vit A (5,000 IU + 30 mg β-carotene) Arm 2: MN Arm 3: MN & Vit A Arm 4: PLACEBO	200,000 IU Vit A PLACEBO 200,000 IU Vit A PLACEBO	♀ postpartum: Vit A MN MN + Vit A PLACEBO

NUTRIENT SUPPLEMENTATION STUDIES (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
S. AFRICA (U.Natal) ☐ 2 arm, Phase III ☐ Completed enrollment PLACEBO STOPPED 2/98 ☐ All ♀: Fe/Folate ante ☐ N = 738 ☐ Improved ♀/infant morbidity/mortality ** (NO EFFICACY TX [VIT A 20%, PL 22%] BUT DECREASE TX IN PRETERM SUBGROUP [VIT A 18%, PL 34%])**	@ 26-32 wks: Arm 1: Vit A (5,000 IU + 30 mg β-carotene) ~~Arm 2: PLACEBO~~	NO DRUG NO DRUG	♀ immediately postpartum: 200,000 IU Vit A PLACEBO
ZIMBABWE (Denmark) ☐ 2 arm, Phase III ☐ Completed enrollment ☐ PLACEBO control ☐ 13 micronutrients (MN) including vit A ☐ N = 1,800 (35% HIV+ = 600) ** (INCOMPLETE FOLLOW-UP)**	@ 24-35 wks Arm 1: 13 MN (with 10,000 IU Vit A) Arm 2: PLACEBO	13 MN PLACEBO	♀ only x 3 mos: 13 MN x 3 mo PP PLACEBO

NUTRIENT SUPPLEMENTATION STUDIES (cont.)			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
ZIMBABWE (Hopkins/USAID/Canada) ☐ Enrolling gen population (expect 30% HIV + ♀) ☐ PLACEBO control ☐ Enroll immediately postpartum, rapid test ☐ HIV tx is a substudy; HIV + population to receive ARV (HIVNET 012 NVP) ☐ N = 14,000 (30% HIV + = 4,200) Ongoing	NO DRUG NO DRUG	NO DRUG HIV + ♀ to receive HIVNET 012 NVP	Arm 1: ♀ 400,000 IU Vit A x1 Infant: 50,000 IU Vit A x1 Arm 2: PLACEBO Infants born to HIV + ♀ receive HIVNET 012 NVP

NUTRIENT SUPPLEMENTATION STUDIES (cont.)			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
ZIMBABWE (Hopkins/USAID/Canada) ☐ Enrolling gen population (expect 30% HIV + ♀) ☐ PLACEBO control ☐ Enroll immediately postpartum, rapid test ☐ HIV tx is a substudy; HIV + population to receive ARV (HIVNET 012 NVP) ☐ N = 14,000 (30% HIV + = 4,200) Ongoing	NO DRUG NO DRUG	NO DRUG HIV + ♀ to receive HIVNET 012 NVP	Arm 1: ♀ 400,000 IU Vit A x1 Infant: 50,000 IU Vit A x1 Arm 2: PLACEBO Infants born to HIV + ♀ receive HIVNET 012 NVP

PASSIVE IMMUNIZATION: POLYCLONAL (HIVIG) & MONOCLONAL

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
USA (PACTG 185) (COMPLETED 4/97) □ 2 arm, Phase III □ HIVIG/IVIG control □ N = 800 ** (ENROLLMENT STOPPED <u>DUE TO UNEXPECTED LOW</u> <u>TX RATE IN BOTH ARMS</u> [HIVIG 4.7%, IVIG 4.8%]) **	@ 20-30 wks Arm 1: HIVIG q mo Arm 2: IVIG q mo (Nonstudy 076 ZDV ± other ARV as needed for maternal health)	IV ZDV IV ZDV	newborn only: HIVIG x1 IVIG x1 (Plus infant 076 ZDV)
UGANDA (Hopkins) □ Phase I dose finding study COMPLETED 12/98 □ 2 arm, Phase III, to start □ After 8/99, REDESIGNED for HIVNET NVP control in Arm 2 □ N = 570	@ 37-38 wks Arm 1: HIVIG (200 mg/kg x 1) Arm 2: NO DRUG	ORAL NVP (300 mg q 3h) ORAL NVP	newborn only: HIVIG (400 mg/kg x1) plus NVP x1 NVP x 1

ACTIVE IMMUNIZATION: VACCINE STUDIES

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
UGANDA (HIVNET 027) ☐ Phase I/II ☐ To start enrollment ☐ <i>ALVAC (canarypox)</i> ☐ Saline placebo vaccine ☐ Newborns of HIV + ♀ ☐ N = 20	Nonstudy	Nonstudy (Oral NVP ♀)	Vaccine to infants (Infant: oral NVP x1 @48-72 hrs)
USA (PACTG 235) ☐ Phase I (COMPLETED) ☐ <i>rgp120 vaccine</i> in pregnant ♀ ☐ N < 20 USA (PACTG 230) ☐ Phase I/II (COMPLETED) ☐ <i>rgp120 vaccines</i> ☐ Newborns of HIV + ♀ ☐ 2 vaccine comparison (Genetech, Chiron), adjuvant controls ☐ N = ~ 120	Vaccine to ♀ (Nonstudy 076 ZDV) Nonstudy (Nonstudy 076 ZDV)	Nonstudy (Nonstudy 076 ZDV) Nonstudy (Nonstudy 076 ZDV)	Nonstudy (Infant nonstudy 076 ZDV) Vaccine to infants (Infant nonstudy 076 ZDV)
USA (PACTG 327) ☐ Phase I/II ongoing ☐ <i>ALVAC (canarypox)</i> ☐ Newborns of HIV + ♀ ☐ N < 20	Nonstudy (Nonstudy 076 ZDV)	Nonstudy (Nonstudy 076 ZDV)	Vaccine to infants (Infant nonstudy 076 ZDV)

ACTIVE IMMUNIZATION: VACCINE STUDIES (cont.)			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
USA (PACTG 389) ☐ Phase I/II ongoing ☐ <i>DNA vaccine</i> ☐ Newborns of HIV + ♀ ☐ N < 20	Nonstudy (Nonstudy 076 ZDV)	Nonstudy (Nonstudy 076 ZDV)	Vaccine to infants (Infant nonstudy 076 ZDV)

MODE OF DELIVERY			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
EUROPE (ECS) □ 2 arm, N = 435 □ Most women either no rx or ZDV alone □ <i>Cesarean vs Vaginal</i> □ Non-breastfeeding <u>** (COMPLETED – CESAREAN SECTION ~70% PROTECTIVE) **</u>	Nonstudy Nonstudy (Nonstudy ARV)	Arm 1: Cesarean Arm 2: Vaginal	Nonstudy Nonstudy
META-ANALYSIS □ No interventions □ Meta-analysis of 8533 pts from 15 cohort studies from U.S. & Europe □ Most cohorts pre-PACTG 076 results □ Non-breastfeeding □ Individual patient-based data analysis <u>** (COMPLETED – CESAREAN SECTION ~50% PROTECTIVE [~85% WITH ZDV]) **</u>	-	Cesarean vs Vaginal	-

VAGINAL CLEANSING			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
MALAWI (NCI) ☐ 2 arm ☐ N = 2,094 (COMPLETED 1996) ☐ <i>Chlorhexidine SWAB</i> ☐ NO WASH control <u>** (COMPLETED:</u> <u>NO EFFECT TX</u> <u>OVERALL, ?EFFECT</u> <u>SUBGROUP WITH</u> <u>ROM > 4h;</u> <u>BENEFIT ♀/NEWBORN</u> <u>RE: REDUCED</u> <u>HOSP/SEPSIS)**</u>	NO DRUG	Arm 1: Swab Arm 2: No swab	Baby wash No wash
KENYA (U. of Ghent, Belgium) ☐ 2 arm ☐ N = 1,000 (HIV+ ♀) ☐ <i>Chlorhexidine LAVAGE</i> (0.25% dilution) ☐ NO LAVAGE control <u>** (COMPLETED:</u> <u>NO EFFECT TX)**</u>	NO DRUG	Arm 1: Lavage Arm 2: No lavage	Baby wash No wash

VAGINAL CLEANSING (cont.)

SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
IVORY COAST (INSERM/ANRS) ☐ Phase II safety, ☐ N = 112 ☐ <i>Benzalkonium chloride</i> <i>suppository</i> ** (COMPLETED, SAFE) **	Start @ 36-38 wks, given daily	Given at onset labor	Baby wash
ZAMBIA (HIVNET 025) ☐ Phase IIA, safety ☐ Ongoing (2% solution currently under study) ☐ N = 225 ☐ <i>Chlorhexidine LAVAGE</i> ☐ Escalating dose design (0.25%, 2%, 4%)	NO DRUG	Lavage	Baby wash

OTHER INTERVENTIONS			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
ZAMBIA/MALAWI (HIVNET 024) ☐ 2 arm, PLACEBO control ☐ In protocol development ☐ Breastfeeding ☐ <i>Antibiotic prophylaxis of chorioamnionitis</i> ☐ Antibiotics: Metronidazole (ME) [NOTE: BEING CHANGED DUE TO ME ASSOC WITH PRETERM DEL]; erythromycin (ER); ampicillin (AMP) ☐ All ♀ get multivitamin supplement ☐ N = 1651	@ 20-24 wks Arm 1: ME & ER x10 d Arm 2: PLACEBO	ME & AMP PLACEBO	NO DRUG NO DRUG

BREAST FEEDING			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
KENYA (Seattle) □ 2 arm, Ph III □ COMPLETED □ <i>Breast vs Formula</i> feeding □ N = 430 ** (~50% REDUCTION BM TX WITH FORMULA, MORTALITY HIGH BUT SIMILAR BOTH ARMS [@24 MOS, DEATHS 20% FORMULA, 24% BREAST]) **	NO DRUG NO DRUG	Arm 1: Breast feed Arm 2: Formula feed	NO DRUG NO DRUG
ZAMBIA (Harvard) □ 2 arm, Ph III □ in development □ All mother/infant pairs receive the single dose IP/PP NVP regimen □ <i>Exclusive Breastfeeding with Abrupt vs Routine Weaning</i> □ N = 1200	NO DRUG NO DRUG	Arm 1: Oral NVP Arm 2: Oral NVP	Newborn: Oral NVP @48 hr PLUS Exclusive Breastfeed X4mos PLUS Abrupt weaning (to replacement feeding) Newborn: Oral NVP @ 48 hr PLUS Exclusive Breast x4 mos PLUS Slow weaning (usual introduction of weaning foods)
Also internat ARV Studies with prolonged PP infant prophylaxis (HIVNET 023, Ethiopia, India, Botswana)			Various designs to study Infant ARV prophylaxis during breastfeeding

BREAST FEEDING			
SITE	ANTEPARTUM	INTRAPARTUM	POSTPARTUM
KENYA (Seattle) □ 2 arm, Ph III □ COMPLETED □ <i>Breast vs Formula</i> feeding □ N = 430 ** (~50% REDUCTION BM TX WITH FORMULA, MORTALITY HIGH BUT SIMILAR BOTH ARMS [@24 MOS, DEATHS 20% FORMULA, 24% BREAST]) **	NO DRUG NO DRUG	Arm 1: Breast feed Arm 2: Formula feed	NO DRUG NO DRUG
ZAMBIA (Harvard) □ 2 arm, Ph III □ in development □ All mother/infant pairs receive the single dose IP/PP NVP regimen □ <i>Exclusive Breastfeeding with Abrupt vs Routine Weaning</i> □ N = 1200	NO DRUG NO DRUG	Arm 1: Oral NVP Arm 2: Oral NVP	Newborn: Oral NVP @48 hr PLUS Exclusive Breastfeed X4mos PLUS Abrupt weaning (to replacement feeding) Newborn: Oral NVP @ 48 hr PLUS Exclusive Breast x4 mos PLUS Slow weaning (usual introduction of weaning foods)
Also internat ARV Studies with prolonged PP infant prophylaxis (HIVNET 023, Ethiopia, India, Botswana)			Various designs to study Infant ARV prophylaxis during breastfeeding

MCTC Issues and Opportunities

Factual Overview

- 1 in 10 new infections annually results from MCTC (600,000 global; 500,000 Africa);
- number of HIV+ pregnant women likely to increase given 55% of new infections are among young girls – 3/4th of whom are between 15 and 24 years old;
- Of 10 infants born to HIV+ mothers, 2 become HIV+ during labor or delivery, 1 becomes HIV+ as a result of breastfeeding, and 7 remain HIV-;
- VCT and ARV interventions have reduced transmission during labor and delivery by 50%:
 - AZT short course = one pill twice daily for last month of pregnancy (\$50-80 in drug costs with company discounts);
 - Nevirapine = one pill at the onset of labor, three drops to newborn (\$4 in drug costs);
- NOTE: drug costs alone underestimate the cost of an effective intervention which would need to include health care infrastructure/training, VCT, replacement feeding, and support services needed increase safety. UNAIDS estimates that the actual cost of preventing MTCT is currently between \$800 and \$5000 each infection averted.
- Failure to breastfeed can not only have social costs but also health implications. In sub-Saharan Africa, the leading cause of child mortality is diarrhea, more children could die from the misuse of breast milk substitutes than would die of AIDS. Also, not breastfeeding carries other health risks, including from 2 to 20 times the risk of infant and child mortality.

US Contribution

- USG has been an active participant in research on reducing MTCT. USG studies through the NIH led to the development of both the AZT and NVP interventions.
- Currently, USAID is spending \$8 million in Kenya, Zambia, and Zimbabwe to further understand the operational challenges in implementing MTCT interventions including:
 - how can antenatal clinics best absorb new, technically complicated tests and service delivery?
 - how can the confidentiality of women be safeguarded?
 - how can partners be engaged in a manner that increases safety for women?
 - how can the stigma related to formula feeding be managed?
 - how can interventions be made affordable and sustainable?
 - how can they be delivered to the half of all African women who deliver outside of the health care setting?
- NIH continues to fund additional MCTC trials as well as work with our global partners on issues of resistance and toxicity.

NVP controversy in SA

- SAG reported to the SA Parliament that 5 women participating in clinical trials that included NVP have died. In response, the SAG says it now wants to see further safety data before using it to prevent MTCT. The trials were not single dose NVP MTCT trials but rather were ongoing combination therapy trials that included 4 drugs – 1 of which was NVP. It is unclear what role NVP played in these deaths.
- It appears that even a single dose of NVP can lead to the development of NVP resistant virus – as was found in approximately 25% of women in one study. While it is unlikely that this would effect the efficacy of the treatment in reducing transmission during delivery, it may pass along resistant virus during breastfeeding and may complicate effective interventions during subsequent pregnancies. WHO monitoring with help from NIH and CDC.



U.S. Agency for International Development

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Office of Sustainable Development
1325 G St., NW Suite 400
Washington, DC 20005

Date:

4/13

To:

Sandy

Phone:

Fax:

From:

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Phone:

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Number of Pages Including Cover Sheet

- Sandy: 6 documents re: MTCT & President
1. Docs are numbered in upper right corner
- # ① USAID activities & MTCT
 - ② update on nevirapine.
 - ③ email to mission on nevirapine
 - ④ 2 pager on MTCT
 - ⑤ 4 pager on " - guidance to missions
 - ⑥ press clippings: see Pf 5 + 7

USAID ACTIVITIES TO PREVENT PERINATAL TRANSMISSION OF HIV

April, 2000

USAID's goals are to compliment the advances made in simple drug regimens with the research necessary to implement actual programs in the field. Recent clinical trials using short course AZT, Combivir, and Nevirapine have paved the way to less costly interventions. However to realize the promise of these findings, additional work is needed to overcome the service delivery barriers, address the critical issues surrounding breastfeeding and replacement feeding, and to understand the impact these interventions will have on the communities they are intended to serve. Our goal is to link prevention of mother to child transmission of HIV (PMTCT) to our overall child survival, HIV prevention, safe motherhood, and reproductive health services. Currently we have activities in Kenya, Zambia, and Zimbabwe. In addition to these current activities, our missions are in discussion with a number of other governments to initiate PMTCT programs. It is likely that we will assist with the provision of VCT services, improvements in antenatal care, as well as monitoring and evaluation.

KENYA/ZAMBIA

This multi-site study in Kenya and Zambia assesses the effectiveness, acceptability, operational barriers, costs, and impact on child morbidity and mortality of a package of services in antenatal clinics. Among other things, the research examines voluntary HIV counseling and testing, the provision of antiretroviral drugs and breast milk substitutes to HIV-infected mothers and the overall efficacy of this package of interventions to prevent HIV infection. Milestones to date include the development of a research protocol, needs assessments in clinics and communities, training materials for health care workers, and development of a monitoring and evaluation plan in line with international guidelines. This research is being carried out with a wide array of local partners including government, academic and community stakeholders.

Objective and Methodological Approach: This study aims to develop a best practice in the prevention of mother to child transmission of HIV in resource constrained settings. The intervention addresses operational issues of access, acceptability, resources, and cost and will assess whether the project activities have resulted in a best practice on measures of availability of services, utilization, effectiveness, absence of adverse outcomes for the baby, and cost. The intervention package includes advocacy, strengthening of antenatal, delivery, and child health services, counseling, voluntary HIV testing, drug therapy, supporting women to make choices regarding infant feeding, and links to care and support.

