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A HealthTech Report

HealthTech V Annual Report
Year 2
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Highlights

- The chlorhexidine work under HealthTech is progressing rapidly with more and more countries expressing interest in introducing chlorhexidine for umbilical cord care; HealthTech and the Chlorhexidine Working Group (CWG) are playing a pivotal role in moving chlorhexidine forward. The CWG, led by HealthTech, has established its position internationally as an authority on the introduction and scale-up of chlorhexidine and now serves as the Chlorhexidine Technical Reference Team for the United Nations Commission on Life Saving Commodities for Women and Children (UNCoLSC). Further, in 2013 the World Health Organization (WHO) added 7.1% chlorhexidine digluconate for umbilical cord care to their Model List of Essential Medicines for Children.
- Implementation of the Cold Chain Equipment Manager (CCEM) is now under way in Laos and Pakistan in collaboration with the United Nations Children's Fund (UNICEF) and in Georgia in collaboration with the WHO regional office for Europe. HealthTech completed the first prototype of a web-based version of CCEM called Cold Chain Equipment Inventory (CCEI) and migrated it to the DHIS2 software platform. Migration of CCEM functionality onto a web-based platform like DHIS2 provides the project with an opportunity to approach countries with a cold chain equipment inventory solution that can be integrated within their national health information system. Furthermore, using a web-based platform provides additional opportunities to make cold chain inventory data useful for temperature monitoring systems, maintenance and repair systems, and facilitates easier data exchange with other tools, including Excel-based tool. A new dynamic collaboration model was created among PATH, the Health Information Systems Programme in Norway and India, UNICEF, and the University of Washington to provide increasing numbers of countries with an opportunity to explore and deploy CCEI tools.
- The Initiative on Multipurpose Prevention Technologies (IMPT) team highlighted multipurpose prevention technologies at a number of important conferences and forums around the world; the Coalition for Advancing Multipurpose Innovations **(**CAMI) and partners also responded to requests from IMPT partners for the development of new MPT online resources and materials. Under CAMI/IMPT, the Scientific Agenda Working Group (SAWG) made preliminary recommendations on MPT product priorities and gaps after an iterative development and vetting process. These FY12-FY13 recommendations will be used to inform a newly formed MPT Supporting Agency Coordination Committee (coordinated by CAMI), and will be reassessed and updated by the SAWG annually. The Communications and Advocacy Working Group expanded outreach with key stakeholders in the United States, established communication plans in Kenya and South Africa and developed new training materials and outreach efforts to reach a broad array of experts and stakeholders across family planning, sexually transmitted infection, and HIV arenas.
- HealthTech participates in the UNCoLSC Neonatal Resuscitation Technical Working Group and leads the efforts around quantification and market sizing. As part of this effort, HealthTech developed a quantification tool and estimated market sizing for bag and mask resuscitation devices, suction devices, and training mannequins for the eight priority countries under UNCoLSC. HealthTech completed bench testing of an innovative resuscitator design made by Laerdal Medical and (with external funding) implemented a user evaluation of the same device in the United States.

- The HealthTech team working on the noninvasive hemoglobin measurement technology for anemia screening is conducting an accuracy study that compares the Pronto devices and the HemoCue point of care device to the reference method used in the laboratories at the Kintampo Health Research Center. The study protocol, and tools were approved by three ethic review boards; the PATH Research Ethics Committee, the Kintampo Institutional Review Board, and the Ghana Health Services Ethics Research Committee. Additionally, the project secured regulatory approval from the Ghana Food and Drugs Administration for use of the noninvasive devices in Ghana for the purpose of conducting the research. By the end of September 2013, the research team had enrolled over half of the 240 participants needed for the study. Concurrently, a market study and cost analysis were conducted in Ghana. The information gathered will be summarized in a planned report and will provide insights into the market opportunity, market segment and cost of current hemoglobin measurement technologies and potential target pricing for noninvasive devices and cost per test.
- Work under HealthTech funding to extend capabilities of a scalable and sustainable electronic logistics management system for requisitions, order processing, and system administration to address supply chain issues has been completed. Plans are currently underway with USAID, the Bill & Melinda Gates Foundation, John Snow Incorporated, PATH, the Rockefeller Foundation, and VillageReach, to build an ongoing, self-sustaining community to support implementations by other countries and ongoing development to address common supply chain and logistics needs. Additionally, interest continues to build around the use of barcode tracking and tracing of commodities as well as the integration of an open source logistics management information system with countries' health management information systems. As funding permits, PATH will continue to participate in efforts to catalyze early-stage work in these areas.
- HealthTech recently completed the bench tests with the paper applicator and tenofovir (TFV) gel. Reports will soon be available to share with key stakeholders. A study design has been agreed upon by CONRAD, CAPRISA, and HealthTech to collect acceptability data on the paper applicator among women in South Africa. HealthTech will continue to facilitate talks between ProPreven and Tekpak with the goal of the two parties reaching a mutually beneficial agreement to supply paper applicators to South Africa and elsewhere in Africa for TFV delivery.
- Regulatory approval for the SILCS Diaphragm was achieved in the second quarter of 2013 in Europe and the device was launched in six countries under the brand name Caya™ contoured diaphragm. HealthTech and partners are implementing health systems assessments, cost/pact modeling, and a gel delivery acceptability study to strengthen the value proposition for the SILCS Diaphragm in developing countries. Pre-clinical studies were completed with Contragel, a lactic-acid based contraceptive gel. Planning is underway for the post-coital study of the barrier effectiveness and the safety study required to validate Contragel as being safe and effective when used with SILCS Diaphragm.

HealthTech Projects

Chlorhexidine for Umbilical Cord Care

Goal

Coordinate and support global rollout of 7.1% chlorhexidine for umbilical cord care including its integration into global programs.

Status of the project as of September 30, 2013

The chlorhexidine work under HealthTech is progressing rapidly. More and more countries are expressing interest in introducing chlorhexidine for umbilical cord care, and HealthTech and the Chlorhexidine Working Group (CWG) are playing a pivotal role in moving chlorhexidine forward. The CWG, led by HealthTech, has established its position internationally as an authority on the introduction and scale-up of chlorhexidine and now serves as the chlorhexidine Technical Reference Team for the United Nations Commission on Life-Saving Commodities for Women and Children (UNCoLSC). Further, in 2013 the World Health Organization (WHO) added 7.1% chlorhexidine digluconate for umbilical cord care to their Model List of Essential Medicines for Children (EMLc). The effort to update the EMLc was initiated jointly by USAID and PATH in 2008 and continued by HealthTech on behalf of the CWG.

Achievements in Year 2

HealthTech achievements as participants in the CWG:

- Convened face-to-face meetings of the CWG in Washington, DC, on January 29, 2013, and August 1, 2013. Teleconferences of the CWG occur every other week.
- The Terms of Reference that address CWG's objectives and roles and the involvement of its members, including pharmaceutical companies, was drafted by USAID and has been reviewed and approved by the full CWG. It is posted on the CWG's page on the Healthy Newborn Network (HNN) website.
- HealthTech and the CWG have developed a generic PowerPoint for use at country technical meetings as well as a technical brief, production brief, country summaries, and frequently asked questions document. These documents are housed on the CWG page on the HNN; this chlorhexidine web page is updated continually by HealthTech with new information about chlorhexidine for umbilical cord care. Whenever feasible, tools and resources were also translated to French and posted on the site.
- CWG took part in numerous dissemination activities; recent examples of these include:
  - A video blog on the Huffington Post in connection with United Nations General Assembly (UNGA) week.
  - Inclusion of chlorhexidine for umbilical cord care in UNGA week activities.
  - Inclusion of chlorhexidine for umbilical cord care in a publication outlining ten breakthrough innovations for the health of women and children.
  - A blog in the Skoll World Forum about innovation which features chlorhexidine for umbilical cord care.

- Publication of a case study by John Snow Inc. entitled, *Chlorhexidine in Nepal: A Public-Private Partnership Case Study*.
- A successful evening session on chlorhexidine was held at the Global Newborn Health Conference in Johannesburg, South Africa, in April 2013. The presentation was well received, and several countries expressed interest in implementing a chlorhexidine program.
- A successful and very well attended talk on chlorhexidine for umbilical cord care was given by members of the CWG at the Women Deliver Conference in Kuala Lumpur, Malaysia, in May 2013.
- Every Newborn Asia Regional Consultation meeting in Kathmandu, Nepal, in August 2013. During this meeting, a CWG member organized and led a field visit to observe the use of chlorhexidine in facility settings. Participants in the field visit included delegation members from Afghanistan, India, and Pakistan.

