HealthTech IV

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PATH
A catalyst for global health

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Highlights and Milestones of the Past Six Months

- Access to Technologies within World Health Organization's (WHO) Immunizations, Vaccines, and Biologicals division is in the process of finalizing a draft policy document entitled "Statement on Prevention of Freezing Damage to Vaccines" that is primarily based on the work that PATH has done under HealthTech.
- The Indonesian Ministry of Health held a national-level workshop on vaccine freezing and finalized its approach to freeze prevention with PATH leadership and participation.
- User materials for needle-remover use have been developed and sent to India and the 11 PEPFAR country safe injection projects for review and future dissemination.
- An appropriate research and development laboratory in Argentina—Instituto Biologico Argentino (Biol) has been identified and validated as a potential supplier of oxytocin and gentamicin in the Uniject™[1] device, to replace Dolphin Laboratories, Ltd. in India. A scope of work for stability testing is currently being negotiated.
- A study conducted by PATH and the Ministry of Health of Vietnam with other funding of oxytocin in Uniject used to prevent post-partum hemorrhage in women in the third stage of pregnancy resulted in positive feedback about the use of the device for delivery of oxytocin. Ninety-eight percent of the midwives participating said that the Uniject device was easier to use than standard syringes. Plus the devices will be less expensive than ampoules if prices at the lower end of likely range become available.
- A report on the study of the RBP-EIA test for vitamin A deficiency in Thailand was completed and the results presented at the annual conference of the International Vitamin A Consultative Group (IVACG). The study showed the first evidence of the biological comparability between serum retinol levels estimated from venous blood and capillary blood and adds to a growing body of research that has demonstrated close correlation between retinol in venous blood samples and RBP in capillary blood.
- The technology transfer recipient of the rapid gonorrhea test—Orchid Biomedical of India—has collaborated with PATH on enhancements to the test, which have improved sensitivity by 30 times over the original test.
- Final results from a comparative evaluation of PATH's rapid gonorrhea test and others in a WHO-sponsored trial in Benin are quite encouraging, demonstrating sensitivity of 71 percent and specificity of 97 percent.

[1] Uniject is a trademark of BD.

- A study of cautery tips used for vasectomy has been completed. Data indicates that cautery tips can be effectively cleaned and disinfected with bleach through standard reprocessing procedures.
- The final report of the delivery kit quantitative study reported on last fall has now been completed and sent to USAID to be used for decision-making about USAID support of delivery kit projects.

Milestones and Accomplishments for Past HealthTech Technologies

PATH has recently confirmed global sales and use of several technologies that were designed and launched under the HealthTech program. These include:

- Uniject device sales by BD had reached 43 million units by the end of 2004, all of which have been for public-sector use, including sales of 1.2 million for Mexico, 1.8 million to Argentina, 1.6 million in India, 37.7 million with hepatitis B vaccine in Indonesia, and .7 million for other countries. Companies that are now filling their vaccines into the Uniject device include hepatitis B by BioFarma of Indonesia, Shantha Biologicals and Panacea of India, Lab Pablo Casara of Argentina, and Beijing Biologics of China, and tetanus toxoid by BioFarma of Indonesia. Biol of Argentina is considering filling gentamicin and oxytocin into the Uniject device; and Pfizer is working on testing the stability of their injectable contraceptives in the device.
- BD also reports that to date, over 2.5 billion immunizations have been administered using BD SoloShot™[2] devices. All SoloShot products are used in public-sector health programs, with a significant majority of sales being made to large international agencies, such as UNICEF and PAHO. These agencies distribute the products to approximately 60 emerging market countries in Africa, Asia Pacific, Latin America, Eastern Europe, and the Middle East.
- Sales of the HIV dipstick by the three remaining licensees—SPAN of India, Yayasan Hati Sahat of Indonesia, and Wiener of Argentina—have now reached over 13 million tests in their various markets. The HIV dipstick is still considered one of the lowest-priced rapid tests on the market at an average price of between US$0.45 and US$0.69 per test.
- Through 2004, TempTime (formerly Lifelines Technology, Inc.) has sold over 1 billion vaccine vial monitors to vaccine manufacturers who are selling their products via UNICEF for use in immunization programs throughout the world. The markers are now being used on all vaccines supplied through UNICEF.

[2] SholoShot is a trademark of BD.

- In Nepal, Maternal Child Health Products reports sales of 814,000 delivery kits since they started production in 1995, when HealthTech provided technical assistance to them regarding production and marketing of the kits.
- The malaria immunochromatographic strip test is being manufactured by SPAN Diagnostics of India and Human GmbH of Germany, both of which have sold over 115,000 tests since product launch. Meanwhile, Orchid Biomedical in India has sold over 10,000,000 malaria tests based on know-how that they received from HealthTech staff.
- Various publications that have been published under the HealthTech program are being widely used. At least 12,000 copies of the manual *Giving Safe Injections: Introducing Auto-disable Syringes.* Have been accessed through PATH's website in the last year. The material on use of autodisable syringes and sharps disposal containers for depot medroxyprogesterone acetate (DMPA) in Spanish was downloaded 2,000 times.

Immunization and Injection Technologies

Cold Chain Technologies

Health Need Addressed

Improperly maintained or outdated refrigeration equipment, poor compliance with cold chain procedures, inadequate monitoring, and poor understanding of the dangers of vaccine freezing contribute to the weakness of the current vaccine cold chain. Emphasis has long been placed on keeping vaccines cold, with less attention devoted to prevention of vaccine damage from freezing. Published reports and field evidence generated under HealthTech support anecdotal reports and demonstrate that accidental freezing of vaccines in the cold chain is commonplace, potentially resulting in widespread delivery of vaccines whose potency has been compromised.

HealthTech IV Solution and Potential Impact

Cold chain technologies, such as the vaccine vial monitor (VVM), new refrigeration technologies, and new vaccine presentations strengthen immunization programs' ability to provide outreach services, improve the reliability of vaccine storage and transport, and reduce unnecessary wastage of valuable vaccines. Most importantly, these technologies will reduce the delivery of ineffective vaccines. Supported by the USAID-funded HealthTech program, and in collaboration with other organizations, PATH is addressing these priorities. Efforts include fostering changes in cold chain policies and an improved global awareness of the magnitude of accidental vaccine freezing. Evaluation and development is directed toward new technologies that improve vaccine storage and transport, prevent accidental freezing, and increase cold chain capacity for important new vaccines and presentations.

Ultimate Goals and Objectives of HealthTech Project

- Increase awareness of the extent and consequences of inadvertent vaccine freezing.
- Build global policy supporting freeze prevention.
- Facilitate development of new freeze-proof cold chain equipment.

Status of Project as of March 2005

The Cold Chain Technologies team continues to promote freeze prevention in the vaccine cold chain at international UNICEF/WHO policy meetings. Working with Ministries of Health in Bolivia, Indonesia, Mozambique, and Viet Nam, PATH is modeling successful cold chain interventions designed to prevent vaccine freezing. Requests for technical assistance with implementation of the WHO-approved freeze assessment protocol demonstrate both increased concern for vaccine freezing as well as awareness of PATH expertise in vaccine freeze prevention.

Changes to cold chain equipment design are part of the solution to vaccine freezing, and the Cold Chain Technologies team will participate in the WHO Performance, Quality and Safety Project (PQS) to improve cold chain equipment and introducing freeze-prevention specifications. Work with equipment manufacturers include both field evaluation as well as guidance with the public-sector immunization market. An in-depth market analysis, informed by both end-user and manufacturer interviews, will support the development and introduction of new technologies by providing market definition and an investment case to manufacturers offering improved cold chain equipment with a freeze prevention design.

Milestones expected in the past six months	Achievements and progress towards milestones
New WHO policies and guidelines to prevent vaccine freezing.	WHO issues draft policy document entitled "Safe vaccine chain for the prevention of freezing and the improvement of immunization coverage". WHO convened a meeting of the Technet subcommittee on vaccine freezing to revise the draft guidelines.
Raise awareness of vaccine freezing problem.	PATH was sponsored by UNICEF and PAHO to initiate and oversee a cold chain temperature study in Bolivia.
Develop freeze-prevention plan as part of national EPI guidelines in Indonesia.	Indonesia held a national-level workshop on vaccine freezing and finalized its approach to freeze prevention.
Refine improved refrigerator technologies.	PATH evaluated a new domestic refrigerator from Japan, Twinbird and began discussions with the company on design refinements to meet WHO and freeze prevention criteria. Work with VaxiCool[1] was discontinued as the company lost interest in the public health market. Field evaluation of a new solar refrigerator design, called SolarChill, is near completion in Indonesia and Senegal. Performance issues were identified and minor equipment modifications will be required. A report to partners will summarize field performance and user feedback.

[1] VaxiCool is a registered trademark of Energy Storage Technologies, Inc.

Problems encountered	Actions taken or plans to resolve
Lots of mixed opinion from experts on the draft WHO policy.	PATH will lead the rewriting of the policy documents to incorporate meeting inputs.
One key element of the WHO plan—using water packs instead of ice packs for vaccine transport—may not provide sufficient cooling for reconstituted vaccines.	An expert committee is reviewing reconstituted vaccine stability and contamination issues. PATH is considering alternative ways to cool reconstituted vaccines.

Milestones expected in the next six months	Planned activities to reach those milestones
Finalize WHO policy to prevent vaccine freezing.	PATH will revise the draft policy document and press WHO for fast action in review and finalization.
Finalize WHO protocol on assessing temperatures in the vaccine cold chain (based on PATH's protocol).	PATH will review drafts.
Finalize PQS specifications for freeze-proof refrigerators.	PATH is a member of the PQS team and is pushing for strong freeze-prevention criteria.
Complete temperature monitoring study in Bolivia (with other funding from UNICEF).	PATH will oversee the study and assist in the analysis.
Establish new procedures in Mozambique to reduce freezing.	PATH will work with the Village Reach program to revise procedures and develop a training plan.
Assistance to manufacturers with the development, refinement, approval, and introduction of improved cold chain equipment.	Specifically we will: • Work with the Twinbird company to modify their domestic refrigerator into a vaccine refrigerator, then conduct laboratory and field evaluations. • Modify the SolarChill refrigerator to improve temperature stability. • Conduct a cold chain equipment market analysis to help manufacturers understand the public health cold chain market needs.
Publish paper presenting a literature review of global evidence of vaccine freezing in the cold chain.	Submit paper to a peer reviewed journal.