The research component will:

1. Evaluate the implementation of a package of antenatal services for the prevention of mother to child transmission of HIV.
2. Systematically examine relevant service delivery variables including acceptability of the intervention by health staff and patients; direct and indirect costs; and use of these findings to enhance the potential for replication and sustainability.
3. Measure the effect of the interventions on the well being of the infant.
4. Measure the effect of the interventions on mother to child transmission of HIV.
5. Assess the effect of the interventions on the choices women make to reduce MTCT.

6. Assess the effect of VCT in the antenatal setting on assisting HIV negative women to protect themselves from infection.

Target Population: Pregnant women, their children, and their partners

Monitoring and Evaluation Plan: During FY00 the implementation of this activity will be monitored through periodic Horizons staff site visits, regular substantive progress reports, financial progress reports, meetings with the implementing organization(s) and principal investigator and research coordinator, and review of the activity work plan time table. This activity will be evaluated at the end of the activity period by Horizons staff together with the staff of the implementing organization(s). The principal evaluation criteria will be to compare the outcome of the activity against the objective(s) of the activity as listed in the activity proposal.

ZIMBABWE/ZVITAMBO

This is a study jointly funded by CIDA and USAID, of postpartum Vitamin A supplementation to newborns and postpartum mothers, whose purpose is to learn if this intervention will reduce infant mortality, reduce transmission of HIV via breastfeeding and reduce postpartum HIV infections of mothers.

The study is a double blind placebo controlled trial of 14000 mother infant pairs. Major outcomes for the study are infant mortality, the rate and timing of vertical HIV transmission, and post partum infection of mothers.

The study is designed to address the following key questions:

1. Does vitamin A supplementation of infants at birth reduce infant mortality?
2. Does vitamin A supplementation of infants at birth reduce the incidence of HIV infection via breastmilk?
3. Does vitamin A supplementation of mothers postpartum reduce the incidence of postpartum HIV infection?
4. What is the best way to inform HIV infected mothers about the risks of breastfeeding to their infants and the options that are available to them?

This study is being carried out in partnership with the University of Zimbabwe and the Harare City Health Department.

ZAMBIA/NDOLA DEMONSTRATION PROJECT

This is a feasibility study that will consist of a package of reproductive health and HIV interventions aimed at promoting maternal-child health clinic attendance and to provide mothers with opportunities to know their HIV status and make and implement informed choices regarding HIV/AIDS and infant feeding. This package will provide mothers with opportunities to know their HIV status and will support them in making and implementing choices regarding HIV/AIDS. The intervention will also include the strengthening of community education, services that will reduce stigma, and increase the support that women living with HIV/AIDS receive from their partners, families and communities.

The study will examine how the expansion of VCT including infant counseling, into ANC and community services influence a woman's ability to make and implement informed choices about HIV (e.g., testing, disclosure of her status, seeking support and care, etc.) and pregnancy (including infant feeding and contraceptive use).

Outcomes of interest include the following.

1. HIV knowledge
2. Stigmatizing attitudes
3. Whether a woman makes a decision to be tested
4. Disclosure of HIV status to spouse and others
5. For HIV+ women: whether a woman seeks medical and/or psychosocial care
6. Prevention, particularly communication with partner and condom use
7. Infant feeding knowledge and practices
8. Childbearing preferences and contraceptive use
9. Partner testing

The following specific questions will be addressed.

1. How does integration of infant feeding and HIV/AIDS counseling into health care and community services influence a woman's ability to make and implement informed choices about infant feeding methods?
2. How does the provision of infant feeding counseling and support influence the rates of exclusive breastfeeding?
3. How does the strengthening of community based services on HIV and Infant Feeding counseling and testing and provision of support, influence the choice of feeding methods and their application among HIV positive and HIV negative mothers?
4. Does the strengthening of Maternal Child Health and Community Based Services by providing infant feeding counseling and VCT influence the uptake of HIV testing by spouses and/or partners?

This activity is being carried out in partnership with national and district health officials as well as a variety of local stakeholders.

HIV/AIDS UPDATE ON NEVIRAPINE

April 13, 2000

In July 1999 the results of an NIH sponsored study of Nevirapine were announced. This study conducted in Uganda demonstrated that a single dose of Nevirapine given to HIV infected women in labor and to their infants after birth, could greatly reduce the transmission of HIV from mother to infant. Since that time many questions have arisen about the use of this drug. Below are responses to the most frequently asked questions regarding the drug Nevirapine.

Background: Since 1994 antiretroviral drugs have been shown to reduce the transmission of HIV to infants. AZT is the most studied drug but other antiretroviral drugs including Combivir (a combination of Lamivudine and AZT) and Nevirapine have shown efficacy in preventing peri-natal transmission in regimens that are realistic for developing country settings. These are not new drugs, simply new uses for existing drugs. They are very similar: they are oral drugs; they suppress HIV in the same way, and in the cases of AZT and Nevirapine, the U.S. price of both is about the same (roughly \$4 per pill). Combivir costs about \$9 per pill.

What is the difference between Nevirapine and other drugs for preventing MTCT?

The table below outlines the difference between the two drugs when used for prevention of MTCT.

	Short Course AZT	Nevirapine	Combivir
Dose	One pill twice a day for the last month of pregnancy.	One pill at the onset of labor, then some drops to newborn	Similar to Short Course AZT Plus one week to infant.
Number of pills	About 70	One + pediatric Syrup	Over 70
Cost	About \$50 in developing countries ¹	About \$5	Over \$100
Efficacy	Effectiveness appears to be similar ²		

Nevirapine clearly has the advantage in cost and ease of use. As this table shows, Nevirapine is currently the only drug that is effective as a single dose for mother and infant. This not only lowers the costs associated with preventing MTCT, it also allows for more discrete treatment of the mother and is only drug regimen that allows for intervention late in pregnancy. In settings where women often do not receive antenatal care this is a significant issue.

Are antiretroviral drugs safe for pregnant women and infants?

AZT has been used by pregnant women and infants for many years now with no evidence of birth defects or tumors. However AZT has produced tumors in the offspring of mice that were given near lethal doses. We have far less experience with Nevirapine in humans but in animal testing, no birth defects or tumors have been reported, even with very high doses. Since this drug is given in labor, after the critical periods of fetal development have passed, it is unlikely to have developmental effects on the infant. The U.S. Centers for Disease Control is maintaining a registry of children exposed to antiretroviral drugs to aid in identifying effects that might not appear until later in life.

Recent news from South Africa has raised new safety issues for Nevirapine. Five deaths have been reported in a trial of combination therapy for people with AIDS. Nevirapine was one of four drugs under study including a new experimental drug. While these results are tragic, it should be pointed out that (1) This trial did not involve pregnant women; (2) This was a trial of continuous treatment rather than a single dose of Nevirapine; and (3) It is not known what role Nevirapine played in these deaths. These results probably have no bearing on the use of Nevirapine for prevention of mother to child transmission.

¹ This price is lower than the \$4/pill cost would suggest because of a major price reduction for developing countries offered by the manufacturer.

² The two regimens have not been directly compared but based on the results of AZT studies in west Africa and one Nevirapine study in Uganda the two appear to have similar efficacy.

Can Nevirapine be used to prevent HIV transmission during breastfeeding? All but one (Thailand) of the short-course anti retroviral trials (and all the trials in Africa) were conducted in breastfeeding populations. Because breastfeeding does increase the risk of postnatal HIV transmission, studies are underway to determine the safety and efficacy of providing Nevirapine to babies to further reduce breastfeeding-related transmission.

Won't increased use of these drugs lead to resistance?

HIV is capable of developing resistance to all antiretroviral drugs and drug resistant virus is found everywhere antiretroviral drugs are in use - including the U.S. HIV develops resistance to Nevirapine very quickly and in fact a number of women who received Nevirapine in the Uganda study developed resistance after receiving a single dose. This does not appear to affect how well the drug prevented HIV infection in the infants born to these women. This does however raise fears that the drug won't be as effective in preventing HIV infection in subsequent pregnancies. This is a complicated question that will require additional study to answer. In the case of AZT, resistance develops much more slowly (on average about 6 months) so that while there are worries about AZT resistance, it is less of a concern.

Is Nevirapine recommended over other drugs for prevention of mother to child transmission? Currently there are no formal recommendations for or against any particular drug. At present most pilot interventions for prevention of MTCT are still using AZT since they had already secured supplies of this drug. In response to the reports of Nevirapine resistance, WHO came out with the position that while pilot studies should continue "[f]urther information on the safety and effectiveness of NVP is required before recommendations on wide-scale use of NVP can be made."