- HealthTech continued the efforts to include 7.1% chlorhexidine digluconate in the WHO's Model List of Essential Medicines (EML), which was initiated jointly by USAID and HealthTech in 2008. The updated EML was published in July 2013 and now includes 7.1% chlorhexidine digluconate which is listed specifically as a medicine for umbilical cord care.
- Through the efforts of HealthTech and the CWG, the United Nations Children's Fund (UNICEF) Supply Catalogue now includes 10-ml bottles of liquid 7.1% chlorhexidine digluconate for single application.
- As of September 2013, the team at RTI International that manages the MANDATE model included 7.1% chlorhexidine digluconate under prevention of omphalitis. We are working with them to ensure that chlorhexidine is included under prevention of neonatal sepsis as well.
- Completed manufacturing, regulatory/policy, and supply chain landscapes for Liberia, Madagascar, and Nigeria. We determined that local production is not feasible in the foreseeable future in Liberia and Madagascar due to the absence of pharmaceutical companies. For Liberia, importing the product from Lomus or UNICEF is a possibility for the short term and importing from Nigeria appears to be a feasible option in the midterm. For Madagascar, importing pharmaceuticals from other African countries is costly, but India might be an option considering the trade status between the two countries. In Nigeria we identified that local production is feasible.
- HealthTech held an initial meeting with an official from the Kenyan Ministry of Health and an official from the USAID East Africa Mission in Kenya to discuss the introduction of chlorhexidine.
- Finalized a scope of work for market research and demand forecasting in Nigeria in collaboration with the USAID Center for Accelerating Innovation and Impact and selected a market research firm through an RFA process. HealthTech's request for a sub-award was submitted to USAID; approval is pending. These market shaping activities being conducted by HealthTech are complementary to with the efforts of the Targeted States High Impact Project and Clinton Health Access Initiatives in Nigeria, which plan to undertake quantification and private-sector market analysis for the 7.1% chlorhexidine digluconate as part of Nigeria's country implementation activities, to leverage each organization's work.
- A manuscript entitled, "Willingness to pay for a 4% chlorhexidine (7.1% chlorhexidine digluconate) product for umbilical cord care in rural Bangladesh: a contingency valuation study," was submitted to

BMC Pregnancy and Childbirth. The editors of *BMC Pregnancy and Childbirth* referred the manuscript to *BMC International Health and Human Rights* where it has been accepted pending author revisions. The manuscript has been provisionally accepted for publication, revisions have been submitted, and we are awaiting editorial communication on the final decision.

PATH achievements as members of the UNCoLSC (not funded under HealthTech):

- PATH provided technical assistance on production, a product introduction strategy, and country-led initiatives to pilot 7.1% w/v chlorhexidine digluconate for umbilical cord care in Liberia, Madagascar, and Nigeria. We also supported the coordination and implementation of regional/country technical meetings with key stakeholders/policymakers in these countries.
- PATH and Promoting the Quality of Medicines Program/United States Pharmacopeia (PQM/USP) traveled to Nepal in September 2013 to meet with Lomus Pharmaceuticals, manufacturers of 7.1% gel chlorhexidine digluconate, to discuss transfer of their formulations to pharmaceutical manufacturers in Nigeria and beyond. Lomus verbally agreed to transfer its formulation to manufacturers in Nigeria. PATH is in the process of establishing the Memorandum of Understanding (MOU) to capture Lomus' intent. During this trip Lomus Pharmaceuticals was invited to participate in the CWG and accepted the invitation (the HNN chlorhexidine page has been updated to reflect this new member).
- In September 2013, PQM/USP and PATH traveled to Nigeria and conducted on-site audits and due diligence for a short list of manufacturers. Three qualified manufacturers were selected, and the results of the visit were discussed with the Nigerian National Agency for Food and Drug Administration and Control and the Federal Ministry of Health. A report on this audit/due diligence is under way. We are working with PQM/USP to provide technical assistance to selected manufacturers in Nigeria so they will be able to obtain regulatory approval. During this process, we will explore how regulatory dossiers might be generalized for other manufacturers.
- Held a technical meeting in the Democratic Republic of the Congo (DRC) in late August 2013. The DRC expressed interest in assessing the feasibility of local production. Planning to visit the country for this assessment is under way.
- Planning is under way for a technical meeting in Burkina Faso in early December 2013. Key stakeholders from four Francophone West Africa countries have been invited to the meeting—Burkina Faso, Côte d'Ivoire, Niger, and Senegal. Key stakeholders from the DRC, Madagascar, and Nigeria have also been invited to share their experiences with implementing chlorhexidine for umbilical cord care. CWG team members are planning to travel to Malawi and Uganda in early November 2013 and to Pakistan in January 2014 to meet with key stakeholders in the ministries of health to discuss the provision of technical assistance.
- Facilitated the inclusion of chlorhexidine for umbilical cord care in programmatic guidance and emergency kits through CWG partner organizations.
- PATH created linkage with Recommendation 1 (shaping global markets), 2 (shaping delivery markets), 6 (supply and awareness), and 7 (demand and awareness) on behalf of the CWG.
- PATH is providing technical assistance to Recommendation 7 on behavior change communication on behalf of the CWG.

Problems encountered and actions taken

We are leveraging funding from the UNCoLSC to complete some of the work surrounding establishing a local/regional supply chain for 7.1% chlorhexidine digluconate, including the development of manufacturing guides for local producers in collaboration with PQM/USP. There have been delays with the subaward to PQM/USP due to limitations in some agreement clauses that were included in the UNICEF award to PATH. PATH has been working with UNICEF's legal group to resolve these issues.

Lomus Pharmaceuticals is currently selling 7.1% gel chlorhexidine digluconate to other countries for studies and pilot introduction purposes. By transferring their gel formulation to interested local manufacturers, Lomus will lose future sales to the countries where they are currently selling their product. However, HealthTech has confirmed with Lomus that they are willing to transfer their gel formulation to other manufacturers in order to achieve an increased supply of quality, affordable product, as long as their costs associated with formulation transfer are covered. We are in the process of establishing an MOU for formulation transfer in Nigeria to capture Lomus' intent.

As Nigeria quickly moves toward introducing the product, more organizations became involved, which made it difficult to effectively coordinate each organization's activities. HealthTech reached out to the organizations who are involved in chlorhexidine work in Nigeria in order to understand each organization's activities and identify areas where synergy could be developed. A matrix of roles and responsibilities for each implementing agency is being developed to address this source of confusion

The WHO recommendation on cord care was not released as early as anticipated. We expect that the recommendation will be published by the end of 2013. We are aware of what the recommendation will most likely include, so we have prepared materials and activities based on this information in order to move forward immediately with dissemination and other activities once the recommendation is published.

Pathway from research to field implementation and use

The project activities will focus on implementing the chlorhexidine intervention over the course of five years. In Year 1, we added to the evidence base by strengthening the application to the WHO EML, leading the development, and managing the implementation of the UNCoLSC plan for chlorhexidine and solidified the strategy for global rollout by convening stakeholders to review a draft plan. The draft plan identified and coordinated programmatic opportunity for integrating chlorhexidine in regional and global platforms as well as building potential supplier bases for regional manufacturing and distribution. In Year 2, we worked toward coordinating the implementation of the global roll-out plan by providing technical support for both supply and demand initiatives in countries with demonstrated and/or strategic interest. In Year 3, we will focus our efforts in priority countries in order to solidify regional hubs for supply and strengthen and disseminate regional evidence to accelerate scale-up in sub-Saharan Africa and South Asia. Years 4 and 5, providing we see favorable results from the randomized controlled trials currently under way in sub-Saharan Africa and additional evidence of program implementation, we anticipate building on the knowledge and implementation base of the CWG and the UNCoLSC to scale the chlorhexidine product quickly worldwide.

Cold Chain Equipment Manager

Goal

Implement the Cold Chain Equipment Manager (CCEM) to make collecting, managing, and using cold chain inventory data a common and sustainable agenda among Expanded Programme on Immunization (EPI) teams and their partners and demonstrate the value of routine use of inventory data for evidence-based cold chain equipment planning and management in low-resource settings.