Sharps Waste Disposal

Health Need Addressed

Each year, more than 16 billion injections are administered worldwide. In some regions, 17 to 75 percent are estimated to be with reused, unsterilized injection equipment.[1] Unsafe reuse has been estimated to cause 20 million hepatitis B infections, 2 million hepatitis C infections, and 250,000 HIV infections annually.[2] The main tool to prevent reuse of unsterile syringes and needles is use of autodisable and safety needles and syringes. However, most syringes currently in use do not prevent reuse. Appropriate sharps and syringe waste management play a critical role in safe injection by disabling syringes to prevent reuse, facilitating the safe and immediate disposal of contaminated sharps, reducing infectious waste volume, and facilitating ultimate disposal.

Safe injection is impaired by the lack of policies on proper disposal of sharps, appropriate equipment, and evidence of cost-effective systems. Currently, sharps waste is dangerous to the community and health care workers; and waste handlers are not protected from hazardous sharps when collecting, storing, transporting or disposing of sharps waste.[3,4,5]

HealthTech IV Solution and Potential Impact

The use of needle removers to separate the needle from the syringe immediately after use reduces the risk of potential infection to patients, health care workers, waste handlers, and the community by:

- Immediately isolating the contaminated sharp.
- Preventing syringe and needle reuse (since the needle remover also destroys the syringe).
- Reducing needle-stick injury risk for waste handlers and scavengers.

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[1] Hutin Y, Hauri A, Armstrong G. Use of injections in healthcare settings worldwide, 2000: literature review and regional estimates. *British Medical Journal*. 8 November 2003;327(7423):1075.

[2] Hutin Y, Hauri A, Chiarello L, et al. Best infection control practices for intradermal, subcutaneous, and intramuscular needle injections. *Bulletin of the World Health Organization*. 2003;81(7):491–450.

[3] Jie L. *Rapid Assessment of Injection Practices in China, Final Report to the Ministry of Health of China and the Secretariat of SIGN*, December 2002.

[4] Dicko M, Oni AQ, Ganivet S, et al. Safety of immunization injections in Africa: not simply a problem of logistics. *Bulletin of the World Health Organization*. 2000;78(2):163–169.

[5] Rajasekara M, Sivagnanam G, Thirumalailolundusubramainan P, et al. Injection practices in southern part of India. *Public Health*. 2003;117:208–231.

By separating the sharp from the syringe, waste disposal systems are more effective and efficient. They:

- Provide an immediate option for sharps disposal via protected needle pits.
- Heighten awareness of contaminated sharps by creating behavioral practices specific to contaminated needle waste management.
- Reduce disposal costs by decreasing or eliminating the requirements for transport and safety boxes.

Taking into account developing-country injections, reuse, needle-stick injury, and infections caused by reuse, we have estimated that needle removal devices could, by 2013:

- Avert more than 9 million hepatitis B, hepatitis C, and HIV infections over a ten-year period (based on an assumption of 20 percent adoption of needle-remover devices by 2013 globally).
- Reduce the overall systems cost of injections (including treatment for inadvertent infection caused by unsafe injection) by more than US$70 million.
- Reduce the cost per safe injection from US$0.077 to US$0.065 over ten years.

Ultimate Goals and Objectives of HealthTech Project

The project goal is to advance, test, and introduce safe needle-removal and disposal systems for health centers and outreach services. The objectives are to:

- Determine the status of point-of-care needle-remover systems.
- Optimize needle-remover systems for use in developing-world health centers and outreach services.
- Validate needle remover systems in developing-world settings.
- Align global and national policies to accommodate needle-remover use.
- Introduce needle-remover systems into practice.
- Evaluate and refine needle-remover and syringe-disposal systems.

Status of Project as of March 2005:

Field trials in two countries (Uganda and Senegal) were completed to evaluate the BD Hub Cutter, the Balcan needle remover, and sharps barrels. The Hopkins needle-remover design has been advanced, and costs of prototyping are being investigated. Generic user materials for needle removers have been developed for device introduction. Specifications for needle removers were drafted for the World Health Organization (WHO).

Milestones expected in the past six months	Achievements and progress towards milestones
Design of Hopkins needle-remover prototype finalized.	Bench testing completed. Design specifications finalized for prototypes for field evaluation. Quotations for injection molded prototypes being solicited from outside vendors.
Acceptability, fit, and function of BD Hub Cutter evaluated in family-planning settings in Uganda.	Data collection completed. Results being analyzed for dissemination.
Appropriate sites for field testing of the Hopkins needle remover identified.	Field evaluation sites not finalized until prototype costs funded.
Generic procurement specifications for needle remover disseminated.	Procurement specifications drafted for WHO Quality and Safety Project (PQS) group.
User materials for needle-remover use developed/disseminated.	User materials developed and sent to India and PEPFAR country safe injection programs.
Design for outreach appropriate needle remover developed by HealthTech in public domain.	PATH submitted the needle remover-device design transfer package to the WHO Health Care Waste Management website to make it available to commercial companies for manufacturing and distribution. The website is currently being redesigned; PATH will continue to monitor when the transfer package is available on line.
Acceptability of Balcan needle remover evaluated after one year of use in a developing-country immunization setting.	Acceptability evaluated in Senegal. Data being analyzed.
Acceptability of sharps barrel as an alternative to the protected needle pit evaluated in a developing-country setting.	Acceptability evaluated in Senegal. Data being analyzed.
Bench testing of electric syringe melter completed.	Melter not received from designer. PATH in discussions with UNICEF and designer to offer our services.

Problems encountered	Actions taken or plans to resolve
Prototyping of the Hopkins needle-remover device is anticipated to be costly, yet it is needed in order to have sufficient numbers of devices for field evaluation.	Once all the vendor quotations are received, we will see if cofunding is needed and raise funds accordingly.
PATH did not receive the electric syringe melter for bench testing, since the developer would prefer to begin evaluations in the field without bench testing.	PATH continues to offer to conduct bench testing. The developer has yet to identify funds for field evaluation. Therefore, he may choose to send device to PATH to build evaluation momentum.

Milestones expected in the next six months	Planned activities to reach those milestones
Go/no go decision about field trial for Hopkins device.	Obtain quotes for prototypes. Determine if funding available. Determine if commercial interest.
Disseminate results of BD Hub Cutter evaluation.	Complete data analysis. Provide information to BD. Hold in-country (Uganda) dissemination meeting for stakeholders. Disseminate findings to interested groups.
Disseminate results of Senegal evaluation of acceptability of needle remover and sharps barrel.	Complete data analysis. Hold in-country dissemination meeting for stakeholders. Publish findings.
Document infection risks of used syringes (without needles).	Review literature for information about the infectivity of defanged syringes. Assess current modes of sharps disinfection and how a study might be designed to measure infectivity of defanged syringes.

Gentamicin in Uniject™ Devices

Health Need Addressed

WHO estimates that at least 4 million neonatal deaths (i.e., death during the first 28 days of life) occur around the world every year. Severe bacterial infections are major contributors of newborn morbidity and mortality. In the developing world each year, an estimated 30 million children develop an infection during the neonatal period, and infectious diseases account for over one-third of all neonatal deaths. In 2000, a WHO advisory committee recommended intramuscular injections of ampicillin and gentamicin as the standard therapy for these bacterial infections and the treatment of neonatal septicemia, meningitis, and pneumonia. Case-fatality rates for severe bacterial infections are high in part due to not administering or delaying the administration of necessary antibiotics. Therefore, it is important that newborns with these infections receive immediate treatment, even before the infectious agent is known. When neonatal infections occur, many deaths can be avoided if the signs are recognized early and the disease is treated promptly.

HealthTech IV Solution and Potential Impact

To improve neonatal survival from infectious diseases, Uniject™[1] injection devices prefilled with a single dose of gentamicin (hereafter called "gentamicin-Uniject") could be easily transported and used in a home setting with an oral antibiotic when the signs of a neonatal infection are first detected. Community-based health workers could be trained to use the gentamicin-Uniject device and a complementary oral antibiotic in order to extend the accessibility and facilitate the administration of antibiotics for early treatment of neonatal infections. Furthermore, gentamicin-Uniject devices could potentially be incorporated into the revised integrated management of childhood illness guidelines, which have been adapted for acute management of common infectious neonatal illnesses. If gentamicin-Uniject is used safely, properly, and efficiently for infants with severe bacterial infections, the Uniject device could make a significant contribution to reducing neonatal mortality in developing countries. HealthTech has recently allocated funds for further development of this application of the Uniject device, with cofunding provided by the Bill & Melinda Gates Foundation.

Uniject device filled with gentamicin.

[1] Uniject is a trademark of BD.

Ultimate Goals and Objectives of HealthTech Project

Create a sustainable, commercial supply of gentamicin-Uniject.

Status of Project as of March 2005

Search for a suitable R&D partner has been completed. Initial scope of work (SOW) with Instituto Biologico Argentino (Biol) to be signed momentarily and R&D effort will begin in earnest.

Milestones expected in the past six months	Achievements and progress towards milestones
Development of a SOW for formulation development with new laboratory facility. The SOW will provide for further investigation of sodium citrate and alternate buffers for stabilizing gentamicin formulations and will include forced degradation studies.	SOW with Biol completed and under negotiation with laboratory in Argentina.
Technical due diligence assessment of new laboratory facility.	Team member and pharmaceutical expert traveled to laboratory facility and conducted due diligence of Biol R&D facilities completed.
Identification and sourcing of bulk product.	Pending signed subcontract with Biol.
On an R&D bench level, fill the Uniject device with the most promising formulations and complete accelerated stability screening studies as per ICH guidelines.	Pending signed subcontract with Biol.
Recommendation for go/no-go decision for further pursuit of gentamicin-Uniject product.	Pending signed subcontract with Biol.
Liaise with Saving Newborn Lives and its collaborators (Johns Hopkins University [JHU] and the International Centre for Diarrheal Disease Research–Bangladesh [ICDDR–B]) on an on-going basis.	Ongoing contact with primary point person, Gary Darmstadt, at JHU.