What should USAID missions do to prevent mother to child transmission? There are number of steps missions can take to prevent mother to child transmission of HIV:

1. Support primary prevention of HIV infection through "Beyond awareness" campaigns, condom promotion, policy dialogue and the promotion of voluntary counseling and testing.
2. Continue to support breastfeeding for all mothers and infants unless the mother has been tested and found to be HIV positive. Continue to support the principles of the Code of Marketing of Breastmilk Substitutes.
3. Support MTCT pilots through assistance with rigorous monitoring and evaluation; support for quality voluntary counseling and testing services; and support for establishing and meeting minimum standards for antenatal care.
4. Continue other activities in Mission portfolios that contribute to increasing infant survival and reducing HIV transmission such as Reproductive health/FP/STI centers, Breastfeeding support networks, Child and Youth initiatives, Maternal health initiatives, Malaria prevention/treatment programs, Health communications, education and counseling programs.

To: s
From: David Stanton@G.PHN.HN@AIDW
Cc:
Subject: urgent update on recent AIDS related news stories
Attachment: BEYOND.RTF
Date: 04/13/2000 8:22 AM

Colleagues,

This email responds to two recent news stories regarding AIDS. The first is the report regarding deaths in South Africa of participants in an AIDS treatment trial. The second is the announcement by WHO and UNAIDS regarding the use of Cotrimoxazole to prevent opportunistic infections.

South Africa: Last week a Reuters article out of South Africa reported that the government had halted a clinical trial of Nevirapine due to the deaths of 5 of the participants. The story gave some false impressions which must be clarified.

There have been no deaths to pregnant women taking single dose Nevirapine to prevent mother to child transmission. The reported deaths were among participants in a treatment trial of combination therapy (of which Nevirapine was one of four drugs under study). To our knowledge no pregnant women were in the study, and without further information it impossible to say which (if any) of the four drugs is considered responsible for these deaths. In her press conference the Minister of Health did state that the South African government wants to see further safety data on Nevirapine before using it to prevent mother to child transmission (MTCT). She cited a recent statement by WHO (attached) stating that it was too soon to move to wide-scale use of Nevirapine for MTCT. This statement did OK continued use in pilot studies.

Cotrimoxazole: Some good news. On April 5th a joint statement by WHO and UNAIDS endorsed (cautiously) the use of the antibiotic Cotrimoxazole for the prevention of opportunistic infections for persons with HIV AIDS in Sub-Saharan Africa. Cotrimoxazole is known by many names: Bactrim, Septra, Septrim, and Trimethoprim-Sulfamethoxazole. Cotrimoxazole is an antibiotic which since the late 1980's has been used in developed countries to prevent a number of life threatening opportunistic infections in persons with AIDS and other forms of immune suppression. The recent decision by UNAIDS and WHO to endorse the similar use of Cotrimoxazole in Africa is welcome news to USAID. The prevention and treatment of opportunistic infections is one of the major aims of the LIFE initiative and this decision paves the way for our programs to provide a significant, realistic, and cost effective intervention to prolong and improve the quality of life of people living with HIV-AIDS. This announcement could also enhance efforts to encourage people to seek voluntary testing and counseling. UNAIDS estimates the annual cost of prophylaxis to run between \$7 and \$18. This is a generic drug (no patents or license issues) and is on probably every essential drug list already.

There are some outstanding issues raised by this announcement. The first of which is the acknowledgment by WHO and UNAIDS that the wide spread use of Cotrimoxazole could lead to increased microbial resistance. This will require monitoring systems currently not in place. Second, even though Cotrimoxazole is safe and well tolerated, some persons will not be able to use it due to allergies and stomach upset. For these persons there is no inexpensive alternative available.

I have attached documents related to these two stories:

- 1 WHO NVP March 2000.doc
- 2 hiv aids update-nevirapine.doc
- 3 MTCT guidance to missions.doc
- 3 cotrimoxazol press release 4_4_00.doc
- 4 UNAIDS guidance on use of Cotrimoxazole.doc

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USAID HIV-AIDS Division

USAID



HIV/AIDS Care and Support for Persons Living in Developing Countries

Discussion Paper on *Mother to Child Transmission of HIV*

Sub-Saharan Africa is suffering tremendously from the HIV/AIDS epidemic. Since the beginning of the epidemic, about 35 million Africans have been infected. As of 1998, there were about 22 million Africans living with HIV, including about 1 million children. In 1998 alone, about 4 million Africans became infected with HIV. This means that every *day* about 10,000 men, women, and children are contracting the virus.

Although the vast majority of people with HIV are adults who have contracted the virus from an infected partner, the problem of mother-to-child transmission has become increasingly important, and is estimated to be the cause of about 10 percent of all *new* infections and nearly 100 percent of all cases of pediatric HIV. In other words, about a half-a-million African babies become infected with HIV every *year*. Mother-to-child infections are likely to increase because of the growing epidemic among women, particularly women less than 25 years of age. Data suggest that about 55 percent of all new infections in Africa occur among women. A startling 70 percent of these occur in women between 15 and 24 years of age - these are new infections among women who are beginning their reproductive lives.

Mother-to-child transmission of HIV can occur during pregnancy, at the time of delivery, and after birth through breastfeeding. In Africa, of 10 children born to HIV infected mothers, it is estimated that 2 will be infected during pregnancy or delivery, 1 will be infected through breastfeeding, and 7 will remain uninfected, even with continued breastfeeding. There are several conditions that make a mother more likely to transmit HIV to her baby. These include:

- high viral load (amount of virus in the body) due to recent HIV infection or advanced disease (AIDS);
- untreated sexually transmitted infections;
- prolonged rupture of membranes during labor;
- invasive delivery procedures that increase the likelihood of blood interchange between mother and baby;
- non-exclusive breastfeeding during the first months of life (i.e., breastfeeding with additional milk, formula, water, solid foods, etc.); and
- breastfeeding while experiencing breast infections, such as mastitis and abscesses.

A combination of interventions are needed to reduce mother-to-child transmission of HIV:

- Primary prevention of HIV among women, including behavior change interventions; decision making and negotiation skills; early diagnosis and treatment of sexually transmitted infections; and increased condom use are important strategies for preventing HIV infections in mothers.
- HIV voluntary and confidential counseling and testing services must be available and accessible to pregnant women and their partners so that families can make informed choices about their reproductive lives.
- Health workers and other care givers need to be skilled in counseling HIV-negative women and their partners about how to avoid risky behaviors, and in counseling HIV-positives on how to discuss their situation with their families and to live positively with the disease.
- Health workers need to understand the risk factors and practices that increase the likelihood of mother-to-child transmission of HIV; they must be able to follow safe birthing practices; and they must be able to counsel women about infant feeding options, including safe breastfeeding and appropriate replacement feeding during the first two years of life.
- A package of antenatal interventions, including essential drugs, must be available for all women without discrimination.
- Antiretroviral drugs, if available, should also be given according to locally agreed upon protocols.

Key Issues Regarding the Use of Anti-retroviral Drugs To Prevent Mother to Child Transmission of HIV (MTCT)

Recently released scientific study results show that a short course of oral antiviral medications (Zidovudine or Nevirapine) can significantly reduce HIV transmission from mother to infant during gestation and birth. However these interventions still have significant safety, cost, capacity, social, and ethical implications, and their ability to provide true public health impact remains in doubt. USAID is now devoting approximately \$6 million to answering key questions surrounding MTCT interventions. The following issues need to be addressed:

Potential for increased deaths from the use of breast milk substitutes: Breast feeding by HIV positive mothers accounts for about one third of all MTCT. In Sub Saharan Africa, where diarrhea is the leading cause of death for children under 5, more children could die from the misuse of breast milk substitutes than would die from AIDS. Also, not breastfeeding carries other health risks, including from 2 to 20 times the risk of infant and child mortality, as well as significantly increased fertility among the mothers.

High costs in addition to the cost of antiretroviral drugs: *Drug prices are only a small fraction of the cost of MTCT interventions.* The actual cost of preventing one HIV infection ranges from \$800 to \$5000 depending on the cost of breastmilk substitutes, the proportion of pregnant women who are infected, and the capacity of existing antenatal services to implement MTCT interventions.

Lack of HIV testing in most of the world: More than 90% of all persons infected with HIV have never been tested. MTCT programs will need to include a substantial investment in voluntary counseling and testing programs in order to have a true impact.

Marginal health systems: Antenatal care programs are often overburdened. MTCT interventions need to be carried out in ways that do not threaten the quality of antenatal care for all women. Health planners need to budget for the cost of maintaining (or bringing antenatal services up to) basic standards of antenatal care.

High risk for discrimination: Women who are infected with HIV are at great risk for discrimination, rejection, and violence by their families and communities. MTCT interventions have the potential to disclose a woman's HIV status. This could happen in the health care setting but also could result from other components of MTCT interventions. For instance taking anti retroviral drugs during labor essentially discloses one's HIV status to those present. In many communities breastfeeding is the norm. To be seen giving breastmilk substitutes also discloses one's HIV status.