Status of the project as of September 30, 2013

In FY2, the CCEM project team drafted and facilitated global debate on standardized definitions for cold chain equipment inventory core data. Active engagement with EPI teams and their partners in a wide range of countries, including Georgia, India, Kenya, Laos, Malawi, Pakistan, and Uganda, provided an opportunity to continue direct support for the continued implementation and use of cold chain equipment inventories.

In FY2, a new dynamic collaboration model was created among PATH, the Health Information Systems Programme (HISP) in Noway and India, the United Nations Children's Fund (UNICEF), and the University of Washington, to provide increasing numbers of countries with an opportunity to explore and deploy cold chain equipment inventory tools. We expect this collaboration to be formalized in FY3. The key technical accomplishment of this collaboration in FY2 is the completion of the first prototype of a web-based version of CCEM called Cold Chain Equipment Inventory (CCEI) and migrating it to the DHIS2 software platform. Migration of CCEM functionality onto a web-based platform like DHIS2 provides the project with an opportunity to approach countries with a cold chain equipment inventory solution that can be integrated within their national health information system. Furthermore, using a web-based platform provides additional opportunities to make cold chain equipment inventory data useful for temperature monitoring systems and maintenance and repair systems and facilitate easier data exchange with other tools, including Excel-based tool.

Achievements in Year 2

- Developed a five-step exercise to give new users an understanding of CCEM functionality. This exercise was also translated into French.
- Presented CCEM as part of a TechNet breakout session on cold chain equipment planning. Distributed copies of CCEM to a Pan American Health Organization representative and to key expert cold chain consultants. Demonstrated the web-based CCEM prototype to UNICEF Programme Division staff.
- HealthTech supported the Clinton Health Access Initiative (CHAI) and the EPI team in Malawi to update 2012 CCEM data using paper-based data collection, managed by district EPI staff; these data will be used for a GAVI Alliance Health System Strengthening application.
- Visited with Kenya's Division of Vaccine and Immunization (DVI), Division of Health Information Systems, and CHAI in July 2013 to discuss how to refine and integrate the web-based CCEM

prototype, DHIS2/CCEI, into the national DHIS2 platform. DVI wants to lead this work and has asked CHAI to manage this effort on their behalf. Work is expected to start in November 2013.

- Visited the Deputy National Programme Manager for the Partnership for Reviving Routine Immunisation in Northern Nigeria's project and began to validate and deploy DHIS2/CCEI in four States. Met with the Nigeria EPI Manager and agreed to keep the National Logistics Working Group up to date with this work to support their eventual consideration of a national DHIS2/CCEI deployment. Met with EPI staff at Ghana Health Services who have requested assistance with the integration of DHIS2/CCEI with the national DHIS2 system.
- Initiated a scope of work with HISP India which will allow developers to incorporate feedback from EPI staff and partners with the goal of finalizing the first version of DHIS2/CCEI by the end of 2013. This will include having a simple data exchange mechanism between DHIS2/CCEI and CCEM and DVD-MT as well as other spreadsheet tools.
- A University of Washington PhD student developed an initial software prototype (HDVis) to support a number of visualizations and utilities that can facilitate data cleaning and validation of a cold chain equipment inventory.
- HealthTech presented draft cold chain equipment inventory data standards to the UNICEF Cold Chain Logistics (CCL) Task Force by leading a debate on these technical standards in a special topic call. This process has launched a broader discussion within the UNICEF CCL Task Force about data standards and the development of other draft data standards (e.g., temperature monitoring).
- In collaboration with WHO, aided in implementing CCEM in Georgia (not funded under HealthTech) using preexisting planning and training materials created by HealthTech and translated into Georgian. We see this as an opportunity to collaborate with the WHO Regional Office for Europe (WHO/Europe) to expand and refine materials into a basic training package for new countries that wish to plan for and implement CCEM.
- In early 2013, the countries of Laos, Myanmar, Tanzania, and Zambia expressed interest in CCEM implementation. CCEM implementation is now under way in Laos and Pakistan in collaboration with UNICEF and in Georgia in collaboration with WHO/Europe. We also met with the Laos EPI team to plan for the deployment of the DHIS2/CCEI tool and design extension of this tool to support monthly reporting of temperature alarm data to trigger managerial response.

Problems encountered and actions taken

HealthTech planned to attend the Eastern and Southern Africa Region (ESAR) EPI managers meeting in March 2013 for the purpose of familiarizing attendees with CCEM. Due to last-minute staffing changes in the team, we were not able to attend. HealthTech will nevertheless pursue opportunities to work with ESAR countries to implement accurate CCEM inventories and design CCEM tools that can overcome common barriers to routine use of inventory data for planning and management decision-making. We continue to look for opportunities and strategies to pursue expressions of interest in CCEM, such as those expressed from partners and EPI teams for Madagascar, Mali, Senegal, Tanzania, and Zambia.

Our recent work with CHAI and EPI teams in Malawi to update 2012 CCEM data reinforced the importance of having easier mechanisms for EPI teams and their partners to independently add new data

fields to the core set contained in the CCEM inventory. Because Malawi wants an up-to-date CCEM inventory to help prepare an evidence-based proposal for a GAVI Alliance Health System Strengthening grant, they added many data fields to the updating form template capturing data on stockouts and temperature monitoring. Many of these data fields are outside the scope of a cold chain equipment inventory data set, but nevertheless the EPI team considered them to be important. Unfortunately, we could not add several of the data points included by Malawi because of how the data tables function in the Access version of CCEM. As an output of this activity, our scope of work for HISP India now contains a request to identify a workflow in the DHIS2/CCEI tool that can make it easier for EPI teams to add new data fields.

Kenya's DVI cold chain manager, data manager, and national logistician are very interested in collaborating with HealthTech and CHAI to migrate their 2011 CCEM inventory from the Access version of CCEM to the web-based DHIS2 prototype version. After a two-day technical meeting in June 2013 with DVI and Kenya's Division of Health Information Systems , we were ready to move this work forward. However, our team encountered difficulties scheduling time with the with Kenya DVI staff who have been busy with recent polio outbreaks and planning for the upcoming Effective Vaccine Management assessment. We continue to keep CHAI, UNICEF, and WHO staff updated on this project activity, and we anticipate that this work will be advanced in FY3.

Work with the EPI teams to identify subregional opportunities to use CCEI data for easier decision-making has been impacted by changes in staff (CHAI Malawi), EPI workloads (DVI Kenya), difficulty timing visits (Uganda), and an intentional delay by PATH to better time CCEI development activities. Extending CCEI solutions that will respond to the needs of subnational EPI staff will advance in Year 3, both from the outputs of the USAID needs assessment and HealthTech's increased effort to demonstrate how the web-based CCEI tool can be easily configured to allow data reporting to be tailored to district-level users and integrated with simple spreadsheet tools.

The work to draft a cold chain equipment inventory data standard has been an important contribution from HealthTech that will potentially allow countries to better coordinate and deploy technologies supporting cold chain equipment management. Initially there was not a clear understanding in the CCL community about data standards and how they can enable innovation and collaboration among developers, allowing technologies to better meet the needs of EPI clients. This initially caused some meetings to focus on better defining the purpose of a data standard and correcting a misconception that these standards are obligatory or static. HealthTech convened a series of discussions, and with the gradual addition of developers of other information and communication technologies, such as HERMES, wVSSM, and eLMIS, the exchange has become more productive.

Benin EPI and the Agence de Médecine Préventive (AMP) have not been able to schedule a time for CCEM training due to EPI administrative deadlines and the implementation of the Logivac program. We will continue to keep AMP management updated on CCEM activities but will no longer plan for a site visit, instead we will send them the training materials developed for WHO/Europe for translation.

Pathway from research to field implementation and use

The project activities for the five years will focus on ensuring that EPI teams and their partners have access to a no-cost and easy-to-use tool that can increase the efficient and sustained use of cold chain inventory data for effective evidence-based cold chain equipment planning and management. In Years 3 we will participate in a USAID-led needs assessment exercise designed to identify how CCEM can better meet the needs of EPI cold chain managers in subnational management positions and help these staff better plan and manage equipment. We will continue to support EPI teams that implement CCEM to identify effective methods for routine inventory data updates and find opportunities to integrate these updates with other immunization program activities. In Years 1 and 2, we have focused on developing regionally based consultants and building the technical capacity of logistics experts in EPI teams in order to broaden the technical resources available to support CCEM implementations at scale. As we build this technical capacity to support CCEM, we will work with EPI teams and partner agencies experienced with CCEM implementations to develop and test CCEM training materials that can support broad, regionally based CCEM training initiatives. Our advocacy efforts will increase in Year 4, and by Year 5 the CCEM software and a comprehensive roll-out package will be finalized and jointly shared with other EPI partner organizations committed to supporting CCEM implementation at scale.