Once an assured supply of gentamicin-Uniject for field evaluation becomes available, prepare criteria for allocation of limited supply to potential, future field evaluations taking place in the 12-24 month time frame.	On hold until product feasibility is determined.

Problems encountered	Actions taken or plans to resolve
Difficulty in identifying suitable R&D lab.	Consultant went to Argentina to determine suitability of facility in December 2004; scheduling difficulties due to construction at lab site permitted due diligence visit of PATH technical staff only in April 2005.

Milestones expected in the next six months	Planned activities to reach those milestones
Collaboration agreement with Biol completed.	Obtain quotation from Biol for revised scope of project; work with PATH Legal Affairs to prepare agreement.
Protocol and preparation for screening and compatibility study completes.	Technical exchange with Biol including regular follow-up phone conferences.
Screening and compatibility study initiated.	Visit by PATH technical staff to review final preparations and assist Biol with filling of gentamicin into the Uniject device.
Interim results of screening and compatibility study available.	Ongoing monitoring and oversight of BIOL.

Oxytocin in Uniject™ Devices

Health Need Addressed

Hemorrhage is the leading cause of maternal mortality and is a particular problem in home deliveries because the short response time makes referral impractical in most cases. The percentage of maternal deaths due to post partum hemorrhage (PPH) has been reported as 25 percent in sub-Saharan Africa, 27 percent in West Africa, and 45 percent in Indonesia. Annually, approximately 130,000 women are known to die due to hemorrhage during childbirth.[1] The use of oxytocin for routine management of the third stage of labor can significantly reduce the incidence of PPH. Active management of the third stage of labor (AMTSL), which includes routine use of a 10-IU dose of oxytocin given intramuscularly, is recommended by the World Health Organization (WHO) for all institutional deliveries and home deliveries attended by a person with midwifery skills.[2]

HealthTech IV Solution and Potential Impact

A prefilled, nonreusable syringe, such as Uniject™[3] is thought to be the safest mechanism for delivering the life-saving benefits of oxytocin to women in peripheral health care settings and homes. This prefilled, easy-to-use, injection-ready format ensures that an accurate premeasured dose is given in a nonreusable, sterile device with minimal preparation and minimum waste. Based on evaluations in Lombok, Indonesia, midwives found oxytocin in Uniject (hereafter called "oxytocin-Uniject") to be safer and more convenient to use during home deliveries than traditional needle and syringe. This study, and results from an upcoming study in Vietnam, may indicate that oxytocin-Uniject can play a major role in facilitating adoption of AMTSL strategies, thus preventing maternal mortality due to hemorrhage.

Ultimate Goals and Objectives of HealthTech Project

Improve and ease adoption of AMTSL initiatives and therefore reduce PPH by engaging one or more pharmaceutical producers to supply oxytocin-Uniject commercially on an ongoing basis. Note that PATH has been supporting a minimal amount of work on this project to date with funding from another source. USAID funding for this project started October 1, 2004.

Status of Project as of March 2005

Project is currently redefining focus and goals in order to match the needs of USAID and Prevention of Postpartum Hemorrhage Initiative (POPPHI) more closely.

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[1] Best practices page. Maternal and neonatal health website. Available at: http://www.mnh.jhpiego.org/best/pphactmng.asp. Accessed April 27, 2005.

[2] Mother-baby package: Implementing safe motherhood in countries. WHO/FHE/MSM/94.11, Geneva, 1994.

[3] Uniject is a trademark of BD.

Milestones expected in the past six months	Achievements and progress towards milestones
Decision on short-term supplier plan.	On hold, pending results of discussions with USAID and final work plan approval.
If not Dolphin Laboratories, engage alternative interim supplier.	Potential supplier (Biol of Argentina) identified, but on hold, pending results of discussions with USAID and final work plan approval.
If Dolphin Laboratories, undertake technical assistance necessary to improve their reliability and quality as an oxytocin-Uniject supplier.	N/A
Participate in the POPPHI uterotonic supplies working group.	PATH technical staff participated in February steering committee and UDD meeting.
If sufficient funding available, identify suitable laboratory partner to conduct formulation investigation.	On hold, pending results of discussions with USAID and final work plan approval.
Complete evaluation of supply allocation criteria.	On hold, pending results of discussions with USAID and final work plan approval.
Develop timetables of oxytocin-Uniject availability for field evaluators, concurrent with development of short-term supplier.	On hold, pending results of discussions with USAID and final work plan approval.
Other milestones and results.	A study conducted by PATH and the Ministry of Health of Vietnam with other funding of oxytocin in Uniject used to prevent post-partum hemorrhage in women in the third stage of pregnancy resulted in positive feedback about the use of the device for delivery of oxytocin. Ninety-eight percent of the midwives participating said that the Uniject device was easier to use than standard syringes. Plus the devices will be less expensive than ampoules if prices at the lower end of likely range become available.

Problems encountered	Actions taken or plans to resolve
Refinement of USAID priorities related to utertonics and oxytocin, and oxytocin-Uniject in particular, have necessitated prolonged discussions with SO2 staff to determine the revised focus for project activities.	Steve Brooke traveled to Washington, DC, to meet with SO2 staff on December 14, 2004, to address these concerns; further discussions via email, telephone, and during POPPHI meetings have ensued. Estimated date of finalization of work plan through September 2006 is at the end of March 2005.

Milestones expected in the next six months (under HealthTech funding)	Planned activities to reach those milestones
Proposed: (but not yet accepted by USAID)	
Complete initial landscape assessment of suppliers of oxytocin.	Desk research, contact existing NGO and agency distributors of essential drugs.
Initiate technical collaboration with Biol on additional stability studies of their oxytocin in ampoules.	Develop and finalize collaborative agreement; jointly develop protocol, get input from others such as USP, WHO, Argentine FDA; and initiate work.
Initiate technical collaboration with Biol on additional stability studies of their oxytocin-Uniject.	Develop and finalize collaborative agreement; jointly develop protocol, get input from others such as USP, WHO, Argentine FDA; and initiate work.
Participate in the POPPHI uterotonic supplies working group.	Activities as requested by POPPHI.

Introduction of Injectable Contraceptives in the Uniject™ Device

Health Need Addressed

Injectable contraceptives are becoming increasingly popular around the globe as women search for safe, highly effective, reversible methods of contraception that do not require compliance with a daily regimen. Depot medroxyprogesterone acetate (DMPA) is administered by injection once every three months, making it highly convenient. Cyclofem®[1] injectable contraceptive (also known as Lunelle and CycloProvera) is administered by injection every month and is formulated to allow women to have more normal menstrual cycles—an advantage in many cultures. Currently, international development and family planning agencies purchase over 25 million doses of DMPA injectable contraceptives annually for distribution to family planning programs throughout developing countries. Approximately 7 million doses of Cyclofem injectable contraceptives were sold in the year 2000.

International development and family planning agencies and recipient governments are continually looking for feasible and affordable methods to reduce unsafe injection practices that can lead to the spread of bloodborne diseases. Provision of one sterile needle and syringe with every dose of injectable contraceptive is the current standard. However, there is a risk with disposable syringes that they will be reused. Autodisable (AD) syringes prevent reuse, but like disposable syringes they can be diverted to other uses during the distribution process. The Uniject™[2] prefill injection device has distinct advantages in terms of both safety and procurement.

HealthTech IV Solution and Potential Impact

A decade ago, prefilled syringes were too costly for use in public-sector health programs, and no prefilled syringe on the market offered an AD feature. Under the HealthTech project, PATH was able to develop the Uniject device, a proprietary, prefilled, AD injection system. The Uniject device prevents reuse, simplifies matching of syringes and supplies, ensures dose accuracy, and is so simple to use that injection at home by the patient or a family member is feasible. Now the device is being considered for use filled with injectable contraceptives. With funding from the USAID Office of Population, PATH has been working for a number of years with the dominant international supplier of DMPA injectable contraceptive to evaluate potential use of Uniject devices. This company was Pharmacia until it merged with Pfizer in April 2003. PATH has also worked with Aplicaciones Farmacéuticas, a Mexican pharmaceutical company which has developed but not yet launched a version of its once-a-month injectable contraceptive, Cyclofem, in Uniject devices.

[1] Cyclofem is a registered trademark of The Concept Foundation.
[2] Uniject is a trademark of BD.

Ultimate Goals and Objectives of HealthTech Project

- To increase the safety, acceptance, and reach of DMPA injectable contraceptives in family planning programs.
- To enable innovative new family planning program options, such as home injection and outreach.

Status of Project as of March 2005

Pfizer and BD have continued negotiating the long-term commercial agreements for exclusive supply of Uniject for DMPA injectable contraceptive over the past six months. Pfizer has also completed additional technical evaluation steps, and no technical barriers have arisen. The project is poised to move into Pfizer's next phase of implementation; however this will only happen if Pfizer and BD come to terms on the commercial supply agreements.

Milestones expected in the past six months	Achievements and progress towards milestones
Continue to encourage progress by BD and Pfizer towards finalizing a Uniject supply agreement, so as to wrap up PATH involvement in the negotiation.	Ongoing.
Complete collection of data needed to update the background paper on volumes and trends in supply of injectable contraceptives to international donor agencies for distribution in developing countries.	Ongoing.
Draft an updated timeline/decision-point diagram to identify and map key milestones and decision points in Pfizer's new-DMPA program (their work to develop, register, and scale up production for new-DMPA in Uniject). Emphasis is on the likely timing of availability of supplies of new-DMPA in Uniject to USAID.	Deferred until BD-Pfizer complete commercial negotiations.
Hold a collaborator meeting between USAID, PATH, Pfizer, and BD to finalize the timeline/decision-point diagram noted above.	Deferred until BD-Pfizer complete commercial negotiations.