Need for additional research: There are many unanswered questions regarding MTCT interventions. The programs involving drugs are largely untested. Some of the issues include: how antenatal clinics can best absorb new, technically complicated tests and service delivery; how best to safely inform or advise women about infant feeding and the risk of HIV infection; how to safeguard confidentiality of women; and how MTCT interventions can be made affordable and sustainable. In addition, policy guidance is needed regarding care of the HIV infected mother after birth.

Realizing opportunities: Despite the current questions and concerns, carefully implemented MTCT programs have the potential not only to save the lives of infants, but also to serve as a catalyst for improving and expanding HIV and antenatal services. MTCT programs highlight the need for expanded voluntary counseling and testing, for high quality prevention programs for women who test negative for HIV, and for expanded programs to care for those infected with HIV. The provision of MTCT services instead of being a burden on antenatal services could bring the resources needed to provide quality services for pregnant women.

MOTHER TO CHILD TRANSMISSION (MTCT) OF HIV

Mother to child transmission (MTCT) accounts for about 10% of new HIV infections. Interest in measures to reduce MTCT in developing countries has increased following a number of studies showing relatively inexpensive doses of antiretroviral medications such as Zidovudine or Nevirapine combined with replacement of breastfeeding reduced pre- and peri-natal transmission of HIV up to 50%.

The current approach to preventing MTCT combines three core elements: voluntary counseling and testing (VCT), antiretroviral drugs (ARV), and replacement feeding (RF). This approach, however, has not been examined outside of research settings and carries risks for the women and children it is intended to help. In addition, this approach may exceed service capacity and has significant cost, behavioral and ethical implications.

This document provides a brief technical discussion of these issues and offers advice, developed by representatives of Global and Regional Bureaus and their cooperating agencies, for USAID missions addressing the question of MTCT of HIV/AIDS.

- **MTCT causes approximately 600,000* of the 6 million new HIV infections annually.** Of 10 children born to HIV infected mothers, about 2 will be infected during pregnancy or delivery, 1 will be infected through breastfeeding, and 7 will remain uninfected, even with continued breastfeeding. The impact of this level of transmission is likely to increase due to the growing epidemic among young women.

- There are many interventions that may reduce MTCT. Recently, much attention has been given to the provision of voluntary counseling and testing (VCT), along with short-term antiretroviral drugs, and replacement feeding (ARV and RF).

- **VCT:** It is estimated that no more than 10% of HIV-infected persons in developing countries have ever been tested. Therefore, voluntary counseling and testing, which is central to many treatment and prevention activities, is a critical component of this approach to prevent MTCT.

- **ARV:** Antiretroviral drugs given during the last weeks of pregnancy, during labor, and to infants, can greatly reduce the transmission of HIV from mother to child.

- **RF:** Children who escape HIV infection during pregnancy and delivery are still at risk for

infection through breastfeeding. The use of breastmilk substitutes, or RF, is a consideration in MTCT interventions. However, not breastfeeding carries other health risks, including 2 to 20 times the risk of infant and child mortality, as well as significantly increased fertility among the mothers.

- UNICEF, funded by the Turner Foundation and in collaboration with the UNAIDS Secretariat, has started to pilot interventions to prevent MTCT in about 11 sites, mostly in Africa.

- USAID has devoted approximately \$5 million in 1999, out of our HIV/AIDS budget of \$125 million, and close to \$1 million in PHN core child survival funds, to address some of the key questions surrounding these and other MTCT approaches.

RECOMMENDATIONS:

- **Continue support for primary prevention of HIV infection.**

- **Continue to support primary health care interventions: breastfeeding, the Code of Marketing of Breastmilk Substitutes, and maternal and child survival efforts.**

- **If a mission chooses to support a prevention of MTCT pilot study, we recommend that process, outcome, and long term monitoring and evaluation of the impact on overall health and mortality be among the first priorities.**

* There are about 12-15 million child deaths annually from all causes combined.

MTCT ISSUES AND CONCERNS

MTCT interventions may have an adverse impact on other health services.

MTCT interventions add a complicated set of tasks to clinical settings, which are often already overburdened. Program managers need to know whether antenatal clinics are able to handle the added burdens of MTCT interventions. While HIV/AIDS is a growing and deadly threat to individuals and to societies, we must be sure that we do not harm active health services currently in place and saving lives in order to more fully address HIV/AIDS. At highest risk are the new maternal health initiatives and preventive child health services. The interventions may divert funding from these critical services. On the other hand, it has been suggested that concerns about HIV/AIDS might serve as catalysts to increase attention to maternal and infant mortality, thus increasing resources.

We have limited experience with implementing programs to inform the general public and counsel HIV+ women about safe breastfeeding and replacement feeding practices

In developing countries, infectious diseases, such as diarrhea and pneumonias, continue to be the leading cause of death among children under 5 years of age. Breastfeeding, through immune activity and nutrition, protects against the morbidity and the mortality of these diseases. Therefore, replacement feeding can be life threatening. RF also leads to significantly increased fertility for the woman. In Africa, where the average duration of breastfeeding approaches 2 years, RF preparation is difficult and costly for the family. Misunderstanding or misuse also could erode community breastfeeding norms. Research is needed to guide the implementation of programs that counsel and support HIV+ women who have been tested and know their status on the risk and options for feeding their infants.

Safeguarding confidentiality of participants is critical and very difficult.

Women who are known, or believed, to be infected with HIV are at great risk of discrimination and rejection by their families and communities. The issues of anonymity begin with the provision of VCT in health care settings and extend to every aspect of MTCT interventions. Childbirth is a social event in some societies with many family members in attendance; taking ARV during labor discloses one's HIV status to those present. In addition, breastfeeding is the norm in many communities, so to be seen using breastmilk substitutes discloses one's HIV status in these settings. Reports from some of the pilot sites confirm that cultural norms and fear of stigma prevent women from using RF even when it is made available at low or no cost.

We do not know the full cost of these interventions.

Drug prices are only a small portion of the overall price tag for MTCT interventions. Other costs include VCT for all women, social and personal costs, costs of training healthcare workers, costs of improvements in healthcare infrastructure, costs of breastmilk substitutes, and the cost of the support services needed to make breastmilk substitutes as safe as possible.

USAID estimates that the total costs per HIV infection prevented by an MTCT program including VCT, ARV, and RF can range from as low as \$800 to as high as \$5000. This amount depends on the proportion of women who are infected, the use and cost of the replacement feeding, and the excess health services that such feeding demands.

WHAT USAID MISSIONS CAN DO TO ADDRESS MTCT

1. DO support primary prevention for women and for the *general population, especially youth, and among pregnant and lactating women.*

Certainly, the best way to prevent mother-to-child transmission is through primary prevention of HIV/AIDS, especially among women of reproductive age or younger. Prevention efforts include behavior change interventions; STI diagnosis, treatment and prevention; and social marketing of condoms. Prevention efforts work and inevitably reduce MTCT. Continued and expanded support of prevention efforts focusing on reduction of HIV/AIDS in the general population, especially among youth and those who are currently of reproductive age, is likely to have the greatest impact on MTCT.

HIV infection during pregnancy and breastfeeding is associated with a higher level of transmission to the infant than occurs if the mother was already infected before pregnancy. This emphasizes the importance of not only testing pregnant women but also investing in prevention before, during and after pregnancy.

The risk of HIV infection to women during the pre- and post-partum period may be higher than at other times for a number of reasons:

- Most new mothers are in the high-risk age group;
- Pregnant women have clearly had unprotected sex;
- In some countries, women are more likely to abstain from sex with husbands or partners during this time. The men may seek sexual relations elsewhere, exposing themselves and, eventually, their partner and her children, to increased risk of HIV;
- Many women in these groups are nutritionally and immunologically compromised.

Data from Uganda show that the percent of pregnant women found to be HIV+ in 12 sentinel sites was significantly decreased following HIV/AIDS education, voluntary counseling and testing, condom promotion, and political leadership. Preventing HIV infection among

women during their pregnancy and during the years of breastfeeding would significantly reduce mother-to-child transmission of HIV/AIDS.

2. DO continue to support breastfeeding for all mothers and infants **UNLESS** the mother has been tested and found to be HIV positive. Continue to support the principles of the Code of Marketing of Breastmilk Substitutes.

Even in countries with the highest levels of HIV infection, the majority of pregnant women remain uninfected. And, even among the HIV+ women, the majority of their infants remain uninfected.

Current guidance suggests that breastfeeding, exclusive for the first six months, and sustained for 2 years or more, is by far the best source of nutrition and the most cost-effective disease fighter in areas with a high burden of infectious disease. In areas of high infant mortality rates, any reduction in breastfeeding will increase fertility rates and can have dire consequences on infant and child survival.