Initiative on Multipurpose Prevention Technologies for Reproductive Health

Goal

Advance development of and access to multipurpose prevention technologies (MPTs) that will simultaneously prevent pregnancy and/or sexually transmitted infections and/or reproductive tract infections.

Status of the project as of September 30, 2013

The Coalition for Advancing Multipurpose Innovations (CAMI), in collaboration with the Initiative on Multipurpose Prevention Technologies (IMPT) partners, made significant advances in all three of the strategic areas in 2013. As noted below, CAMI and partners highlighted MPTs at a number of important conferences and forums around the world; CAMI also responded to requests from IMPT partners for the development of new MPT online resources and materials. Under CAMI/IMPT, the Scientific Agenda Working Group (SAWG) made preliminary recommendations on MPT product priorities and gaps after an iterative development and vetting process. These FY12-FY13 recommendations will be used to inform a newly formed MPT Supporting Agency Coordination Committee (coordinated by CAMI) and will be reassessed and updated by the SAWG annually. Lastly, the Communications and Advocacy Working Group expanded outreach with key stakeholders in the United States, established communication plans in Kenya and South Africa, and developed new training materials and outreach efforts to reach a broad array of experts and stakeholders across family planning, sexually transmitted infection (STI), and HIV arenas.

Achievements in Year 2

- Preliminary recommendations on MPT product priorities and gaps generated by IMPT's SAWG were vetted with donors and others with relevant MPT technical expertise at a meeting in Washington, DC, in October 2012. Outcomes of this meeting are available in the meeting report, shared to the CAMI/IMPT listserv and available on the website. This meeting was one element of the process for the first MPT product prioritization and gap analysis.
- The SAWG MPT product priorities and gap recommendations were vetted among a wider cadre of key stakeholder audiences, including with MPT product developers, at the annual MPT meeting in Baltimore (February 2013), the CONRAD Product development meeting in Arlington (February 2013), and other venues.
- The final SAWG FY12-FY13 MPT product priorities and gap recommendations has been accepted for publication in a special supplement of *AIDS Treatment and Prevention* (November 2013). Recommendations have been summarized and incorporated into CAMI/IMPT PowerPoint presentation templates made available on the CAMI websites (www.cami-health.org and www.mpts101.org).

- In collaboration with the Indian Council for Medical Research, CAMI/IMPT helped organize the first ever regional stakeholder meeting in India in December 2012. The final meeting report was distributed via a listserv of nearly 1,000 members and disseminated in the CAMI and ICMR websites.
- Presented, prepared, and distributed outreach materials at the CONRAD-sponsored Product Development Workshop 2013: HIV Prevention and MPTs (February 20-21, 2013) and at USAID's Annual Meeting for Microbicide Account Cooperating Agencies (March 7-8, 2013).
- Gave a presentation on IMPT to domestic and international reproductive and sexual health advocates in February 2013 in Washington, DC.
- Staff members from CAMI/Public Health Institute participated in the UN Commission on the Status of Women in March 2013.
- In May 2013, CAMI/IMPT partners coordinated and presented on a MPT panel at the European Conference on Contraception in Copenhagen, Denmark.
- CAMI/IMPT partners organized and presented on a MPT panel and distributed MPT materials at a booth at Women Deliver in Kuala Lumpur, Malaysia, in May 2013.
- Presented a poster with an IMPT partner in China at the STI & AIDS World Congress in Vienna, Austria, July 2013.
- Drafted an IMPT terms of reference (TOR) and governance structure and convened and facilitated an IMPT Strategy Meeting in Washington, DC, on March 25, 2013 where the TOR and governance structure was discussed. The IMPT strategic plan and IMPT TOR were revised based on outcomes of the March 2013 strategy meeting.
- In August 2013, CAMI hosted a meeting in San Francisco with several IMPT partners to discuss and outline timelines for MPT product pipeline database revisions, advancing the MPT scientific agenda, and goals for CAMI/IMPT's new participation in the Sexually Transmitted Infections Clinical Trials Group. A socio-behavioral literature review was also presented and discussed during this meeting with IMPT partners.
- Outreach materials were presented at Reproductive Health 2013, Denver, CO, September 2013.
- MPTs were featured by IMPT partners who developed slides developed by CAMI/IMPT during a Research Update Symposium and a dedicated breakout session at the South Africa Women's HIV-Prevention Summit (September 2-3, 2013).
- CAMI/IMPT assisted Indian Council for Medical Research staff in preparing a presentation on MPTs as part of the 35th Annual Conference of Association of Obstetricians and Gynaecologists of Delhi (September 21-22, 2013, New Delhi, India).
- Maintained and updated the CAMI website and distributed information via listserv. The following are some of materials posted to the CAMI website and distributed via listserv:
  - Report on the MPT Product Prioritization Stakeholder Meeting http://www.cami-health.org/documents/2012-SAWG-Report-FinalReport.pdf.
  - Funding opportunities including the Bill & Melinda Gates Foundation Call for Concepts and Grand Challenges Explorations "Develop the Next Generation of Condom," and USAID's AIDS Supplement and Family Planning Call for Papers http://www.cami-health.org/ resources/funding-opportunities.php.

  - The recently published article, "Developing Multipurpose Reproductive Health Technologies." http://www.hindawi.com/ journals/art/2013/790154/.
  - A link to a blog on MPTs (*New MPTs could provide many benefits to women*) from RH Reality Check.
  - A technical brief on hormonal contraception and HIV, prepared in collaboration between the U.S. President's Emergency Plan for AIDS Relief and USAID.
  - IMPT event calendar http://www.cami-health.org/resources/ events.php.
- Performed numerous website updates and expanded the range of information presented, examples include:
  - Developing new content and designing a MPT web page for use as a key outreach tool.
  - Reorganizing and updating the Presentations and Convenings pages for easier navigation and use.
  - Redesigning and posting an MPT fact sheet and Global Reproductive Health Diary booklets.
- In September 2013, launched www.MPTs101.org and developed the MPT 101 PowerPoint presentation and complementary presentations and accompanying materials for presenters.
- In July 2013, CAMI's Senior Scientific Advisor and a University of California, Berkeley intern initiated revisions to the MPT pipeline database in order to reorganize it and make it more user friendly.
- HealthTech with CAMI/IMPT assessed interest/availability among family planning, STI, and HIV experts in the Caribbean to determine the ability to develop a Communication Advisory Committee in the Caribbean. Experts expressed interest but lack of time to lead/champion this effort. Based on response, HealthTech and CAMI determined further outreach in the Latin America/Caribbean (LAC) region is needed in 2014 to build IMPT interest and support in LAC.
- HealthTech in collaboration with IMPT regional representatives at the Kenya Medical Research Institute and Wits Reproductive Health and HIV Initiative established MPT communication advisory committees in Kenya and South Africa, respectively. The AIDS Vaccine Advocacy Coalition, among other local and international partners, is a member of both the Kenya and South Africa committees.
- HealthTech facilitated monthly calls with IMPT communication advisory committees in Kenya and South Africa, established consensus on communication objectives and specific activities for the 2013–2014 year, and established consensus on key features of a communication strategy.
- Identified key convenings in China for regional partners' participation.
- CAMI/IMPT facilitated a strategy for coordinated MPT outreach at several upcoming conferences including the American Public Health Association, the International Conference on Family Planning, the International Congress on AIDS in Asia and the Pacific, and the International Conference on AIDS and STIs in Africa. Activities relevant to MPTs will include panel sessions, an MPT booth, discussion tables/forums, a survey of MPT preferences, and development of infographics and materials.
- Held a briefing and strategy session with staff of a senator from California in February 2013.
- In 2013, IMPT expanded its funding base with the additional support provided to CAMI from the Bill & Melinda Gates Foundation. This support is co-funding two key components of the IMPT strategy, namely (1) supporting CAMI as secretariat for IMPT, and (2) facilitating the MPT scientific agenda. The activities under the third IMPT strategy, enabling a supportive global policy environment for the

development of MPTs, are not supported under the Gates Foundation funding. These activities are carried out by HealthTech, the Guttmacher Institute and Association of Reproductive Health Professionals in conjunction with CAMI and IMPT partners.

