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A HealthTech Report

HealthTech V Annual Report

Year 3

October 1, 2013 to September 30, 2014

Cooperative Agreement AID-OAA-A-11-00051

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Highlights

- The Alternative Methods for the Delivery of Rilpivirine for HIV Preexposure Prophylaxis team drafted a landscape of existing alternative delivery technologies and related formulation technologies for ripliverine and created a draft target product profile for alternative delivery methods of ripilverine.
- Completed market research in Nigeria that uncovered the key strategy for chlorhexidine implementation in the country: Possibility of introducing liquid and gel forms of chlorhexidine since almost half of respondents prefer liquid over gel; Use of private-sector distribution channels (i.e., patent proprietary medicine vendors and pharmacies) to increase access to chlorhexidine products since the vast majority of respondents are already buying cord care substances at these outlets; Use of antenatal care (ANC) as an educational avenue for women, including community-based ANC outreach programs conducted by community health extension workers.
- Completed a feasibility assessment in Kenya that indicated local production of 7.1% chlorhexidine digluconate is feasible in the country. Began manufacturer selection for local production of the chlorhexidine product. Engaged with the Kenya Pharmaceutical Manufacturers Association to solicit interest from member companies, and an invitation for an expression of interest was posted in a newspaper.
- Developed the *Country Guidance for Implementation of Chlorhexidine for Umbilical Cord Care* document, which was released in conjunction with the World Health Organization's (WHO) recommendation on cord care. A supplementary country guidance document was also developed to assist countries with the implementation of the WHO recommendation on cord care.
- Developed a country status matrix to communicate the status of each country's interest or uptake of chlorhexidine for umbilical cord care, including dosage forms and application regimens selected by each country. More than 25 countries are now engaged in some stage of the process, from early consideration to scale-up.
- Health Information Systems Programme (HISP) finished the development of a District Health Information System 2/Cold Chain Equipment Inventory (DHIS2/CCEI) module that captures some of the core functionality of the Microsoft Access-based Cold Chain Equipment Manager tool. In April 2014, the final prototype of the core CCEI module in DHIS2 was made available at http://www.dhis2.org/downloads. The availability of the DHIS2/CCEI module and its development by HealthTech was announced on the DHIS2 user's global listserv with approximately 500 active members (https://launchpad.net/dhis2).
- CAMI Health hosted or co-hosted the following live webinars: in November 2013, with the Association of Reproductive Health Professionals "Developing Technologies for Preventing Unintended Pregnancy, and Sexually Transmitted Infections"; in January 2014, "Multipurpose Prevention Technologies (MPT) Product Development and Regulatory Issues 101"; and in September 2014 "MPT Manufacturing Issues". Recordings of the webinars are available on the CAMI Health website.
- Based on extensive consultation with the Communication Advisory Committees (CACs), key MPT messages were developed for Kenyan and South African target audiences. HealthTech developed and

vetted a Microsoft® PowerPoint® presentation on MPTs with the Kenya CAC and an MPT factsheet with the South Africa CAC.

- CAMI Health produced a three-minute video on MPTs, entitled "MPTs for a Better World," that was launched in September 2014 and can be found on the CAMI Health website. WHO also highlights MPTs and the CAMI Health MPT video on the home page of their website.
- As part of the Injectable Antibiotics (IA) Quality Subgroup of the United Nations Commistion on Lifesaving Commodities (UNCoLC) the IA for Newborn Sepsis Treatment team, conducted a literature review to locate reports and evidence of counterfeit/substandard antimicrobials in African countries, with a focus on gentamicin, oral amoxicillin, and procaine penicillin. This report was shared with the IA Technical Resource Team and USAID. A manuscript is being drafted based on the literature review.
- The Microbicide Delivery team completed Phase 1 of a manufacturing scan to identify potential microbicide applicator manufacturers in China, India, and South Africa. Phase 2, which includes manufacturer visits and assessments, was completed in India and South Africa and is underway in China.
- The Microbicide Delivery team developed five placebo fast-dissolving tablet (FDT) formulations, conducted physical characterization and stability studies on placebo FDTs, and sent them to CONRAD for evaluation and feedback. Based on feedback from CONRAD, the team designed three formulations of tenofovir FDTs, which are currently undergoing physical characterization at PATH. Feedback from CONRAD on these formulations will identify lead formulation candidates to be taken forward for preclinical evaluation by CONRAD.
- The following reports were completed and are now available on the PATH website, the Health Newborn Network website, and the Helping Babies Breathe website: *Quantification Tool for Neonatal Resuscitation Devices* and *Market Sizing Estimates for Neonatal Resuscitation Equipment*.
- Finalized the following guides on commercially available technologies related to the Survive and Thrive Global Development Alliance: continuous positive airway pressure devices, thermoregulation devices, rechargeable lighting, cesarean section/birth simulators, and portable ultrasound.
- In Year 3, the Noninvasive Hemoglobin Measurement Technology for Anemia Screening team successfully completed a study to assess the performance of two noninvasive hemoglobin (Hb) measurement devices, the Pronto and the Pronto-7, at the Kintampo Health Research Center (KHRC) in Ghana. The results were shared with the product developer (Masimo Corporation) and other key stakeholders. A follow-up study to collect waveform raw data, to confirm performance, was designed by Masimo and conducted by the research team at KHRC.
- In Year 3 HealthTech provided support to the USAID Center for Accelerating Innovation and Impact (CII) in achieving its goal of developing and disseminating a comprehensive toolkit for effective planning for introduction and scale-up of global health innovations. Based on a literature review and stakeholder feedback, HealthTech wrote case studies and examples of best practices for the examples section of the User's Guide; drafted best practices, lessons learned, and critical success factors for each of the four sections of the toolkit; and co-wrote draft narrative content for the introduction, framework overview, and description of phases and key activities. HealthTech developed two design

directions for the toolkit to USAID to select from and delivered the first fully complete layout of the document to USAID in September 2014.