Although current advice in the United States is that women who test positive should not breastfeed, breastfeeding still should be considered in many situations worldwide. Why? Even if a woman is HIV positive, chances are nearly 2 out of 3 or better that her infant will not become infected. Those children who are denied the benefits of being breastfed may suffer 2-20 times the mortality of their breastfed peers. These risks must be considered in program and policy decisions.

This difficult and complex decision concerning infant feeding choice should be based on adequate counseling, ready availability and affordability of RF, and the judgement as to the adequacy of the health care facilities available to handle the increased incidence of other diseases that will occur when children are not breastfed.

If breastmilk substitutes are available, affordable, and safe, and if adequate health care is available and affordable, then RF should be promoted as being safer than breastfeeding. If HIV-positive mothers are encouraged to use RF, then

breastfeeding should be promoted and protected among the general population.

We know very little about replacement feeding strategies; preliminary studies indicate that current recommendations cannot be implemented in impoverished settings due to complexity and cost. Local options for replacement feeding must be identified and evaluated, as well as counseling methods for imparting that information to mothers. Feasible recommendations must be developed that will maximize the health and well being of mothers, their infants, and their families. This should be accomplished in a manner that is not in violation of the International Code of Marketing of Breastmilk Substitutes.

3. It is in USAID's interest to encourage the rigorous monitoring and evaluation of current MTCT pilot programs.

Missions considering support for the UNICEF or other such pilots should take steps to ensure the quality of evaluation. The replicability, as well as the generalizability, of findings from the pilot sites are of great significance at this early stage of the development of these interventions. Of special importance is the long-term monitoring of the impact of these interventions on overall health and survival.

USAID is currently supporting studies that will allow us to assess other interventions and to better understand the risks inherent in alternative MTCT interventions. Perhaps, more importantly, USAID studies are being designed to discover how these risks can be minimized. If a mission chooses to support a MTCT pilot study, we recommend that process, outcome, and long term monitoring and evaluation of the impact on overall health and mortality be among the first priorities.

Mission support of the evaluations might include technical input into development of plans and policies for pilot activities, including support for monitoring and evaluation. The greatest concern is that the outcomes of these costly and specially selected "pilots" will be misinterpreted and/or over generalized, and then replicated in areas or circumstances where the findings do not apply.

Another important area for study is how to reduce transmission through breastfeeding. Informed women choose to breastfeed for a variety of social, cultural, and economic reasons, as well as for infant and child survival, and economic reasons. There are conditions, including mastitis, cracked nipples, and damage to the infant's mouth or gut caused by infections or by use of other milks, that may enhance passage of the virus.

4. Do continue other activities in Mission portfolios that might contribute to increasing infant survival and reducing HIV transmission, with concomitant reduction of MTCT, such as:

HIV/AIDS Programs –

- "Beyond awareness" campaigns
- Condom promotion
- Policy dialogue
- VCT for all

Other Health Programs –

- Reproductive health/FP/STI centers
- Breastfeeding support networks
- Child and Youth initiatives
- Maternal health initiatives
- Malaria prevention/treatment programs
- Health communications, education and counseling programs

QUESTIONS?

Detailed documents and technical assistance on these issues are available. For further information, please contact:

David Stanton or Linda Sussman
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Kristen Marsh or Miriam Labbok
G/PHN/HN/NMH

employees are treated like any other employee with a chronic life threatening condition," declared Fantan.

An AIDS activist Helen Ditsebe-Mhone who has also gone public about her positive HIV status, said she supports the Debswana move. "If you send people for training you would expect those people to work.

I think they are right," said Mhone, approving the Debswana stand. She does not feel that testing people for HIV and rejecting those who are positive is discriminatory.

However, Mhone suggested that those candidates who are found to be HIV positive should be counselled and empowered. She suggests that maybe Debswana should sponsor them for short-term courses.

"I do not want to see a situation where they are just telling people that you have tested HIV positive so we cannot give you a scholarship. They should not just dump them," she said.

If the candidates who are HIV positive were neglected, she said they would suffer two blows. Firstly they would lose the scholarship and then face the stigma of being HIV positive.

Mhone stressed that Debswana should come up with a comprehensive programme to address the problem. When contacted for comment, officials of Ditshwanelo - the Botswana Centre for Human Rights said they have arranged a meeting to discuss the matter with Debswana.

Candidates who are given scholarships by the government do not undergo an HIV test. Government policy on AIDS/HIV discourages discrimination against people who are HIV positive.

>>>>Reuters 11 April 00

AIDS KILLING MORE PEOPLE THAN FAMINE IN ETHIOPIA.

ADDIS ABABA, April 11 (Reuters) - Food shortages may be threatening the lives of up to eight million people in Ethiopia but certain death awaits at least three million people infected with HIV in the next eight years, health experts say.

Last year, nearly 300,000 people in Ethiopia died of AIDS-related illness - a rate of over 800 per day - and a further three million are believed to be infected with the HIV virus that will eventually lead to the deadly disease.

The toll is far higher than any figures relating to the food shortages in the Horn of Africa country and also threatens the most economically productive part of the population.

"AIDS is a far greater crisis facing Ethiopia than famine," one health expert told Reuters on Tuesday.

"At risk of sounding cynical, I am amazed at the reaction of the Ethiopian government and the West to the food shortages compared to their reaction to the AIDS crisis."

Last week, latest figures on Ethiopia's AIDS crisis showed that nearly 10 percent of the sexually active population - those aged between 15 and 49 - were infected with HIV.

Some 27 million of Ethiopia's 61 million people fall in that age group and those infected are projected not only to pass on the virus to tens of thousands of others, but also produce thousands of HIV-positive babies who will become orphans before probably falling to the disease themselves.

These figures are conservative estimates and based on testing at pregnancy clinics in mainly urban areas, experts say. The Ethiopian government has introduced public awareness campaigns, but health experts say privately that these are half-hearted and have had little impact.

"Perhaps the government feels vulnerable to blame if there is a national food shortage whereas contracting HIV is considered the fault of the individual," one said.

>>>>Reuters 11 April 00 SOUTH AFRICA FAILING TO TACKLE AIDS, WARNS BANK.

By Steven Swindells

JOHANNESBURG, April 10 (Reuters) - South Africa, with one of the world's highest HIV infection rates, is failing to act quickly enough to keep AIDS from ravaging the country, a leading investment bank warned on Monday.

The criticism by bankers ING Barings was the latest assault on Pretoria, which has been criticised for questioning the causal link between the Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS).

"The government really needs to formulate an AIDS strategy. It doesn't help when the government debates whether HIV causes AIDS. We can't waste any time," Kristina Quattek, chief economist at bankers ING Barings told Reuters after the bank presented a study of the future economic impact of AIDS.

South Africa's government has incensed the scientific world by inviting AIDS dissidents - scientists who question the link between HIV and AIDS - to an international AIDS conference in July and allowing them on a panel of international experts.

Pretoria also attracted controversy by refusing to give the AIDS-retardant drug AZT to HIV-infected pregnant women or rape victims, citing conflicting scientific reports and its cost.

President Thabo Mbeki, who succeeded Nelson Mandela last June, questioned the efficacy of AZT in preventing infection and reducing the likelihood of transmission in the womb.

The country's health minister has also fanned the flames by accusing the scientific community of using South Africa as a dumping ground where drugs could be tried but most people would never benefit from them because they were unaffordable.

The need for a clear policy was made all the more pressing by the estimated 1,700 South Africans who become infected each day with HIV.

According to government statistics, about 12 percent of the country's 40 million people are HIV positive.

ING Barings' report, a year in the making, forecast that HIV infection rates would peak at almost 17 percent by 2006 and AIDS related deaths top off five years later at 256 AIDS deaths per 100 normal deaths.

AZT treatment could significantly change the future growth of HIV-AIDS, the bank said.

"The fact that there is a lack of policy response means that the AIDS epidemic is a dark cloud on the horizon," said Quattek.

The ING-Barings study showed that the population growth rate would stagnate by 2010, by which time 2.5 times as many South Africans would die of AIDS than any other causes.

>>>>Associated Press 11 April 00 AIDS to slash South Africa's economic growth, reports find

JOHANNESBURG, South Africa (AP) _ The AIDS crisis will cut South Africa's economic growth, increase inflation and exacerbate the country's shortage of highly skilled labor, according to newspaper reports Tuesday.

A new report from ING Barings concluded that the epidemic will cut South Africa's annual growth rate by .3 to .4 percentage points over the next 15 years, the Business Day daily reported.

Though the infection rate among highly skilled labor is only a third of that among less skilled, it is still enough to cause a shortage of highly skilled people, the Star newspaper said, citing the Barings report. That shortage is likely to increase inflation.

A third of South Africans are unemployed, but most of the jobless lack skills.

Barings criticized public and private policy for not presenting a clear strategy to combat the epidemic. It noted that uncertainty about the epidemic's effects deterred foreign investors.