Clarify needs for any training and information materials—during 2005—to support potential clinical and field evaluations of new-DMPA in Uniject.	Product for clinical evaluation now not expected before 2006.

Problems encountered	Actions taken or plans to resolve
BD-Pfizer negotiations for long-term supply and exclusivity agreement of Uniject for injectable contraceptives not completed during this six month period. Slow communication process between these two large organizations.	Continue interaction with both; encourage resolution as soon as possible.

Milestones expected in the next six months	Planned activities to reach those milestones
BD and Pfizer conclude commercial negotiations.	Ongoing follow-up with both parties
PATH provide formal concurrence with exclusivity terms of BD-Pfizer agreement.	Keep Chris Elias informed of status of negotiations; work with PATH Legal Affairs to provide formal concurrence when appropriate.
Identify and map key milestones and decision points in Pfizer's new-DMPA program (their work to develop, register, and scale up production for new-DMPA in Uniject). Emphasis is on the likely timing of availability of supplies of new-DMPA in Uniject to USAID.	Contact with Pfizer particularly important for this, and they will drive the process.
Provide USAID with updated background paper on volumes and trends in supply of injectable contraceptives to international donor agencies for distribution in developing countries.	Team members complete draft in May, internal review and final production, provide to USAID.
Hold a collaborator meeting between USAID, PATH, Pfizer, and BD to review the timeline/decision-point diagram noted above and discuss collaborative activities in next phase of Pfizer work.	Timing contingent on conclusion of Pfizer-BD commercial negotiations.

Diagnostic Technologies

Retinol Binding Protein Enzyme Immunoassay

Health Need Addressed

Micronutrient malnutrition has emerged as one of the greatest public health concerns in the world today. Almost one third of children in developing countries are affected to some degree by vitamin A deficiency (VAD), which impairs their growth, development, vision, and immune function (including resistance to disease), and in extreme cases leads to blindness and death.[1,2,3]

A body of knowledge and experience exists that effectively addresses VAD through both short-term and long-term interventions. Global efforts have promoted capsule supplementation, food fortification, nutrition education, and the so-called food-based strategies to combat VAD. However, the targeting and implementation of effective interventions requires accurate and timely data. Generating information on VAD at a country and subnational level has been hampered by technology constraints. The lack of affordable, valid, and reliable screening methods has made it difficult and expensive to conduct badly needed vitamin A assessments. The development and introduction of the retinol binding protein-enzyme immunoassay (RBP-EIA) to assess VAD alleviates this constraint by generating prevalence data and information to promote the planning, implementation, and evaluation of vitamin A interventions to improve child health and nutrition.

HealthTech IV Solution and Potential Impact

The RBP-EIA is a competitive assay, which detects and quantifies retinol binding protein in human serum. The test uses purified human RBP adsorbed to microtest strip wells to compete with natural RBP found in serum. The test results for 96 determinations are available in as few as 35 to 40 minutes after the start of the assay; however, it is strongly recommended that all samples, including calibrators, be performed in duplicate. Therefore, the kit provides a total of 48 results. The RBP-EIA is designed to access and monitor the vitamin A status in populations. While the results for the assay are quantitative, it should not be considered a diagnostic test for detection of VAD in individual patients, but rather, as a research and epidemiological surveillance tool to be used at a population level.

This technology addresses USAID's strategic objective to increase the use of key child health and nutrition interventions (SO3). It does this by improving the quality and

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[1] UN ACC/SCN (United Nations Administrative Committee on Coordination/Subcommittee on Nutrition). *Third report on the world nutrition situation.* Geneva:ACC/SCN; 1997.

[2] World Health Organization, *Global prevalence of vitamin A deficiency: Micronutrient deficiency information system. WHO MDIS Working paper #2.* Geneva:WHO; 1995.

[3] Sommer A, West KP. *Vitamin A deficiency: health, survival, and vision.* New York, NY and Oxford, UK: Oxford University Press; 1996.

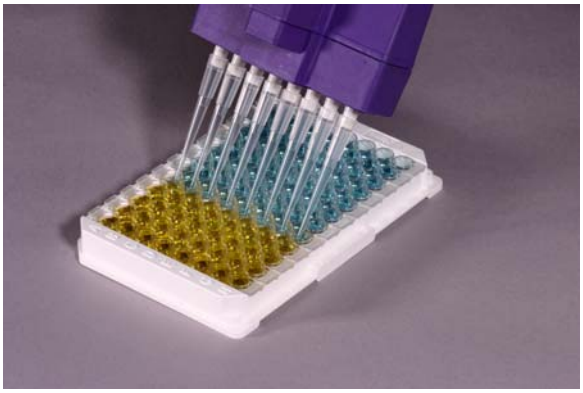
availability of key screening services (IR 3.4), improving preventive behaviors related to child health and nutrition (IR 3.3), and providing information to improve policies and increase global, national, and local resources for appropriate child health interventions (IR 3.2).

The RBP-EIA offers a rapid, inexpensive, and quantitative tool for determining vitamin A status at the population level. Vitamin A status is currently being determined by "gold standard" HPLC methodologies that are expensive and require significant investments in training and time to carry out. The RBP-EIA test developed at PATH is simple and requires a relatively small amount of specimen. It reduces reliance on centralized laboratory facilities in developing countries and saves time and money by eliminating the need to transport specimens to a developed country for analysis using overly sophisticated and costly tests such as HPLC. It provides a more cost-effective tool for the monitoring and recognition of VAD in targeted populations, will assist surveillance units in the field with the assessment of VAD status at the population level, and reduces the time between assessment and implementation of interventions to address VAD. We expect that the RBP-EIA will facilitate the ease of conducting vitamin A field assessments and increase the number of countries that conduct prevalence surveys to assess VAD, especially in countries where they have not yet been performed but where the need may be the greatest.

Ultimate Goals and Objectives of HealthTech Project

Our goal is to enhance the reliability and ease of VAD assessment and decrease the associated cost. Our objectives are to:

- Improve the consistency of the results of vitamin A assessment, including ease of specimen analysis and interpretation.
- Improve the reliability of VAD estimates.



RBP-EIA Enzyme immunoassay test for determining vitamin A status.

Status of Project as of March 2005

Field evaluations and commercial transfer of the RBP-EIA are near completion. Current activities support the informed selection of the RBP-EIA and are targeted to ensure proper use of the RBP-EIA in field settings. Training materials and job aids are being developed to ensure proper sample collection, handling and storage, and to assist new users with conducting the test with the commercially manufactured RBP-EIA test kit.

Milestones expected in the past six months	Achievements and progress towards milestones
Complete results and final report for Thailand evaluation.	Study completed. Results: • Showed the first evidence of the biological comparability between serum retinol levels estimated from venous blood and capillary blood. • Adds to a growing body of research that has demonstrated close correspondence between retinol in venous blood samples and RBP in capillary blood.
Complete data analysis of dried blood spots stability study conducted in Tanzania.	The Tanzania study comparing retinol and RBP from venous blood has been completed by London School of Hygiene and Tropical Medicine and the results have been reviewed and approved by PATH. Correlation and validity of the RBP-EIA test performed in a laboratory in Tanzania were similar to tests performed in the United States. Serum RBP correlated well with HPLC serum retinol concentrations. Sensitivity was high at 92.5 percent, while specificity was only moderate (65.2 percent). The association between serum retinol and RBP did not change after adjustment for infectious disease or signs of malnutrition.

Meet with key donors of existing micronutrient programs to foster informed selection of the test, publish journal articles, develop briefing materials, participate in international nutrition meetings, and conduct test demonstrations.	International Vitamin A Consultative Group meeting accomplishments held in November 2004 included: • Oral presentation on RBP-EIA at plenary session. A lot of positive interest in the test was expressed. • Presented results from Thailand evaluation in an evening session. • Introduced Scimedx representative to potential users.
Senegal sample analysis for retinol completed by CDC as a result of multiple problems with the original retinol analysis. Complete analysis of the RBP from serum collected for a micronutrient intervention conducted in Senegal in conjunction with University of California at Davis, the University of Dakar, and the Micronutrient Initiative.	See problems encountered below.
Job aids developed and field-tested in support of field use of the RBP-EIA. End-user feedback obtained and incorporated into the RBP-EIA and supporting materials.	Job aid for sample collection, handling, and storage completed. End-user feedback questionnaire developed and distributed to four researchers conducting the RBP-EIA label review.
Candidate "early adopters" are selected and provided with RBP-EIA tests and Q&A technical support at no cost to gain exposure for the test, build a market, and demonstrate the technology. Quality control activities are implemented to ensure that both retinol and RBP assessments are precise and accurate.	Tests purchased from Scimedx to support early adopters. Developed matrix to screen potential users. Identified three potential studies in Myanmar (UNICEF), PNG (CDC), and Mali (CDC) where the RBP-EIA is being considered.
RBP-EIA introduced to key stakeholders and the broader consumer audience. Communication tools developed and introduced to describe and promote the RBP-EIA test.	Created CD for distribution to stakeholders that provides critical documents and information on the RBP-EIA. Technical Bulletin developed with Scimedx.

Problems encountered	Actions taken or plans to resolve
Subagreement with consultant to develop new training aids for end users and complete data analysis required a lot of negotiation with the University of Washington and was not signed until late March 2005.	Subagreement has been signed and the deadlines extended to accommodate the work.