Problems encountered and actions taken

No problems to report.

Pathway from research to field implementation and use

As part of a global coalition with the goal of advancing MPTs for reproductive health, the project team will participate on four activities over five years. These activities include supporting CAMI as the secretariat for IMPT, expanding global support for MPTs, facilitating the MPT scientific agenda, and developing a MPT communication strategy. The focus in Years 1 and 2 was on identifying regulatory pathways for MPTs; the focus will expand to include access and delivery in Years 3 through 5.

Neonatal Resuscitators

Goal

Conduct independent, third-party evaluation of new designs of neonatal resuscitators and/or component pieces (i.e., face/device interface) as part of the Helping Babies Breathe (HBB) Global Development Alliance (GDA) to reduce neonatal mortality by improving newborn resuscitation.

Status of the project as of September 30, 2013

HealthTech participated in the United Nations Commission on Life Saving Commodities for Women and Children (UNCoLSC) Neonatal Resuscitation Technical Working Group and leads the efforts around quantification and market sizing. As part of this effort, developed a quantification tool and estimated market sizing for bag and mask resuscitation devices, suction devices and training mannequins for the eight priority countries under UNCoLSC. Completed bench testing of an innovative resuscitator design made by Laerdal Medical and (with external funding) implemented a user evaluation of the same device in the United States.

Achievements in Year 2

- Participated in meetings related to the UNCoLSC Neonatal Resuscitation Technical Working Group as well as the HBB Global Development Alliance.
- Completed guides to selection of equipment that would be complementary to the aims of the Survive and Thrive GDA; topics include rechargeable lighting, continuous positive airway pressure, thermoregulation devices for preterm infants, birth simulators, and portable ultrasound. These are currently being reviewed by USAID. A summary of fetal monitors is in process.
- Drafted a technology landscape on face/ventilation interfaces.
- Conducted a third round of bench evaluations on the most recent prototype of the upright resuscitator design from Laerdal and disseminated the evaluation report to both USAID and Laerdal.
- Conducted a third round of bench evaluations on the most recent prototype of theUpright resuscitator design from Laerdal and disseminated the evaluation report to both USAID and Laerdal.
- Conducted a user evaluation of the upright resuscitator at Seattle Children's Hospital (funded by Laerdal Global); data were obtained from 40 participants. Preliminary results have been communicated to Laerdal and Save the Children (for the purpose of moving forward with field evaluations in Uttar Pradesh).
- HealthTech has completed initial discussions with UNCoLSC teams for resuscitation and Recommendation 6 (supply) regarding timing and work plans for the quantification tool and market sizing.
- Participated in the World Health Organization's (WHO's) consultation for technical specifications for procurement and regulatory pathway of medical devices determined by the UNCoLSC.
- Advocated for and provided technical support to include resuscitation equipment in the WHO and Interagency List of Essential Medical Devices.

- Determined algorithms for market sizing in support of the development of a simple model for estimating the size of global and country-specific market for resuscitation equipment. Data collection has been completed, and the market size estimation is in process.
- HealthTech developed a preliminary quantification tool to assist countries in estimating the quantities of resuscitation equipment needed in various settings and geographies. It was reviewed by the UNCoLSC Resuscitation Working Group and was then field tested in Tanzania and Uganda in August 2013. In September 2013 it was presented at the HBB meeting in Chicago. The quantification tool will be finalized and disseminated in HealthTech year 3.

Problems encountered and actions taken

The planned evaluation of the new device (NeoBreathe) has not begun due to delays on the part of the device developer. The developer has agreed to contact us when the device is ready for evaluation.

Pathway from research to field implementation and use

Project activities focus on identifying and evaluating any innovation in this product category over the course of five years as well as on development tools that will facilitate product introduction and scale-up within newborn care programs. Of immediate interest are the simplified resuscitator designs being developed by Laerdal Medical. In Year 1, we evaluated these devices in bench testing. In Years 1 and 2, we sought funding to conduct independent evaluation of these devices in developed- and developing-country settings. HealthTech also developed a quantification tool and is performing market sizing for bag and mask resuscitation devices, suction devices, and training manikins for the eight priority countries under UNCoLSC. The quantification tool and market sizing will enable countries to better manage supply and manufacturers to understand required production capacity to meet the demand of countries. In Years 3 to 5, provided we see favorable results from the independent user evaluations in various settings, we anticipate joining a wider group of partners in integrating the new devices into the existing HBB programmatic platform to achieve global scale.

Noninvasive Hemoglobin Measurement Technology for Anemia Screening

Goal

Advance the introduction of noninvasive anemia screening technologies in low-resource settings.

Status of the project as of September 30, 2013

The HealthTech Team is conducting an accuracy study that compares the Pronto devices and the HemoCue point-of-care device to the reference method used in the laboratories at the Kintampo Health Research Center (KHRC). The study protocol and tools were approved by three ethic review boards: the PATH Research Ethics Committee (REC), the Kintampo Institutional Review Board (IRB), and the Ghana Health Services (GHS) Ethics Research Committee (ERC). Additionally, the project secured regulatory approval from the Ghana Food and Drugs Administration (GFDA) for use of the noninvasive devices in Ghana for the purpose of conducting the research. By the end of September 2013, the research team had enrolled over half of the 240 participants needed for the study.

Concurrently, a market study and cost analysis was conducted in Ghana. Members of the HealthTech project team traveled to Ghana in July 2013 to gather information on the current methods of hemoglobin (Hb) screening in antenatal care and conduct a market assessment for the noninvasive devices. Meetings and interviews were held with over 30 stakeholders in the public and private sector including policy leaders, facility administrators, clinicians, procurement specialists, medical device distributors, and officials from the National Health Insurance office. The information gathered will be summarized in a planned report and will provide insights into the market opportunity, market segment, cost of current Hb measurement technologies, potential target pricing for noninvasive devices, and cost per test.

Achievements in Year 2

- Finalized plans to conduct the validation part of the performance study of two noninvasive devices with local principal investigator and study team at the KHRC, including study design, budgets, and timelines.
- PATH's REC deemed the calibration part of the performance study to not be human subjects research.
- Received a grant from Masimo to cover the cost of the calibration part of the study.
- HealthTech and Masimo conducted a study initiation visit to KHRC that included review of study tools and training on device use and maintenance.
- Performance study protocol was submitted to USAID for final review; it was also finalized and submitted to the PATH REC, KHRC IRB, and GHS ERC.
- Received PATH REC study approval in December 2012 contingent upon Ghana regulatory approval. Approvals from KHRC IRB, the GHS ERC, and the GFDA were granted by June 2013, and final PATH REC approval was given in July 2013.

- HealthTech trained the study research team and finalized the study tools. Consent and enrollment of women started in September 2013.
- Conducted secondary research for a forthcoming report that included background information on anemia prevalence and current anemia control programs in Ghana.
- Initiated discussions with the collaborating team in Kintampo for conducting an operational feasibility study of the Pronto and Pronto-7 devices in existing maternal health facilities in Ghana. HealthTech outlined study objectives and preliminary study design in consultation with monitoring and evaluation experts, drafted study instruments, and in July 2013, HealthTech team members traveled to Ghana to meet with the collaborating team in Kintampo where they discussed roles and responsibilities, study needs, and coordination.
- HealthTech received non-research determination from the PATH REC to conduct interviews and site visits in Ghana as part of the planning activities for the operational feasibility study planning.
- Signed a Memorandum of Understanding (MOU) with Masimo. It will provide tiered pricing and enable a novel business plan for low- and middle-income countries.
- Identified appropriate pricing for noninvasive devices in Central and East Africa and communicated this range to Masimo as a possible target price. This target has been acknowledged as part of our MOU and will be further refined for Ghana through the cost analysis.
- Initiated on-going discussions with the GHS the possible inclusion of the devices within their new postpartum hemorrhage strategy. Discussions are ongoing.
- HealthTech held discussions with MCHIP and MEASURE Demographic Health Survey (MEASURE DHS) regarding programmatic opportunities to include noninvasive screening for anemia within health programs. With this same aim, HealthTech attended the International Congress of Nutrition in Granada in September 2013 and connected with the Micronutrient Initiative's Regional Director, Asia; members of the steering committee for the Micronutrient Forum; and MEASURE DHS Uganda.