A paper prepared by the World Bank to be discussed at a meeting next week of the International Monetary Fund and the World Bank in Washington, said "the epidemic poses the foremost challenge to development in sub-Saharan Africa."

Inaction by governments has played a crucial role in the disease's spread, the paper said.

Once the prevalence of AIDS in a population reaches 8 percent, the per capita growth is reduced by .4 percent a year, the paper said. According to the Actuarial Society of South Africa, 12 percent of South Africans are infected with HIV. The society predicts the infection rate will peak at 17 percent in 2006 and AIDS-related deaths will begin to decline about five years later.

In countries such as Zimbabwe, where the infection rate exceeds 25 percent, the annual per capita growth is slashed by at least a full percentage point, the World Bank paper said.

>>>>Associated Press 11 April 2000

UNESCO sponsors world education conference in Senegal in late April

PARIS (AP) _ A UNESCO-sponsored summit later this month on worldwide education will look at ways to improve learning amid debilitating crises such as widespread AIDS in Africa and gender discrimination, the group's director said Tuesday.

The World Education Forum, to be held in the Senegalese capital of Dakar from April 26 to 28, is expected to draw leaders including U.N. Secretary-General Kofi Annan and the presidents of Egypt, Nigeria, Senegal and Uganda.

Legislation prevents mandatory screening for HIV/AIDS on recruits or personnel of the SANDF.

Defence force spokesman Maj Fanie Pretorius said recently 254 SANDF members had committed suicide between 1994 and the end of January this year. Afusa secretary-general Nare Makgakga said: "We are opposed to compulsory tests for HIV/AIDS because they are illegal and will lead to many more soldiers committing suicide."

Makgakga quoted soldiers from the Seventh Battalion of the medical contingent saying they had been put under pressure to take the tests in February. Members of the battalion said authorities demanded everybody be tested, saying these were the orders of defence force chief Gen Sphiwe Nyanda.

Defence Minister Mosiuoa Lekota's spokesman, Sam Mkhwanazi, said it was not government policy to test troops unless they were part of a contingent that was to be deployed on a United Nations mission outside SA.

The union, which is on a recruitment drive, told a meeting in Johannesburg last week that it was concerned blacks had had to contend with more obstacles than any other grouping since integration. Makgakga called for an investigation of the "nature of the causes of suicide in the defence force", saying the problems seemed to afflict blacks more than others. He said it was disconcerting that 98% of cases of people going absent without leave, most dismissals and most cases of disciplinary action involved African soldiers.

The union said in light of a court martial moratorium passed last year by former defence minister Joe Modise, it was calling on all cases of soldiers court marshalled since 1994 to be reviewed.

The union again expressed disappointment with the low percentage of black, "particularly African soldiers", in positions of influence within the SANDF.

It also alleged that several soldiers from the former liberation forces occupied the same positions they had three years ago. "In terms of defence force regulations, a soldier must be considered for promotion after three years; or at the least, if there are no posts available, have a salary increment," Makgakga said.

He said: "We are working to end discrimination within the defence force. We want a person to be promoted on merit and nothing else. If the minister wants us to be a pressure group in that sense, then we are prepared to do that."

Referring to poor salaries, Makgakga said one of the problems was that soldiers working on a stand-by basis were "paid only R16,50 a day".

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>>>> Boehringer Ingelheim, 10 April, 2000 Boehringer Ingelheim Clarifies AIDS Drug reports

Ingelheim, Germany (Boehringer Ingelheim, April 10, 2000) - Media reports have focused on a triple combination study of AIDS drugs in HIV-infected adults in South Africa (FTC 302) conducted by Triangle Pharmaceuticals (located in Durham, North Carolina) to assess their investigational drug FTC (emtricitabine). Boehringer Ingelheim's AIDS drug nevirapine (VIRAMUNE) is one of the products involved in this trial.

News reports implied that nevirapine may have been associated with five deaths in the study. According to investigator reports, of the 470 patients enrolled in the trial (394 receiving nevirapine in combination with other antiretroviral treatments), two hepatic deaths were possibly related to nevirapine.

However, in a clinical trial in which patients are taking multiple drugs, it is not possible to determine with certainty, which drug, if any, may have caused the two deaths. The other three deaths were due to other specifically identified causes. According to news reports, there was also a higher than expected incidence of liver toxicity in the study. In fact, the incidence of liver toxicity seen in the study is in line with what is commonly seen in similar studies of triple combination antiretroviral therapies in HIV-infected individuals.

As with all potent antiretroviral treatments, there are known side effects of nevirapine as described in the product labeling. Boehringer Ingelheim takes all adverse events seriously and reports events to the health authorities internationally, and the company is further evaluating the study and intends to meet with the South African authorities to address questions.

Nevirapine has been studied extensively and has been approved in over 60 countries including Australia, Canada, South Africa, United States and in European countries. Large, multi-center international trials have shown that nevirapine, when used in combination therapy, can durably suppress the amount of HIV in the blood to undetectable levels (Atlantic, INCAS).

While not currently a labeled indication, nevirapine has also been shown to reduce mother-to-child transmission (MTCT) of HIV in a trial in Uganda (The Lancet, Sept 4, 1999). It has recently been added to the World Health Organization essential drug list as an option for the prevention of MTCT of HIV in the developing world. Contact: Ulrich Bock Corporate Public Relations Division
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>>>> All Africa News Agency, 10 April, 2000

AIDS: Rising Infection Rate Worries Prison Authorities

Blantyre (All Africa News Agency, April 10, 2000) - The first study of its kind in Africa initiated by the Penal Reform International PRI in 1998 to critically analyse the HIV/AIDS situation in Malawi's prisons has revealed that the spread of the epidemic has reached dangerous proportions in the country's gallows.

The findings of the study, which was initiated after the 1998 conference on HIV/AIDS in African prisons held in Dakar, Senegal, are published in a report called HIV/AIDS In Malawi Prisons.

The report says that over 50 prisoners die everyday in the country's prisons. Of the 8,400 cases treated at Zomba Central Prison Clinic during 1997, 25 percent

Laimi, who appears perfectly healthy, said she regretted that many Namibians refused to believe that a healthy-looking person could have the HIV virus.

"This is not the case. Look at me. I am looking healthy and fat but I have the virus, so be careful," she said.

Laimi appealed to those infected with the virus which causes AIDS not to spread it to others, but to go to counsellors for advice, and appealed to people in general "to be brave" and go for tests.

She also urged those with the virus not to commit suicide as was happening at present.

"Lastly, I thank God for sparing me to this date when He gave me courage to go public and tell my fellow people that I am HIV positive. Let the Lord be praised," she said.

Director of Health for the North West, Dr Naftali Hamata, Governor of the Oshana Region, Klemens Kashuupulwa, and Chief of the Nursing Staff in the Region, Lely Nunes, applauded Laimi's bravery.

Hamata said hers was a truly brave decision because, as was always the case with those living with HIV-AIDS, fingers were pointed and people started judging them and discriminating against them.

The Health Director said from their side they would assist HIV- positive people with counselling and, where people did not have money for medication would help with medical treatment.

Kashuupulwa said despite the ongoing campaign against HIV-AIDS the disease continued unabated.

"We need to go for openness and enter into public discussions on issues related to HIV-AIDS, to create a friendly environment acceptable to people living with HIV-AIDS to undo the stigma attached to the disease," Kashuupulwa said.

Independent Online (South Africa), 6 April 2000

Nevirapine can still be used - minister

>By Lynne Altenroxel and Anso Thom

>

>The Aids drug Nevirapine could still be used to prevent mother-to-child

>transmission of the disease, in spite of the deaths of five women during

>clinical trials involving the drug, according to Health Minister Manto

>Tshabalala-Msimang.

>

>She said on Thursday that she had "just a while ago signed a letter to

>support the studies being done at Bara (Chris Hani Baragwanath Hospital).

We

>

>have even asked them to ensure they have more than one site so that we can
>get really good results."
>
>The minister said the government had not stopped any trials other than the
>FTC302 trials being conducted by Quintiles Clindepharm at Kalafong Hospital
>in Pretoria.
>
>"I was talking about one study, the FTC study," Tshabalala-Msimang said.
Dr
>
>Frank Rousseau, chief medical officer for Triangle Pharmaceutical, which
>manufactures FTC, said from the US on Thursday night that he did not
believe
>
>there was any evidence to attribute the deaths to one of the drugs.
>
>"I think it's highly unfortunate that anyone died," he said. "The other
side
>
>of the coin is that the rest of the patients are doing very well." Two of
>the
>patients had died of hepatitis, two of central nervous system disorders
>(meningitis) and one of pancreatitis, he said. PAC health secretary Dr
>Costa
>Gazi said the people agreeing to be human guinea-pigs were desperate for
>medication. "Because the minister doesn't make anti-retrovirals available,
>these women flock to these trials," Gazi said. "It's an outrage."
>
>Quintiles Clindepharm's US spokesperson, Pat Grebe, said the company had a
>confidentiality agreement with Triangle Pharmaceutical and was therefore
>unable to comment.