Milestones expected in the next six months	Planned activities to reach those milestones
Senegal sample analysis for retinol completed by CDC as a result of multiple problems with the original retinol analysis. Complete analysis of the RBP from serum collected for a micronutrient intervention conducted in Senegal in conjunction with UC Davis, the University of Dakar, and the Micronutrient Initiative.	Complete data analysis.
Job aids developed and field-tested in support of field use of the RBP-EIA. End-user feedback obtained and incorporated into the RBP-EIA and supporting materials.	Develop new training material to accompany test kit and to be used in conjunction with test kit insert. Test and revise new training materials through end-user benchmarking. Produce electronic versions and laminated job aids for distribution to users of the RBP-EIA.
Candidate “early adopters” are selected and provided with RBP-EIA tests and Q&A technical support at no cost to gain exposure for the test, build a market, and demonstrate the technology.	Distribute tests to CDC for use in analysis of serum from Mali and PNG to assess VAD. Obtain continued end-user feedback through a questionnaire. Quality control activities to ensure that RBP-EIA is used appropriately in the field. Complete label review and end-user feedback for commercial RBP-EIA test kit.
RBP-EIA introduced to key stakeholders and the broader consumer audience.	Organize meetings between Scimedx and potential buyers of the RBP-EIA.

Immunochromatographic Strip Test for Gonorrhea

Health Need Addressed

Despite long-standing, global public health efforts to control sexually transmitted infections (STIs), infections caused by *Neisseria gonorrhoeae* still occur in epidemic proportions in the developing world and in specific regions of the United States. For effective control of gonorrhea (GC), STD control programs must offer early and accurate diagnosis of symptomatic infection and identification of invasive, complicated, or asymptomatic infections. Control of STDs is also considered to be an essential component in the control of HIV/AIDS transmission.

HealthTech IV Solution and Potential Impact

The immunochromatographic strip (ICS) test for diagnosis of GC, developed under HealthTech III and IV, utilizes relatively inexpensive, off-the-shelf components and is formatted to identify L7/L12, a specific gonoccocal antigen, directly from clinical specimens. The strips are stable at ambient temperatures when packaged appropriately. This simple, rapid test will allow testing to be performed on direct clinical specimens from patients in rural or smaller clinics, regional hospitals, and STD clinics in the developing world, or in other resource-limited settings. Results can be returned within one hour, thereby allowing effective patient follow-up, additional counseling, and prescription of therapeutic drugs, if needed. Epidemiological surveillance teams in the field may also use the test to gather baseline data or to assess the effect of public health interventions.

Ultimate Goals and Objectives of HealthTech Project

- Commercial availability of rapid gonorrhea test for use in developing countries.
- Published data supporting the utility of this test in the developing world.
- Endorsement of the test by the World Health Organization (WHO).

Status of Project as of March 2005

The technology transfer of the GC ICS test to our first recipient is nearly complete with both supply agreements and licensing in the final stages of negotiation. The test was evaluated in a WHO-sponsored trial in Benin with encouraging results that showed sensitivity of 71 percent and specificity of 97 percent.

Milestones expected in the past six months	Achievements and progress towards milestones
Collaboration with our technology transfer partner to improve the performance of the test.	The collaboration with Orchid Biomedical has proved to be successful. The latest iteration of the test appears to be at least 30 times more sensitive than the original test.
Increased coverage of use of the GC test by identifying additional commercial partners outside of the current partner's area of distribution.	We are in preliminary discussions with manufacturers in Brazil who may be candidates for a technology transfer.
Collaboration with developing-country partner on validation/introduction study.	Licensing issues have not allowed us to pursue this task during the past six months.
Other milestones and results.	Further analysis of the results of WHO-sponsored trial in Benin of the PATH tests and others were much more positive than previously reported. The encouraging results showed sensitivity of 71 percent and specificity of 97 percent for the PATH test.

Problems encountered	Actions taken or plans to resolve
Licensing and supply agreements to the antibodies that are a fundamental component of the test have taken much longer than expected.	We worked through contacts at Thermo and Asahi (the owners of the antibodies) to emphasize our desire to gain access to the IP necessary for this test. A license agreement for all parties is now expected in May 2005.

Milestones expected in the next six months	Planned activities to reach those milestones
An introduction and validation study with our first technology transfer recipient.	We will review and advise the development of study protocols created by our first technology transfer recipient. These studies will allow the recipient to obtain regulatory clearance with the India central government.
Initiation of technology transfer activities to a second recipient.	PATH representatives will be in contact with potential candidates, will conduct due diligence on those who are deemed appropriate, and then begin the process of technology transfer with this institution.
Enhancements of test based on the improvements accomplished by our technology transfer recipient.	PATH will work with Orchid Biomedical to apply the improvements to the test and increase sensitivity that way.
Publication of results of Benin trial of gonorrhea tests in which the PATH test achieved 71 percent sensitivity and 97 percent specificity, considered very good results.	Coauthored an abstract for presentation at the International Society for Sexually Transmitted Disease Research meetings to be held in Amsterdam, July 2005. Abstract was accepted, and study results will be presented.

Immunochromatographic Strip Test for Chlamydia

Health Need Addressed

Accurate diagnosis and control of sexually transmitted infections (STIs) continues to be a challenge for health care providers in many developing countries. Although there are many simple and rapid tests available for the diagnosis of *Chlamydia trachomatis* (CT) infection, the sensitivity of many are low, and most, if not all, are too expensive for use in developing countries. The development of a rapid immunochromatographic strip (ICS) test for Chlamydia that is sufficiently sensitive, specific, rapid, and affordable would be an extremely valuable tool.

HealthTech IV Solution and Potential Impact

The ICS test for Chlamydia, developed under HealthTech III, utilizes relatively inexpensive, off-the-shelf components and is formatted to identify a Chlamydia-specific antigen obtained directly from clinical specimens. The strips are stable at ambient temperatures if packaged appropriately. This simple, rapid test will allow testing to be performed on direct clinical specimens from patients at the point of care in rural or smaller clinics, hospitals in the developing world, or other resource-limited settings. Results can be returned within one hour, thereby allowing effective patient follow-up, additional counseling, and the prescribing of appropriate therapeutic drugs if needed. Epidemiological surveillance teams in the field may also use the test to gather baseline data or to assess the effect of public health interventions.

Ultimate Goals and Objectives of HealthTech Project

- Commercial availability of rapid Chlamydia test for use in developing countries.
- Published data supporting the utility of this test in the developing world.
- Endorsement of the test by the World Health Organization.

Chlamydia 20-minute ICS test.

Status of Project as of March 2005

The CT ICS test project is moving ahead quickly. The laboratory based development is nearly complete and we are preparing for a field trial in Bolivia and technology transfer to a commercial manufacturer in India.

Milestones expected in the past six months	Achievements and progress towards milestones
Retrospective evaluation of clinical samples and assay verification has been completed on the two-step extraction system prototypes but remains to be done using the single-step extraction version.	Endocervical, vaginal, and mucous swab samples from the Planned Parenthood Mar Monte study have been evaluated. The assay has now been verified with the two-step extraction only. This extraction process provides the most robust and consistent results. The decision was made to not move forward with the single-step extraction version as the two-step process provides the most consistent results.
Development of the CT ICS test to continue once the assay reagents and components are verified with the retrospective evaluation.	We have now screened new, inexpensive antibodies for use in the CT ICS system. These antibodies performed exceptionally well and were substituted in the assay.
Documents describing the processes and procedures for manufacturing the assay and its components (e.g., standard operating procedures [SOPs]) to be drafted and refined as the product is developed.	The SOPs have been drafted, revised, and finalized. These documents will be used in our first technology transfer of the CT ICS test.
Investigation of signal enhancement systems to improve the assays sensitivity.	We investigated the use of new sample collection systems (flocked swabs) and new detection systems (fluorescence-based detection). These efforts are ongoing.

Problems encountered	Actions taken or plans to resolve
Uncertainty about original antibody (controlled by Thermo) cost and availability for our test.	We evaluated other CT antibodies and decided to use a commercially available antibody that has equal performance, is available worldwide, and is approximately 1/6 the cost of the Thermo antibody.

Milestones expected in the next six months	Planned activities to reach those milestones
Preliminary results from a final evaluation of the test.	We will initiate a field-based evaluation of the CT ICS test in Bolivia. This evaluation will determine the sensitivity and specificity of the test in uncontrolled clinical settings. It will also determine the utility of new sample collection devices with our test. Approximately 1,800 women will be screened with the test.
Technology transfer to a commercial manufacturer in the developing world.	We will sign licensing agreements with suppliers and manufacturers and transfer the SOPs to a manufacturer in India. This technology transfer process will be unique in that we will partner with our recipient to make improvements to the test and share all innovations that results from this process.
Identification of a second technology transfer recipient, preferably in South America.	We will contact manufacturers in Brazil who have expressed interest in our rapid test portfolio. We will also contact manufacturers in Vietnam.

Rapid Diagnostics for Tuberculosis

Health Need Addressed

Tuberculosis (TB), the disease produced by the bacterium *Mycobacterium tuberculosis*, continues to cause significant morbidity and mortality worldwide. Recently, the increasing incidence of TB—particularly in the developing world—has been associated with HIV infection, the emergence of multiple drug-resistant strains, and the breakdown of preexisting screening programs. Globally, TB is already the leading cause of death among people with AIDS, accounting for about 40 percent of fatalities in Africa. While worldwide reporting reflects incomplete data, it is estimated that globally as many as 3 to 4 million deaths can be attributed to TB each year. Astonishingly, this figure exceeds the estimate for malaria or acute respiratory infections and ranks TB as one of the most important infectious disease problems today. The available data indicate that 95 percent of the clinical cases and 98 percent of the deaths attributable to TB occur in the developing world.

The general consensus is that the top priority for TB-control programs should be active case detection, confirmation of infection, and therapy for all infectious cases in both low- and high-prevalence areas. Since 1996, the World Health Organization (WHO) has promoted the Directly Observed Therapy Short Course (DOTS) strategy for TB control, one aspect of which is case detection through sputum smear microscopy of TB suspects. The emphasis on TB diagnosis by sputum smear microscopy is, however, problematic. The method is simple and relatively inexpensive but requires quality microscopes, experienced microscopists, and exacting quality control. The specificity of smear microscopy has been reported to be as high as 99.2 percent, but reports of sensitivity range from 40 to 60 percent for a combination of three examinations and may be as low as 20 to 25 percent in high HIV sero-prevalent populations (personal communication, Michael Iademarco, CDC).