Problems encountered and actions taken

The performance studies to evaluate the devices in Ghana were originally scheduled to begin in the middle of February 2013 but were delayed because additional approvals and documentation were requested by the PATH REC. The GHC ERC approved the study in January 2013. The PATH REC approved the study contingent on receiving a letter from the Ghana regulatory authority allowing use of the devices. Currently in Ghana, drugs are regulated through the GFDA, but there is no body that regulates medical devices. The GFDA reviews requests for medical use and registration in some cases. Prior to GFDA review, the GHS IRB must approve the study. This caused several more months of delay in order to submit the required documentation, including an appropriate United States Food and Drug Administration certificate to governments and the CE Declaration of Conformity for the devices, and secure final approvals. In May 2013, the GFDA requested more documentation including proprietary information. Final approval was granted the end of June 2013. In July 2013, enrollment of 109 women into the study was started prior to final approvals and study release by the PATH REC resulting in a serious noncompliance determination. Once this occurrence was identified, the study was stopped, and a report was submitted to the PATH REC. The team developed a communication plan and informed

partners, all IRB committees, and USAID of this noncompliance. Approval to start the study was granted in early September 2013.

Delays in the start of the performance study have pushed back the other project activities, most notably the pilot introduction study that is contingent on the successful completion of the validation study.

Pathway from research to field implementation and use

The project activities follow a progression over the course of five years. In Years 1 and 2 we conducted technology validation and operational research. Starting in Year 3 if funding is secured, we will conduct demonstration pilots to generate demand and create sustainable business models which will lead to successful larger-scale introduction in developing-country programs. HealthTech will work closely with stakeholders to ensure that the noninvasive technologies support and integrate with other efforts to combat anemia. Partnerships to conduct pilot introductions with country programs and ministries of health, the Global Alliance for Improved Nutrition, the Maternal and Child Health Integrated Program, MEASURE DHS, and others in developing countries will inform and support plans for scale-up

OpenLMIS

Goal

Extend capabilities of a scalable and sustainable electronic logistics management information system (eLMIS) for requisitions, order processing, and system administration to address supply chain issues such as poor data for supply chain decision-making, poor quantification and forecasting of commodities, poor distribution channels and storage, and poor stock inventory management.

Status of the project as of September 30, 2013

Work under HealthTech funding to extend capabilities of a scalable and sustainable eLMIS for requisitions, order processing, and system administration to address supply chain issues has been completed. Plans are currently under way with USAID, the Bill & Melinda Gates Foundation, John Snow Incorporated (JSI), PATH, the Rockefeller Foundation, and VillageReach to build an ongoing, self-sustaining community to support implementations by other countries and ongoing development to address common supply chain and logistics needs. Additionally, interest continues to build around the use of barcode tracking and tracing of commodities as well as the integration of an open source logistics management information system (OpenLMIS) with countries' health management information systems, and as funding permits, PATH will continue to participate in efforts to catalyze early-stage work in these areas.

Achievements in Year 2

- Performed a third-party evaluation of the OpenLMIS platform to inform future investment.
- Completed an analysis and documented requirements for a vaccine supply chain within Tanzania.
- Completed user acceptance testing and initial round of training within Tanzania and Zambia.
- Began deployment, supporting supplies and logistics at national and subnational locations for essential medicines and HIV/AIDS programs within Tanzania and Zambia.
- Both VillageReach and JSI released the OpenLMIS software as open source.

Problems encountered and actions taken

Coordination between development partners continues to be a challenge. Ongoing levels of facilitation and negotiation are needed to meet the needs of country stakeholders. HealthTech continues to play a role, fostering collaboration both locally and globally.

Funding for country-specific development ends at the end of the calendar year, and we are working with donors to assist with bridging funds to address issues during early 2014.

Additional work products for training, testing, and deployment plans are currently country specific. However, these are seen as valuable components to assist with adoption by other countries. PATH intends to generically package and release these items as part of the OpenLMIS effort, contributing to the creative commons.

Pathway from research to field implementation and use

Beginning from a published set of global common requirements for the suppy chain that involved research across five countries, Tanzania and Zambia adopted these requirements for their local context. In Year 2, the USAID/DELIVER project facilitated a joint request for proposal of an eLMIS using the global common requirements as a base. During Year 2, to capture the advantages of speeding introduction through the use of the OpenLMIS software, JSI, PATH, ThoughtWorks, and VillageReach formed a wider joint development effort, and this effort is now transitioning to field implementation and use. Concurrently, the Bill & Melinda Gates Foundation, PATH, and the Rockefeller Foundation invested in the development of OpenLMIS also using common requirements. We do not anticipate further role under HealthTech for OpenLMIS, as it has now been released as open source software.

Paper Applicator for Microbicide Delivery

Goal

Facilitate adoption and use of a low-cost paper applicator for the delivery of tenofovir (TFV) 1% gel in clinical trials and for broader commercial introduction and use in South Africa and elsewhere.

Status of the project as of September 30, 2013

In close partnership with key stakeholders, including CONRAD, ProPreven, Tekpak, and CAPRISA, HealthTech focused on three areas of activities in 2012-2013: (1) technical data—conducting bench tests with the paper applicator and TFV gel to inform future TFV user instructions, as well as to understand feasibility of applicator reuse; (2) acceptability data—advancing plans for conducting acceptability research of the paper applicator among women in South Africa; and (3) commercialization—facilitating discussions between ProPreven and Tekpak around short- and long-term supply of paper applicators for TFV delivery in South Africa.

The bench tests have recently been completed, and the reports will soon be available to share with CONRAD and other key stakeholders. A study design has been agreed upon by CONRAD, CAPRISA and HealthTech to collect acceptability data on the paper applicator among women in South Africa; these research plans can move forward once CONRAD secures funding to support these research activities. Regarding supply of paper applicators to South Africa and elsewhere in Africa for TFV delivery, HealthTech's understanding from ProPreven and Tekpak is that they are both interested in partnering for this purpose. HealthTech will continue to facilitate these talks with the goal of the two parties reaching a mutually beneficial agreement. These talks will continue into 2014.

Achievements in Year 2

- Completed a bench test with the paper applicator and TFV 1% gel to identify the optimal time between filling and dispensing the gel. HealthTech is analyzing results for discussion with CONRAD.
- Completed a bench test with the paper applicator and TFV 1% gel to assess the potential for the paper applicator to be reused. HealthTech is analyzing results for discussion with CONRAD.
- Established interest among CONRAD and CAPRISA for conducting acceptability research on paper applicators among women in South Africa. HealthTech, CONRAD, and CAPRISA agreed to design the applicator acceptability study as a follow on to CAPRISA 008.
- Executed a Confidential Disclosure Agreement with CAPRISA for the purpose of sharing of confidential background materials relevant to study development.
- HealthTech met with the CAPRISA study team in KwaZulu Natal, South Africa, to discuss study design and reached an agreement on study design with CONRAD and CAPRISA. Developed study schema and outlined key roles and responsibilities for conducting the study.
- HealthTech facilitated numerous discussions between CONRAD, ProPreven, and Tekpak beginning in November 2012 about future supply of paper applicators to South Africa. ProPreven expressed their interest in partnering with Tekpak for supply (short term) and technology transfer (longer term).

ProPreven provided Tekpak with an outline of partnering terms. Tekpak also expressed interest in partnering with ProPreven for this purpose; partnering scope and plan are still under discussion.

- Tekpak provided ProPreven with applicator cost and price estimates for a range of applicator volumes. ProPreven has incorporated data into the TFV manufacturing cost analysis. Discussions around applicator supply are ongoing.

Problems encountered and actions taken

CONRAD experienced a delay in the manufacture of TFV 1% gel in multi-dose format in 2012, resulting in a delayed shipment of TFV gel to HealthTech for bench testing. This delay in receipt of TFV gel resulted in bench testing being completed by HealthTech in September 2013.

In our initial discussions with Tekpak and ProPreven, Tekpak expressed concerns about potential reverse engineering and profit loss if they transferred their production know-how to a manufacturer in South Africa. To address these concerns, ProPreven prepared high-level terms for further discussion with Tekpak. In July 2013, ProPreven proposed to HealthTech that they negotiate directly with Tekpak without HealthTech's involvement, which we supported. However, over the last five months, to our knowledge, no discussions between the parties have taken place. Our understanding from conversations with both ProPreven and Tekpak is that they are still interested in partnering. Therefore, HealthTech will resume facilitating these discussions between ProPreven and Tekpak with the goal of these parties developing a suitable partnership for applicator supply.