>Political tension over Nevirapine reached fever pitch on Thursday as the row
>
>over the deaths deepened.
>
>Experts have questioned whether Nevirapine could have caused the deaths, as
>the drug had already undergone clinical trials of its own before being
>registered for use in 1998.
>"How can you know if it's Nevirapine (which caused the deaths) if it's a
>cocktail of three drugs?" asked PAC MP Patricia de Lille, echoing the
>thoughts of experts who pointed out that the women may have died as result
>of
>complications of HIV.
>
>The men and women on the trial were given different mixtures of three
>registered anti-retrovirals, as well as the new drug, FTC. None of the
women
>
>were pregnant and the FTC 302 trial had no relation to Nevirapine tests
>which
>have been undertaken in South Africa to determine the effectiveness of
>Nevirapine in preventing mother- to-child transmission of HIV.
>
>The minister, in saying "five South African women have died during the
>course
>of an ongoing clinical trial involving Nevirapine", has been accused of
>using
>the deaths to justify the government's refusal to provide pregnant women
>with
>anti-retroviral drugs. "It is unfortunate that she has used the tragic
>event

>of deaths during the trials to make a political point that justifies her
>doing nothing to stop mother-to-child transmission," De Lille said.
>
>Drugs used in the study
>
>Nevirapine (anti-retroviral)
>Approved for use in the United States in 1996, for use in Canada in 1998,
>and
>for use in South Africa in 1998. In Uganda the drug has been approved for
>use
>in preventing mother-to-child transmission since February and is expected
to
>
>be approved for this use in South Africa soon.
Manufactured by
>Boehringer-Ingelheim.
>
>Lamivudine (anti-retroviral)
>Similar to AZT, commonly known as 3TC, Lamivudine was approved in South
>Africa in June 1996. Manufactured by Glaxo-Wellcome.
>
>Stavudine (anti-retroviral)
>Similar to AZT, commonly known as d4T, Stavudine was approved in South
>Africa
>in January 1998. Manufactured by Bristol-Myers-Squibb..
>
>FTC
>The experimental drug manufactured by US company Triangle Pharmaceutical.
>
>The study in which five people died
>
>According to a Medicines Control Council report handed to the minister, 510
>patients had been recruited for the trial. The trial aimed to compare FTC
>with Lamivudine in a triple combination regimen in people who were HIV
>positive and who had not yet taken any anti-retroviral drugs.

>

>The trial had two groups. One group received FTC and the other Lamivudine.

>Within each group, there were three sub-groups of patients. The patients in

>

>sub-group one and two received Nevirapine as part of their drug cocktail and

>

>sub-group three did not. Some also received Stavudine.

Use of Nevirapine to Reduce Mother-to-Child Transmission of HIV (MTCT)

WHO Review of Reported Drug Resistance

Geneva, 24 March 2000

A recent early report that a single dose of Nevirapine given to HIV-infected women during labour to reduce the risk of mother-to-child transmission (MTCT) of HIV can lead to the selection of Nevirapine (NVP)-resistant virus at 6-weeks in the mother does not warrant exclusion of NVP from pilot MTCT-prevention programmes or research studies. Further information on the safety and effectiveness of NVP is required before recommendations on wide-scale use of NVP can be made.

In the past two years, evidence has accumulated that short and cost-effective antiretroviral regimens can reduce the transmission of HIV-1 from mother to child during labour and delivery. Results from the first of these studies demonstrated that a one-month course of Zidovudine (ZDV) used from 36 weeks' gestation until delivery was well-tolerated, safe and reduced the risk of transmission by half in women who did not breastfeed. Following these results, recommendations on the use of such a ZDV regimen were published in the WHO Epidemiological Record in October 1998 [WER 98].

In 1999, clinical trials demonstrated the efficacy of 1-month ZDV regimens in predominantly breastfeeding populations, the efficacy of a regimen combining two antiretrovirals (ZDV and Lamivudine [3TC]) as well as the efficacy of NVP given at a single dose to the mother at the beginning of labour and a single dose given to the infant within 72 hours of life. There is little to differentiate between currently available regimens (ZDV from 36th week to delivery, ZDV plus 3TC from onset of labour to 1 week post-partum, one dose of NVP at onset of labour and one to the new-born) in terms of efficacy. The low cost of NVP and simplicity of administration make it a good candidate for low-income countries where women generally attend antenatal care irregularly or late during pregnancy, or where many deliveries occur in home settings [WER00 in press; Lancet 1999; 354: 795-802].

Safety data are mainly available for ZDV and 3TC, which have been widely used for several years in developed countries, although for longer therapeutic protocols. To date, experience with single dose NVP administered to mother at onset of labour and to the neonate is based on over 700 mother-infants pairs enrolled in two Phase I safety studies conducted in the USA and Uganda, and an efficacy trial in Uganda. More extensive safety data are available with use of NVP and ZDV for long-term treatment. During use of both ZDV (alone or in combination with 3TC) and NVP for longer periods than that recommended to prevent MTCT in low income countries, rare but severe cases of toxicity have been observed (mitochondrial disease and Stevens-Johnson syndrome) [WER00 in press].

The recent report from a phase II study (HIVNET006) showing that a single dose of Nevirapine led to the selection of NVP-resistant virus in 3 out of 14 women at 6 weeks post-partum raised

concerns about the potential adverse effects of NVP on the mother and infant health. WHO convened a Technical Consultation of investigators, virologists, epidemiologists, representatives of the manufacturer, representatives from NIH, CDC, ANRS, UNAIDS and UNICEF on 16 February 2000 to explore the potential implications of this report. A confidential copy of the full report from the study was made available to the meeting participants. The four main conclusions of the Technical Consultation were:

1. Rapid emergence of NVP resistant virus has been previously observed in adults receiving chronic NVP treatment as a single agent [J of Virology, 1996; 70: 7894-7899]. Given the pharmacokinetics of the drug (long half life) and its high potency, selection of resistant virus even after a single dose was not wholly unexpected. Indeed, the profound decrease in the quantity of drug-sensitive virus particles strongly favours replication of resistant virus present before treatment.
2. Since NVP is given at onset of labour, the consultation considered it unlikely that selection of resistant virus occurred in the few hours before delivery. It is also unlikely that resistant virus be transmitted during labour or delivery to infants infected despite treatment, given that resistant virus would probably not be selected until at least several days following delivery. However, the rapid selection of resistant virus may compromise the efficacy of the NVP prophylactic dose given to the infant and the likelihood of transmission of resistant virus during breastfeeding is of greater concern. In addition, the use of NVP may be less effective in reducing the risk of transmission during a subsequent pregnancy in women in whom resistant virus was selected in their first pregnancy.
3. Although the infectivity and pathogenicity of selected NVP-resistant variants is unknown, previous studies on other drug-resistant viruses do not suggest that such variants are more transmissible or worsen the prognosis of HIV infection. In addition, resistant virus is expected to reach undetectable levels within a few weeks or months after cessation of treatment [JAMA 1996; 279: 1984-1991]. The temporary selection of resistant virus induced by a single dose of NVP during labour is therefore not expected to lead to emergence of NVP-resistant strains in the population. Of greater concern is potential emergence of NVP-resistant strains in the population if NVP were used in sub-optimal treatment regimens.
4. The implications for future therapeutic options for women and children with resistant virus were discussed. The efficacy of combination therapies not including NVP or other Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) antiretrovirals should not be altered in such patients. In theory potent combination therapies which include NVP or another NNRTI should not allow re-emergence of resistant virus, but the use of a NNRTI in sub-optimal combinations should be avoided. Research studies will be needed to assess the impact of previous NVP administration on the effectiveness of subsequent antiretroviral treatment, should such options become available

Given the potential value of NVP in reversing the dramatic trends of AIDS-related paediatric mortality in developing countries, and the anticipated low impact of temporary selection of resistant virus in a minority of treated women, the new information is not considered sufficient to interfere with plans to make NVP more widely available in pilot MTCT-prevention programmes or in research settings. The most recent report is based on only 3 cases of NVP resistance. New

information on the effectiveness of NVP for MTCT-prevention from other research studies and further information from the HIVNET012 study on NVP-resistance 6 weeks after delivery are anticipated to be available within the next 6 months. At that time WHO will review the potential programmatic implications of the new data. There is currently insufficient information to recommend wide-scale implementation of NVP for MTCT-prevention. Long-term follow-up of mothers and children exposed to NVP or other antiretrovirals for the prevention of MTCT is required. Research should in addition explore options to reduce transmission through breastmilk, and potent and affordable long-term combination therapies.

24 March 2000

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