In developing countries, diagnostic sensitivity may be improved by sputum culture. However, a sputum culture takes weeks to yield results and requires dedicated equipment and technical expertise. Long delays can result in the patient being treated empirically and inappropriately, and the cost of some of the current culture systems may also be beyond what many control programs in resource-poor countries can afford. Recently, several new diagnostic methods for TB have been developed, including nucleic acid detection and amplification techniques. Although they provide advantages in terms of sensitivity, these methods are still too technically complex and expensive for use in most developing-country settings.

HealthTech IV Solution and Potential Impact

Serodiagnostic technology offers the potential for development of rapid, inexpensive tests for TB. They can be fairly simple to use, formatted as high- (e.g., ELISA-based assays) or low-volume assays (e.g., immunochromatographic strip tests [ICS]), and can be relatively inexpensive. There have been efforts to develop TB serodiagnostic tests for many years, but early tests had unacceptably low specificity. High test specificity is required because a false positive result can commit the patient to a long course of inappropriate therapy, with risk of stigma, high costs of antibiotics, and the potential for side effects.

For the developing world, inexpensive and less complex serodiagnostic tests can be developed in simple dipstick, strip, or particle agglutination formats, which can be performed in clinics with lower patient volumes. These could be used at the peripheral or district health care level to fortify syndromic diagnosis of TB in sputum-positive patients and to detect suspected cases of sputum-negative or extra-pulmonary TB. This would be especially effective in specialty applications (e.g., testing of HIV-positive persons), since the clinical signs and symptoms of TB are often atypical, and skin test anergy may be present.

The development of a TB ICS test could provide an alternative diagnostic tool to supplement or replace microscopic diagnosis of TB-positive sputum smears or identify suspected cases of TB-negative sputum smears or extra pulmonary TB infection and therefore will:

- Extend or enhance immediate or same-day return of results in intermediate to peripheral hospitals and clinics to allow appropriate therapy to be administered.
- Provide a back-up tool to microscopic examination of stained sputum smears for use in central or specialty clinics where high-volume diagnosis is currently performed well.
- Potentially reduce testing costs through technology transfer for commercial manufacturing in the developing world.

Ultimate Goals and Objectives of HealthTech Project

- To develop an accurate and simple serodiagnostic test for TB, which is affordable to populations in the developing world.
- To understand the need and market for rapid diagnostics for TB in order to make informed decisions about investments in development of tests.

Status of Project as of March 2005

TB ICS test development has been discontinued due to poor results from field trials in Botswana, Ukraine, and India. PATH has started to evaluate the feasibility of a phage-based approach to a point-of-care test for tuberculosis. Meanwhile the study of the need and market for a rapid TB test is ongoing.

Milestones expected in the past six months	Achievements and progress towards milestones
An understanding of the demand for rapid TB diagnostics in the public sector, taking into account the geographic, demographic, and health system variations present in five countries in the developing world.	This market study, which was meant to inform the Gates Foundation Global Forum on Diagnostics, has been put on hold until a consensus is reached on what data are needed.
Develop and conduct a market analysis that will study the economic and public health impact of the introduction and uptake of new diagnostic tests. The study is planned to take place in five countries.	On hold as explained above.
Formal collaboration with partner for the development of a new rapid assay approach to TB diagnosis that employs macrophage replication as a mechanism for signal detection in sputum samples.	We have established a collaboration with the Seattle Biomedical Research Institute and Macrophage, a private sector company in Denver, to develop a phage-based assay for TB diagnosis.
Proof of principle of a TB diagnostic using phage replication and lateral flow technologies.	Laboratory-based work has moved more slowly than expected but we are nearing proof of principle on the assay.
Identification and early development of another new serodiagnostic test for TB. Report on results from new experiments.	Budget constraints did not allow us to develop a new serodiagnostic test.
Recommendations about the future of serodiagnostic tests for TB.	We completed a draft of a TB manuscript for submission to a peer-reviewed journal that details our recommendations for new TB diagnostics including serodiagnostics.

Problems encountered	Actions taken or plans to resolve
The Gates Foundation Global Forum on Diagnostics delayed our work on market and infrastructure demands for new TB diagnostic tests.	We had several conference calls with USAID and Gates Foundation representatives to resolve these issues. They remain unresolved.

Milestones expected in the next six months	Planned activities to reach those milestones
Manuscript about TB diagnostics submitted to a peer-reviewed journal.	We will revise the current manuscript draft, select an appropriate journal, and submit it.
Proof of principle attained for a phage-based TB assay.	Further laboratory experiments to reduce phage replication time and development of lateral flow detection system will take place.
Explore funding opportunities for new TB diagnostics.	We are developing a proposal to Foundation for Innovative New Diagnostics (FIND) to fund the development of a new lateral-flow-based assay using sputum that has an instrumented detection system. This detection system may be more sensitive than current ICS-based platforms.
A final plan for the TB market and infrastructure analysis.	We will develop a revised concept paper and get support from all stakeholders for our work. We will also begin this work in several countries, either with archived or prospectively collected data.

Diagnostics for Surveillance

Health Need Addressed

Measles is a highly infectious, acute viral illness that is a leading cause of childhood death, malnutrition, diarrhea, mental retardation, visual and hearing impairment, and immune suppression in mostly developing countries. Despite the worldwide decline in the incidence of measles cases, the disease remains a major cause of mortality and morbidity, accounting for over 800,000 deaths annually[1,2] with more than 50 percent of these deaths occurring in Africa.[3] Because of the high burden of the disease in some African countries, World Health Organization/Regional Office for Africa (WHO/AFRO) has recommended case-based surveillance in conjunction with immunization as a means of controlling and preventing measles outbreaks.[4]

Currently, the confirmation of suspected cases of measles is made from serum samples using an enzyme immunoassay (EIA) as mandated by the WHO.[5] Measles diagnosis from serum requires that venipuncture be performed, a process that involves the use of syringe and needle, centrifugation of the blood sample to separate the serum, cold chain for shipment of the separated serum, and the handling and disposal of infectious waste. These factors increase the costs associated with measles diagnosis, costs that are already a financial strain in resource-poor countries. An alternative to serum is the dried blood spot (DBS), which the WHO has identified as an appropriate sample for the detection of measles-specific IgM.

HealthTech IV Solution and Potential Impact

The use of DBS instead of sera can potentially reduce the costs and infrastructure requirements associated with measles detection and surveillance. Demonstration of DBS samples as an economical, convenient, and equally effective alternative to sera for the detection of measles-specific IgM can give further support to WHO and country surveillance programs for the use of this sampling technique for measles detection. Moreover, because of the convenience of sample collection, transport, and storage of the filter paper cards, incorporation of the DBS sampling method in measles surveillance can conceivably lead to an increase in coverage of suspected measles cases. PATH is

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1 de Quadros CA. Can measles be eradicated globally? Public health reviews. *Bulletin of the World Health Organization*. 2004;82(2):134–138.

2 Bellini WJ, Helfand RF. The challenges and strategies for laboratory diagnosis of measles in an international setting. *Journal of Infectious Disease*. 2003;187(S1):S283–S290.

3 El Mubarak HS, Yuksel S, Mustafa OM, et al. Surveillance of measles in the Sudan using filter paper blood samples. *Journal of Medical Virology*. 2004;73:624–630.

4 World Health Organization/Regional Office for Africa (WHO/AFRO), Vaccine Preventable Disease Unit, WHO/African Region. Measles surveillance in the African Region. *Vaccine Preventable Diseases Bulletin*. 2003;35:1–3.

5 WHO, Department of Vaccines and Biologicals, Geneva. Research related to measles control and elimination. *Measles Bulletin*. 2000;3:2.

collaborating with Ghana's Public Health Reference Laboratory (PHRL), National Surveillance Unit (NSU), and Health Research Unit (HRU), as well as the USAID-supported Partners for Health Reform*Plus* (PHR+) project to evaluate the impact of DBS sampling technique on the Ghanaian Integrated Disease Surveillance and Response measles surveillance system. The operational success of this study may facilitate a wider application of DBS as a preferred collection method for other infectious diseases.

Ultimate Goals and Objectives of HealthTech Project

To evaluate the operational feasibility of DBS samples for measles surveillance in a developing country, the following objectives have been identified:

- Collaborate with the Ghanaian ministry of health (MOH) to design and prepare for technical and operational assessment of DBS in current measles control activities.
- Assist PHRL with training for collection, transport, and analysis of DBS for measles diagnosis using an EIA.
- Collect quantitative and qualitative data on costs, benefits, utility, and performance of DBS for measles case confirmation in existing surveillance system.
- Evaluate the technical performance of DBS collected from finger-stick blood to detect measles-specific IgM with a commercially available EIA.
- Participate in WHO-led policy discussions on the application of DBS as an alternative specimen for global measles surveillance activities.
- Write up and disseminate study results with assistance of PHRL, NSU, and HRU.

Status of Project as of March 2005

Proposed study of measles surveillance in Ghana is on hold pending more funding from USAID for this purpose.

Milestones expected in the past six months	Achievements and progress towards milestones
All arrangements formalized for study to be completed by December 2005.	USAID confirmed WHO support of proposed study.
Training plan and materials developed by end of December 2004.	On hold pending funding.
Specimen and data collection standard operating procedures (SOPs) and forms produced by February 2005.	On hold pending funding.
Initiation of study by March 2005, if further funds can be identified.	On hold pending funding.

Problems encountered	Actions taken or plans to resolve
Lack of funding has prevented implementation of the study.	Formal request for additional funding has been made to USAID.

Milestones expected in the next six months	Planned activities to reach those milestones
All arrangements formalized with MOH and Partners for study to be completed by June 2006.	Contact MOH Ghana and Partners.
Training plans and materials developed by July 2005.	Develop training plan in conjunction with MOH Ghana and Partners; share plan with WHO.
Specimen and data collection (SOPs) and forms produced by September 2005.	Draft data collection SOPs in collaboration with MOH.
In-country training of field workers and health personnel conducted by MOH with assistance from PATH by November 2005.	Travel to Ghana to assist the MOH with training and coordination of study activities.