Pathway from research to field implementation and use

The project activities over five years were designed to lead to introduction of TFV 1% gel with a low-cost paper applicator in South Africa. In Years 1 and 2, we worked to establish support for the paper applicator with ProPreven, the South African joint venture responsible for registration, manufacture, and distribution of TFV 1% gel, and facilitated discussions with Tekpak, the applicator manufacturer; these will continue in year 3. In parallel, in Years 1 and 2, we ensured necessary technical data were generated to support registration and user instructions, and in Years 3 through 5, we will provide technical assistance to ensure appropriate clinical data are collected to inform introduction of TFV with the paper applicator in South Africa. This project will work closely with key stakeholders, including CONRAD, ProPreven, CAPRISA, and Tekpak.

SILCS Diaphragm, a Nonhormonal Barrier Method for Contraception and Dual Protection

Goal

Advance the commercialization of the SILCS Diaphragm by conducting developing-country assessments, scaling production, pursuing regulatory approvals, and building evidence for appropriate gels to be coupled with the device.

Status of the project as of September 30, 2013

Significant progress has been made on all five objectives to support this project. Preclinical studies were completed with Contragel, a lactic-acid–based contraceptive gel. Planning is under way for the postcoital study of the barrier effectiveness and the safety study required to validate Contragel as being safe and effective when used with SILCS Diaphragm. Health systems assessments in two countries are being implemented as well as the associated market research to explore target markets, product positioning, and messaging. Economic modeling to explore the cost/impact of the introduction of the SILCS Diaphragm in a developing country has been completed. Discussions under way with USAID will determine whether additional modeling can be supported to expand this work to other countries and also to include the impact of the SILCS Diaphragm as a multipurpose prevention technology (MPT) by focusing on the added value of the SILCS Diaphragm as a microbicide gel delivery system compared to gel delivered by a vaginal applicator. A gel delivery acceptability study with the SILCS Diaphragm is being implemented in South Africa to assess feasibility and acceptability of this strategy in a developing-country setting. The health systems assessments, cost/pact modeling, and the gel delivery acceptability study will strengthen the value proposition for the SILCS Diaphragm in developing countries. Regulatory approval was achieved in the second quarter of 2013 in Europe, and the SILCS Diaphragm was launched in six countries under the brand name Caya™ contoured diaphragm. A regulatory submission to the United States Food and Drug Administration (USFDA) is scheduled for submission in the fourth quarter of 2013.

Achievements in Year 2

- Completed bench testing on two contraceptive gels, Contragel and Amphora, in November 2012. Results were shared with gel manufacturers. Both gel products are physically compatible with the SILCS Diaphragm in terms of dose delivery. Results will help inform protocols for future studies involving the SILCS Diaphragm with various gel products. Developed a materials transfer agreement with CONRAD for access to tenofovir (TFV) gel. Similar bench testing of physical compatibility of SILCS with TFV gel will be completed by the end of 2013.
- Completed two laboratory studies using Contragel in rabbits: (1) a vaginal irritation test and (2) a contraceptive efficacy study. Findings were presented to USAID in November 2012. The safety study showed good results and no concerns. The contraceptive effectiveness in rabbits showed that Contragel was not effective when used alone for contraception. HealthTech received CONRAD's final report in August 2013 and shared it with USAID.

- Worked with CONRAD to establish study designs and budgets for two clinical studies in women evaluating SILCS Diaphragm used with Contragel: (1) a postcoital study of barrier effectiveness and (2) a safety study. These studies are required to build evidence of the safety and efficacy of Contragel used with the SILCS Diaphragm. The subagreement covering these studies and the associated regulatory work to support them have been drafted and reviewed by CONRAD.
- In conjunction with CONRAD, engaged in consultations with the USFDA on regulatory requirements for two clinical studies. The USFDA advised that the postcoital study could proceed as a nonsignificant risk study and that the SILCS Diaphragm with Contragel safety study may require a new Investigational Device Exemption (IDE). The USFDA requested a pre-IDE submission to examine the protocol and determine the issues.
- Developed evaluation tools and protocol for a health systems assessment of the SILCS Diaphragm in India and received the required ethics approval for the assessment. Interviewed 22 national-level stakeholders in Delhi in December 2012. Implemented state-level interviews and conducted nine focus group discussions (FGDs) with potential users in the states of Rajasthan in the north and Karnataka in the south to examine regional differences between attitudes and practices. Completed the research activities assessment in September 2013. The final report has been drafted and is being reviewed.
- Selected through a competitive bid process IMRB-SRI International of Delhi, India, to implement market research in India to identify the potential target segments who will be interested in the SILCS Diaphragm and explore appropriate positioning and messages to drive success among these target market segments. Developed the subagreement for this activity and submitted it to USAID for review in July 2013. USAID approval and concurrence for this activity was achieved in September 2013. The market research activity was immediately launched.
- Through a competitive bid process, selected MatCH of Durban, South Africa, to conduct an in-country assessment of opportunities and challenges for future introduction of the SILCS Diaphragm in South Africa both as a contraceptive method and as a reusable delivery system for microbicide gel. The project was launched in September 2012 after USAID approval/concurrence of the subagreement was received. Completed an analysis of family planning, sexual and reproductive health, and HIV prevention policies that will influence and shape future introduction of the SILCS Diaphragm in South Africa in January 2013. Developed interview guides, FGD protocol, discussion guides, and facility surveys. These were submitted to the University of Witwatersrand institutional review board (IRB) in February, and ethics approval was received in May 2013. By August 2013, roughly half of the assessment activities were completed. We are now waiting for additional required provincial- and district-level approvals in order to complete the final interviews and implement the facility assessments and FGDs. An abstract on this health systems assessment was accepted for presentation as part of a panel on development of MPTs at the International Family Planning Conference in Ethiopia, scheduled for November 2013.
- Through a competitive bid process, selected Added Value of South Africa to conduct market research that will define target segments and product positioning for the SILCS Diaphragm as a contraceptive and explore consumer interest in the SILCS Diaphragm as a reusable delivery system for microbicide gel in South Africa. The subagreement with Added Value was developed and submitted to USAID in

April 2013. USAID approval and concurrence were received in August 2013. The activity—which assesses target market segments, market sizing, and cultural insights to inform product positioning and key promotional messages—was immediately launched.

- After receiving USAID approval and concurrence in April 2013 for the subaward to MatCH for the gel delivery acceptability study, drafted the study protocol and related study tools in preparation for submission to the PATH and the University of Witwatersrand ethics committees. Arranged for supply of study inventory of hydroxyethylcellulose placebo gel in prefilled plastic applicators and negotiated supply by donation of SILCS Diaphragms from Kessel. Submitted study protocol and related documents to PATH's Research Ethics Committee (REC) in September 2013. Now that we have PATH REC approval, the study documents will be submitted to the University of Witwatersrand IRB for review as well.
- Evaluated existing economic models to see if these could be adapted to illustrate health impact and cost of introduction of the SILCS Diaphragm as a contraceptive and/or for multipurpose prevention (i.e., reusable delivery system for microbicide gel) in target countries. Confirmed that existing models are not sufficient. After consultation with economic modeling groups, engaged consultants from the London School of Hygiene and Tropical Medicine to conduct a cost-impact analysis of the SILCS Diaphragm. Completed a model illustrating the cost/impact of the introduction of the SILCS Diaphragm in South Africa as a contraceptive aimed at women with an unmet need for family planning. The model was reviewed by external experts, and revisions were incorporated. A funding request for an expanded model to look at impact as a reusable delivery system for TFV gel for HIV/sexually transmitted infection protection and to expand the model beyond South Africa is under discussion with USAID.
- Completed documentation required for the SILCS Diaphragm technical file and achieved successful review by the Notified Body (European regulatory auditor). Manufacturing and facility audits have been completed, and CE Mark approval was achieved in March 2013. HealthTech issued a joint press announcement in conjunction with CONRAD in June 2013 to coincide with Kessel's public announcement of CE Mark approval. Kessel launched the SILCS Diaphragm (marketed as the Caya™ contoured diaphragm) in six European Union (EU) countries.
- Clarified issues with the USFDA regarding the 510(k) application. To expedite and simplify the USFDA review, we agreed not to seek an over-the-counter designation at this time. Received confirmation from the USFDA that the 510(k) submission can move forward with no pre-510(k) meeting required. Translated and compiled the technical documents for the 510(k) submission and supplemented the 510(k) application with additional documentation required for the US filing. Engaged a regulatory consultant who reviewed the submission in September 2013. Additional revisions based on these review comments are under way.
- Provided technical assistance to Kessel in support of production optimization and scale-up. Initiated pilot production with the optimized two-step production process at the WEFO-tec factory in December 2012; it was validated by February 2013. Kessel implemented three production batches at the WEFO-tec factory since February 2013. A new pressure test device was validated as part of the quality assurance testing and validation for the SILCS Diaphragm at WEFO-tec. Conducted quality testing on the pilot production and the subsequent batches to ensure the SILCS Diaphragm units met

product specifications and comply with International Organization for Standardization guidelines for diaphragms. HealthTech agreed to continue quality analysis on a spot-check basis during the first year of production and/or while Kessel/WEFO-tec/HealthTech continue to refine the manufacturing process to improve yield and reduce cost.