Rapid Diagnostic Tests Website

Health Need Addressed

Program planners, managers, and laboratory staff need clear, well-documented information about available diagnostic tests in order to make informed decisions, particularly when resources are limited. Because rapid diagnostic tests are a relatively new and underutilized group of technologies, comprehensive information is difficult to find. Examples and information on how rapid diagnostics can be appropriate by utilized in resource-limited settings improves access and the programmatic benefits of rapid diagnostic tests.

HealthTech IV Solution and Potential Impact

PATH has substantial experience and knowledge about rapid diagnostic test development and introduction. With the support of HealthTech, PATH has developed the Rapid Diagnostic Tests website to provide information on rapid test performance, references to peer-reviewed literature, and links to available online resources. The website strives to promote the appropriate use of rapid diagnostic tests. In addition to general information, there are sections on rapid test technologies for hepatitis B, HIV, malaria, and syphilis which provide important information on the availability and accuracy of these tests as well as describing their appropriate use. A comprehensive table for each disease includes manufacturer contact information for available rapid diagnostic tests for these four main diseases. Potential impact of this website includes the ability of planners, managers, and laboratory staff to make better diagnostic test choices and improve program design both for individual diagnosis and disease surveillance.

Ultimate Goals and Objectives of HealthTech Project

- Provide current and relevant information to support proper use of rapid diagnostic tests.
- Improve contact between manufacturers and developing-country end users of rapid diagnostic tests.
- Make recent rapid diagnostic test information easily available to policymakers with limited internet access.

Status of Project as of March 2005

The rapid diagnostics website has been updated as of April 2005. New links have been added, manufacturer information confirmed, and public access articles on rapid diagnostic tests highlighted.

Milestones expected in the past six months	Achievements and progress towards milestones
In November 2004 the final update will be posted.	Final update was completed in March 2005.
Inquiries to potentially interested organizations will attempt to secure funding for continued updates and potential expansion of website.	Pending a publicity campaign in May 2005, a strategy to identify funds for ongoing maintenance or expansion will be identified.

Problems encountered	Actions taken or plans to resolve
Availability of website technical staff was limited, postponing the final update until March 2005.	Material was updated and posted in March 2005.

Milestones expected in the next six months	Planned activities to reach those milestones
A publicity campaign to manufacturers, technical listservs, and programmatically relevant audiences will announce the updated website.	In the first week of May 2005, announcements of updated website will be released.
User statistics will be monitored to inform decisions on website continuation.	Discussions in May-July 2005 will evaluate the future funding possibilities for the rapid-diagnostics.org website.

Other Technologies

Development of Single-Dose Packaging of Nevirapine Oral Suspension

Health Need Addressed

Clinical trials have shown nevirapine (NVP) to be an efficacious therapy for reducing mother to child transmission (MTCT) of HIV.[1,2] Study results demonstrated that NVP is both low cost and practical. However, administration of NVP in resource-limited settings can be problematic given the requirement to deliver infant doses within 72 hours of birth, the high prevalence of home births, and the reluctance of health workers to open multi-dose bottles for single use due to wastage concerns. This is especially challenging in areas where there is limited use and limited availability of health care services. One important barrier to expansion of use is the absence of single-dose packaging for the pediatric oral suspension of NVP. As has been documented in immunization programs, health workers may be reluctant to open a 20-ml bottle of NVP (approximately 30 pediatric doses) to administer a single dose to an infant out of concern that the remaining doses will not be used before the expiration period of six weeks described on the label.[3] Single-dose packaging will be necessary in rural settings characterized by limited clinical capacity and/or low client load. It will also be essential for use in home births.

HealthTech IV Solution and Potential Impact

PATH is participating in a public-/private-sector collaboration with USAID, Population Services International (PSI), Boehringer Ingelheim (BI, the manufacturer of nevirapine), and other partners to develop and introduce a single-dose package capable of delivering a pediatric dose of NVP oral suspension.

Now with HealthTech funding, PATH is conducting a detailed feasibility and implementation analysis of packaging options, new presentation development plans, and manufacturing scenarios that could create a sustainable supply of NVP in single-dose packages.

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[1] Guay LA, Musoke P, Fleming T, et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial. *The Lancet*. 1999;354(9181):795–802.

[2] Moodley D, Moodley J, Coovadia H, et al. A multicenter randomized controlled trial of nevirapine versus a combination of zidovudine and lamivudine to reduce intrapartum and early postpartum mother-to-child transmission of human immunodeficiency virus type 1. *Journal of Infectious Diseases*. 2003;187(5):725–735.

[3] Drain PK, Nelson CM, Lloyd JS. Single-dose versus multi-dose vaccine vials for immunization programmes in developing countries. *Bulletin of the World Health Organization*. 2003;81(10):726-731.

Ultimate Goals and Objectives of HealthTech Project

The goal is to increase ease of use, availability, and ultimately the uptake of the infant oral dose of NVP for prevention of mother-to-child transmission (PMTCT) of HIV. In order to achieve this goal, PATH will:

- Develop a detailed feasibility and implementation analysis of single-dose packaging options, new presentation development plans, manufacturing scenarios that could create a sustainable supply of NVP in single- or small-dose packaging, and the development of an implementation plan for the large-scale programmatic delivery of this PMTCT product and associated services.
- Identify, evaluate, and work with partners to introduce single-dose packaging capable of delivering the pediatric dose of NVP oral suspension.

Status of Project as of March 2005

As of March 2005, PATH's work was for the most part on hold pending outcome of USAID-BI discussions. PATH is poised to carry forward as appropriate and as identified by USAID.

Milestones expected in the past six months	Achievements and progress towards milestones
Stability studies of NVP in Uniject™[4] DP completed at BI.	Stability studies of NVP in Uniject DP were completed at BI. Final data determined loss of parabens was significant and Uniject DP was ruled out as a final packaging candidate.
Effectiveness of foil pouch to increase stability of Exacta-Med®[5] dispenser demonstrated.	Interim data suggest that a foil pouch significantly reduces moisture loss and may potentially increase stability of NVP in the Exacta-Med dispenser.
Demonstration of acceptability of Uniject DP device and Exacta-Med dispenser.	Acceptability studies of Uniject DP and Exacta-Med dispenser were completed in Tanzania and Zambia. Users found both devices to be acceptable. Pouch design and labeling will be important components of the final packaging design.

[4] Uniject is a trademark of BD.
[5] Exacta-Med is a registered trademark of Baxa Corporation.

Request transfer of the NVP analytical method and BI corporate support for development of the USP Monograph for NVP.	PATH requested transfer of BI's analytical method in order to facilitate stability study testing at alternate sites. BI has denied PATH's request to transfer the method, but has agreed to conduct the next set of stability studies for the project at BI's testing facility. BI agreed to be the official sponsor for the USP monograph on NVP.

Problems encountered	**Actions taken or plans to resolve**
In a December conference call, BI announced to PATH that they identified several points of concern with the NVP project. After consulting with their legal team, BI determined the following issues and conditions upon which the project would move forward: • Uniject DP is no longer a viable candidate based on the results of the stability study. • There are no scenarios in which maintaining a supply of prefilled devices would be acceptable and an "on-demand approach" will be the only accepted strategy. • Machine-fill scenarios are not acceptable due to potential quality assurance issues and a hand-fill scenario is the only way to move forward.	PATH summarized the conference call details and immediately shared them with USAID. USAID placed a hold on the project until the issues that BI outlined could be explored and USAID and BI could find a mutually acceptable plan for project continuation. PATH provided USAID with a series of documents outlining the critical issues including detailed analysis of the implications. Exacta-Med's 1 ml dispenser will be the device that they can support into the next phase of the project. BI supports further study of pouching the Exacta-Med dispenser to potentially increase stability and will be willing to conduct stability studies for the project.

Milestones expected in the next six months	Planned activities to reach those milestones
Final results for study to determine effectiveness of foil pouch to decrease moisture loss of NVP in Exacta-Med dispenser.	Complete evaluation of evaporative loss; share report with USAID and BI.
Plan and initiate stability studies of NVP in pouched Exacta-Med dispenser at BI. PATH role will likely be to supply the filled, pouched samples for the study.	Contact R&D staff at BI to determine their needs for study, procure appropriate supplies, assemble samples, and deliver to BI.
Support USAID's development of a revised structure and plan for the next phase of the project, taking into account the constraints of filling and pouching Exacta-Med dispensers with NVP for on-demand use.	The project will change significantly as a result of the guidelines laid out by BI for continuation. PATH will work with USAID to determine next steps and potential plans for the next phase of the project.

Microbicides Applicator Evaluation

Health Need Addressed

AIDS is the leading cause of mortality among adults aged 15 to 59 years.[1] Women are increasingly bearing the disproportionate burden of the AIDS epidemic. In 2003, women accounted for nearly 50 percent of all people living with HIV, compared to 41 percent in 1997.[2] In Africa, women are 1.3 times more likely than men to be infected with HIV; young women aged 15 to 24 are 2.5 times more likely to be infected than young men.[3]

Due to social norms, gender inequalities, and economic disparities, women are often unable to protect themselves from HIV through abstinence, mutual monogamy, or male condom use. Safe, effective microbicides could provide urgently needed options for women and men seeking protection from HIV and other sexually transmitted infections.

With over 60 potential microbicides in preclinical or clinical trials, most research has focused on the gels/creams intended for topical application, with much less targeted research on the devices (applicators) that will be used to deliver the microbicides. The applicator devices will be critical in ensuring a safe, effective microbicide product. The applicator impacts the overall product's safety (relationship with product purity and stability, avoidance of local trauma associated with insertion or use), efficacy (consistent delivery of the required amount of product in the intended location) and acceptability (comfort, ease of use, disposability). Acceptability of the applicator, in addition to the microbicide, will greatly impact whether the product is used consistently and correctly. From past female condom research,[4] it is clear that user acceptability, in addition to product cost, is a major determinant of product uptake and actual use. Finally, the design of a product for worldwide users estimated at 34 to 88 million women per year[5] has a potential environmental impact in terms of waste disposal.

HealthTech IV Solution and Potential Impact

Modeling efforts have shown that a partially effective microbicide could avert over 2.3 million cases of HIV in three years, given certain levels of uptake, coverage, and use.[6] As noted above, the applicator will play a critical role in product uptake and use. We have the opportunity to evaluate and address these important issues before microbicide product

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[1] World Health Organization. *Facts and Figures from The World Health Report 2003-Shaping the future*. Geneva:*WHO*; 2003.
[2] UNAIDS. *Report on the Global AIDS Epidemic.* UNAIDS; 2004.
[3] UNFPA. *State of the World Population.* UNFPA; 2004.
[4] Hoffman S, et al. The Future of the Female Condom. *Perspectives on Sexual and Reproductive Health*. 2004;36(3):120-126.
[5] Pharmaco-Economics Working Group of the Microbicide Initiative. The Economics of Microbicide Development: A Case for Investment.
[6] Public Health Working Group of the Microbicide Initiative. The Public Health benefits of Microbicides in Low Resource Settings: Model Projections.

introduction, so that appropriate applicators can be as accessible and acceptable as possible, leading to much greater levels of use-effectiveness and greater rates of HIV protection.

Ultimate Goals and Objectives of HealthTech Project

The goal of the project is to ensure that safe, appropriate, affordable applicators are available for use in low-resource settings at the time of microbicide introduction. The objectives of this project are to:

- Provide data that can inform product selection of devices for use in low-resource settings.
- Provide data on status and availability of existing applicators that meet cost, user, product, and manufacturing requirements.
- Strengthen linkages between applicator and microbicide researchers, developers, and sponsors to ensure timely and effective product introduction.

Status of Project as of March 2005

PATH is gathering information from manufacturers on their products and manufacturing and business capacity. PATH is also organizing an applicator regulatory meeting for microbides sponsors and stakeholders and is working on publication of results of findings to date; these finding will be submitted to peer reviewed journals.

Milestones expected in the past six months	Achievements and progress towards milestones
Finalize manuscripts for both clinical safety study and acceptability study for publication in peer-reviewed journals.	Clinical safety study manuscript completed. Manuscript submitted to *Contraception*. Acceptability study manuscript to be submitted to *AIDS* by end of April.
Conduct international search for applicators.	Completed. Search was conducted in South Africa and India, and interviews conducted with manufacturers in each country. Results indicate numerous applicator manufacturers in India that have potential and interest in supplying applicators for microbicide products.
Organize microbicide meeting to discuss regulatory needs and research priorities for bridging current microbicide products with lower cost, alternative applicators for product introduction.	In progress. Now working with Family Health International (FHI) to convene pre-IND meeting with FDA to discuss regulatory pathways for new applicators. Once we receive information from the FDA meeting, we will be able to share this with the broader group of stakeholders.

Problems encountered	Actions taken or plans to resolve
FDA was not willing to participate in our proposed regulatory meeting. Their participation was considered a critical component of this meeting since the goal was to learn about US regulatory needs and research requirements for use of new applicators.	FDA said that they would discuss this information only with product sponsors in the context of specific devices; therefore, we have since contacted FHI and are now discussing a collaboration whereby they will request a pre-IND meeting with the FDA—as trial sponsors—and we will work with them to incorporate information in the pre-IND packet on cardboard, user-filled applicators. Personnel from FHI, PATH, and USAID will participate in this pre-IND meeting. Once we learn more information from the FDA on this topic, we will then be able to convene a larger group of stakeholders and share this information with them as originally planned.
Clinical safety study manuscript rejected by *AIDS*.	Submitted article to *Contraception*.

Milestones expected in the next six months	Planned activities to reach those milestones
Submit acceptability article to *AIDS* for publication.	Finalize manuscript. Seek external review and comments. Submit to *AIDS*.
Participate in pre-IND meeting with FDA to discuss regulatory pathways for new applicators.	Develop collaboration with FHI. Complete pre-IND packet for FDA with FHI. Participate in pre-IND meeting with FDA.
Convene microbicide meeting to discuss regulatory needs and research priorities for bridging current microbicide products with lower cost, alternative applicators for product introduction.	Compile recommendations from FDA meeting. Determine appropriate participant list and date in conjunction with USAID. Convene meeting in PATH office in DC in Fall of 2005.

Vasectomy Technologies

Health Need Addressed

Recently published evidence suggests that the rate of vasectomy failure (measured by unintended pregnancy) is around 4 percent[1,2] with methods commonly used globally. Incorporation of improved methods, such as fascial interposition and thermal cautery, could help lower the rate of failure and increase acceptance of vasectomy.

HealthTech IV Solution and Potential Impact

Family Health International (FHI) and EngenderHealth (EH) have recently published evidence confirming the clinical advantages of fascial interposition[3] and indicating possible advantages of thermal cautery.[4] To complement this research, PATH was asked to evaluate the physical durability and the potential for reuse of a thermal cautery device along with potential redesign or cost-reduction opportunities. The long-term goal of this collaboration is to permit introduction of a cautery vasectomy technique, in conjunction with recommended procedural and reuse methods, for introduction into low-resource settings.

Ultimate Goals and Objectives of HealthTech Project

- Verify that a cautery device (designated by the manufacturer as single use) is safe and effective for multiple uses.
- Provide technical assistance to other project partners for review of new devices, sourcing of generic devices, and sperm analysis.
- Conduct a cost-effectiveness evaluation for different currently used vasectomy methods.

Status of Project as of March 2005

- PATH is finalizing instructional materials on reprocessing of cautery tips and planning distribution.
- PATH is conducting a cost-effectiveness evaluation for vasectomy methods in multiple low-resource clinics.

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[1] Wang D. Contraceptive failure in China. *Contraception*. 2002;66:173–178.
[2] Nazerali H, Thapa S, Hays M. Vasectomy effectiveness in Nepal: A retrospective study, *Contraception*. 2003;67:397–401.
[3] Sokal D, Irsula B, Hays M. Vasectomy by ligation and excision, with or without fascial interposition: A randomized controlled trial. *BMC Medicine.* 2004;2:6.
[4] Barone M, Chen-Mok M, Sokal D. *BMC Urology*. 2004;4(1):10.

Milestones expected in the past six months	Achievements and progress towards milestones
Completion of cleaning and disinfection follow-up study.	Study completed–data indicates that cautery tips can be effectively cleaned and disinfected with bleach through standard reprocessing procedures. Draft report reviewed by FHI and Michel Labrecque (Universite Laval, Quebec) and revised. Reprocessing instructional materials drafted and currently in review at FHI and EH.
Complete clinic visits for cost-effectiveness analysis.	Clinical visits complete in Kenyan and Indian sites by regional PATH staff. Clinical visits scheduled in Mexico for end of May.
Compile and begin analysis of data from clinical visits.	Data analysis from two sites to begin in April.

Problems encountered	Actions taken or plans to resolve
Approval for clinical visits in Mexico delayed by local authorities.	Study permission was recently granted and research scheduled for end of May (delayed in April and May due to PATH staff travel and leave schedules).

Milestones expected in the next six months	Planned activities to reach those milestones
Finalization of instructional materials and distribution through posting on PATH and EH websites.	Review and approval by each partner. Website posting. Follow-up with clinics currently using cautery to distribute reuse recommendations.
Complete clinical visits and data analysis, and draft report on cost-effectiveness and practicality of the cautery vasectomy technique	Clinical visits in Mexico (May). Data analysis (April–July). Draft and finalize report (August–September).

Basic Delivery Kit

Health Need Addressed

High rates of maternal and perinatal mortality in developing countries indicate a crucial need for new and innovative interventions for pregnancy and neonatal care. Most women have no access to maternity services due to distance, cost, and local customs; many give birth alone. High rates of neonatal and maternal tetanus and sepsis indicate a need for education and materials focused on clean birth practices.

HealthTech IV Solution and Potential Impact

The basic delivery kit is an inexpensive, simple kit designed to help create a clean birthing environment, particularly for home births. Based on a needs assessment in rural community settings, the contents selected for inclusion in the kit sold in Nepal include a clean razor blade, clean cord ties, a small bar of soap, a cord-cutting surface, pictorial instructions, and a polyethylene delivery sheet. The delivery kit is designed for use by trained and untrained traditional birth attendants, family members, and women who give birth unassisted in the home. The potential impact of the development and promotion of kits in local communities in Africa is great. To demonstrate the health effects of kit use, PATH has completed the first cross-sectional observation study of single-use delivery kits in Africa. PATH is currently exploring partnership opportunities with a group in Ethiopia and is seeking funding for a local kit production project in that country.

Ultimate Goals and Objectives of HealthTech Project

The purpose of the study entitled “Evaluation of a clean delivery kit intervention in preventing cord infection and puerperal sepsis in Mwanza, Tanzania” was to determine the impact of a delivery kit intervention on reducing cord infection and puerperal sepsis among newborns and their mothers in rural Tanzania.

Status of Project as of March 2005

Report on the delivery kit study in Tanzania is now complete. We are working on an article for publication and will make a presentation at the annual Global Health Council conference. We expect to have further discussions with USAID and other donors about the implications of the study findings and what that might mean in terms of future investments in delivery kit projects.

Milestones expected in the past six months	Achievements and progress towards milestones
Submit final report on Tanzania delivery kit study.	Completed March 2005.
Prepare and submit article on Tanzania delivery kit study to peer-review journal.	Article completed; expected submission in June 2005.

Problems encountered	Actions taken or plans to resolve
Draft of report included some statistics that had to be reanalyzed. Delayed the submission of the final report to USAID.	Clarified the questioned results and slightly changed to findings accordingly. Report completed now.

Milestones expected in the next six months	Planned activities to reach those milestones
Concept paper for a pilot project to develop a local delivery kit in Oromia Region, Ethiopia.	Develop and write up paper in collaboration with local entity.
Funding for Ethiopia project.	Will discuss funding possibilities with USAID and other possible donors.

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