Problems encountered and actions taken

Progress toward the clinical studies of Contragel used with the SILCS Diaphragm was delayed over the past year while CONRAD/HealthTech engaged with the USFDA to clarify the regulatory requirements for these studies. During this time, the USFDA provided guidance on regulatory determinations (i.e., whether the studies are considered significant risk vs. non-significant risk). Regulatory considerations impacted both the order for feasibly implementing these studies and also decisions regarding which clinical sites could be used (i.e., whether inside or outside the United States). The need to engage with the USFDA and their recommendations delayed the finalization of study budgets and establishing the subagreement with CONRAD. These issues have all been resolved satisfactorily. A benefit of this delay is that USAID has now allocated funding in both FY11 and FY12 to apply to the CONRAD scope of work (SOW) in support of these studies, so we will seek to establish one subagreement with CONRAD that covers both clinical studies and the regulatory activities needed to support these. This should result in efficiencies compared to establishing separate subagreements for all three activities. **Note:** Since current USAID allocations are not sufficient to fully fund all three activities, HealthTech will request as part of the FY14 proposed work plan a final allocation to fully fund the CONRAD SOW.

The health systems assessment of the SILCS Diaphragm in South Africa was delayed when it took longer than anticipated to achieve USAID concurrence for this activity. The additional approvals required at the provincial-, district-, and facility-levels have further delayed implementation of some activities. We requested and have received an extension until December 31, 2013, to allow MatCH to complete these final activities.

The European regulatory filing and the 510(k) filing were delayed due to technical challenges in establishing production. Kessel and HealthTech staff worked together to address these. Production scale-up and validation progressed in a step-wise manner, moving from 500 units to 4,500 units to 10,000 units, with quality verified at each step. Validation of pilot production was the final step required before European approval; the CE Mark was granted in March 2013. Since then, the focus shifted to the 510(k) submission, which is expected to be ready for submission to the USFDA by December 2013.

HealthTech negotiated with two groups of health economists to undertake this cost/benefit analysis before determining that staff from the London School of Hygiene and Tropical Medicine, due to their expertise and availability, were the better fit for this project. However, FY12 funding for this activity was sufficient to cover only a portion of the outputs needed to illustrate the SILCS Diaphragm's value as a contraceptive method and as a MPT. HealthTech submitted a request for additional funding to USAID under the Microbicide Account FY13 work plan to cover a second phase of economic modeling by the London School to further establish the value proposition of the SILCS Diaphragm as a microbicide gel delivery

system as compared to gel delivery via other scenarios, such as prefilled applicators or disposable paper applicators. This work plan is being reviewed.

Pathway from research to field implementation and use

Over five years, project activities will focus on advancing the commercialization of the SILCS Diaphragm. Activities will include validating a contraceptive gel for use with the device in developing countries; conducting developing-country market assessments and demonstration studies to clarify the value proposition for the SILCS Diaphragm as both a barrier contraceptive and as a microbicide delivery system for dual protection; building strategies for market introduction, regulatory submissions, and scaling up production to bring the SILCS Diaphragm to key developing-country markets; and supporting market development to ensure awareness, access, and sustainable supply.

Skunkworks

Injectable Antibiotics

This skunkworks funding allowed HealthTech to participate actively in the United Nations Commission on Life-Saving Commodities for Women and Children injectable antibiotics for newborn sepsis commodity group Technical Resource Team (convened by Save the Children). HealthTech catalyzed action in this group which culminated in a face-to-face meeting of the Technical Resource Team in August 2013. As part of that meeting, HealthTech prepared a manufacturer landscape of gentamicin, procaine penicillin, and ceftriaxone suppliers and assessed the current supply chain from manufacturer to country of use. During preparation for the meeting, HealthTech worked closely with colleagues from the USAID Center for Advancing Impact and Innovation to understand the market shaping requirements of injectable antibiotics both at global and country levels.

Local Manufacture of Noninvasive Hemoglobin Measurement Device

The purpose of this work was to support time in Kenya for a commercialization officer to meet with manufacturers to understand local manufacturing capacity with regard to manufacture of a low-cost noninvasive hemoglobin measurement device using the Masimo Corporation's original equipment manufacturer technology.

This skunkworks project has concluded. We conducted a meeting with a manufacturer in Kenya where manufacturing capacity and business relationships were discussed as well as complementary business models were being tested for sustainability and access for low-resource populations. Similar discussions have also been conducted with manufacturers in South Africa. The information gathered from these conversations combined with the findings from a market opportunity evaluation (conducted by PATH commercialization staff under a project funded by USAID that focused on a malaria anemia etiology tool), as well as the stated level of commitment from partners in Kenya and South Africa to seek complementary funding, helped us to select an organization in South Africa as the local manufacturing partner. A technology transfer is currently in process.

Participation in Best Practice Pneumonia Demonstration Projects Roundtable

HealthTech supported participation in a roundtable discussion on Best Practice Pneumonia Demonstration Projects in New York in April 2013. The Roundtable is an initiative of the Pneumonia and Diarrhea Working Group chaired by United Nations Children's Fund and the Clinton Health Access Initiative and is in support of the United Nations Secretary-General's *Every Woman, Every Child* movement. Pneumonia and diarrhea are two of the leading causes of death for children under five and are responsible for nearly one-third of these deaths. This activity supports and reinforces our work through the United

Nations Commission on Life-Saving Commodities for Women and Children amoxicillin commodity group.

A HealthTech staff member attended the Pneumonia Roundtable and successfully represented PATH with a presentation on pneumonia innovations and a panel discussion. She also presented on pneumonia diagnostics on behalf of Debbie Burgess from the Bill & Melinda Gates Foundation.

mPneumonia Pilot

The goal of this work is to improve frontline health workers' ability to manage childhood pneumonia through the use of an innovative cell-phone–based application. Our mPneumonia application integrates a digital version of Integrated Management of Childhood Illnesses protocol and applications for assessing respiratory rate and oxygen saturation into a user-friendly diagnostic and management algorithm for childhood pneumonia. Through field testing in Africa and a small pilot study, the team will assess the feasibility, acceptability, and usability of the mPneumonia application.

This skunkworks funding supports a larger effort being conducted by the United Nations Commission on Life-Saving Commodities for Women and Children. Work on the mPneumonia pilot project has begun. Ghana was selected as the country setting and Kintampo Health Research Center as the implementing partner. The mPneumonia application is being readied for initial field testing (Phase 1) in Ghana which is planned for early January 2014. The mPneumonia team has already developed the pilot (Phase 2) protocol, and ethical review is planned. We plan to proceed with field testing (Phase 1), and when we feel comfortable with the application, will move on to the pilot (Phase 2) in the coming year.

Opinion Paper: Uterine Balloon Tamponade

HealthTech used skunkworks funding to research and write a paper on the use of uterine balloon tamponades that will be submitted for publication in a peer-reviewed journal. The paper will focus on identifying key research questions and gaps in evidence that need to be addressed to inform introduction and scale-up of the technology within maternal health programs.

Working closely with the knowledge services team at PATH, keywords and search terms were identified, and a literature search initiated. Editors at two journals were contacted to assess interest level in an opinion piece on the uterine balloon tamponade. We received positive feedback and were encouraged to proceed. We are currently developing an outline for the paper and will be proceeding with writing.

Sickle Cell Disease Literature Review and Technology Landscape

HealthTech supported a literature review of disease prevention, diagnosis, management, and treatment of sickle cell disease in newborns and produced a landscape of technologies associated with the continuum of care. These results will be used to identify technology innovation ideas for potential future

development. The literature review has been drafted and is now being reviewed by technical experts to determine the most likely areas for investment in technology innovation.