- The qualitative and quantitative market research reports on IMRB International's evaluations of country preparedness, market segments, and distribution channels for the introduction of the SILCS Diaphragm in India were finalized and submitted to USAID in August 2014. These reports have been shared with other organizations working to introduce reproductive health products in India.
- HealthTech and MatCH finalized for distribution desk research of policies and guidelines for introduction of the SILCS Diaphragm in South Africa. MatCH shared the report at the March 2014 Stakeholder Consultation on Priority Implementation Research to Inform Development of World Health Organization Normative Guidance on Topical Pre-Exposure Prophylaxis meeting in Durban, South Africa. This report has been shared with other nongovernmental organizations evaluating policies for microbicide introduction.
- The SILCS Diaphragm project submitted the 510(k) market submission for the Caya™ diaphragm to the US Food and Drug Administration (USFDA) in February 2014, and responded to several requests for additional information. The USFDA completed their review of the 510(k) submission and granted market clearance in late August 2014.
- Kessel and HealthTech worked closely with WomanCare Global staff on product registration in Malawi and Zambia, both of which were received by August 2014. HealthTech and Kessel contributed to development of instructions and provider materials to support the introduction of the Caya™ diaphragm in Malawi and Zambia through the Effective Contraceptive Options project.

HealthTech Projects

Alternative Methods for the Delivery of Rilpivirine for HIV Preexposure Prophylaxis

Goal

Investigate the feasibility of alternative delivery systems for the use of long-acting rilpivirine for HIV preexposure prophylaxis (HIV PrEP).

Status of the project as of September 30, 2014

HealthTech conducted an analysis of potential alternative delivery methods that could be applied to rilpivirine for use for HIV PrEP. Additional antiretroviral drug (ARV) presentation and delivery options have been identified as a critical area of public health need to prevent HIV infection. HealthTech's analysis included discussions with stakeholders, review of the current landscape of products in development for PrEP (both short and long acting), and identification of other technologies that could potentially be used for rilpivirine delivery. We developed a target product profile (TPP) listing attributes for PrEP technologies for systemic and local delivery of rilpivirine and received input from internal and external experts.

The landscape analysis identified a variety of technologies that could be used for the delivery of rilpivirine, including vaginal gels and fast-dissolving tablets, intravaginal rings, the SILCS Diaphragm, microneedles, intrauterine devices (IUDs), and implants. Following the review of the technology landscape, identification of gaps in current research efforts, as well as discussion with stakeholders, we used the criteria in the TPP to identify technologies to recommend for further development for rilpivirine delivery and feasibility assessment. A key area of emphasis was the identification of technologies suitable for the delivery of a long-acting rilpivirine formulation. Our initial analysis identified three top candidate technologies: a drug-eluting IUD, a dissolving microneedle patch (MNP) for local (vaginal) delivery, and a hydrogel MNP for systemic delivery. After further investigation and comparison with the TPP, we selected dissolving and hydrogel microneedles for further exploration, and developed a work plan for technical feasibility assessment. The two microneedle-based technologies represent different forms of protection against HIV infection (systemic and vaginal), and could each potentially be self-administered at home by users.

Achievements in Year 3

- Reviewed currently available and development-stage technologies that could be applied to HIV PrEP.
- Completed a draft TPP for alternative delivery methods.
- Drafted a landscape of alternative delivery technologies and related formulation technologies.
- Developed a work plan for a feasibility assessment of two technologies and submitted it to the US Agency for International Development.

Problems encountered and actions taken

No problems encountered.

Pathway from research to field implementation and use

The project activities over the remaining 2.5 years of HealthTech are designed to investigate the feasibility of alternative delivery systems for the use of long-acting rilpivirine for HIV PrEP. In HealthTech Year 3 we will develop a draft TPP, identify the most promising alternative delivery methods, and develop a preclinical product development plan. Pending future support, in HealthTech Years 4 and 5 we will initiate preclinical development to determine initial technical feasibility of alternative delivery methods.

Chlorhexidine for Umbilical Cord Care

Goal

Coordinate and support efforts to accelerate introduction and global scale-up of chlorhexidine for umbilical cord care to at least ten countries by the year 2016.

Status of the project as of September 30, 2014

The chlorhexidine for umbilical cord care project made great progress during the program year. Major highlights: registration of the first African chlorhexidine for umbilical cord care product on the market with technical assistance provided by PATH and the United States Pharmacopeial Convention (USP), completion of market research in Nigeria, undertaking of market research in Kenya, and completion of a multiyear operational plan for Madagascar. Interest continues to grow in this innovative intervention, and more than 25 countries are now engaged in some stage of the process, from early consideration to scale-up.

Achievements in Year 3

HealthTech achievements as a participant in the Chlorhexidine Working Group (CWG):

- Completed market research in Nigeria that uncovered the key strategy for chlorhexidine implementation in the country:
  - Possibility of introducing liquid and gel forms of chlorhexidine since almost half of respondents prefer liquid over gel. This possibility should, however, be carefully examined, since splitting demand to two product forms will lead to low production quantity and high production cost for each of the forms if the demand is small.
  - Use of private-sector distribution channels (i.e., patent proprietary medicine vendors and pharmacies) to increase access to chlorhexidine products since the vast majority of respondents are already buying cord care substances at these outlets.
  - Use of antenatal care (ANC) as an educational avenue for women, including community-based ANC outreach programs conducted by community health extension workers.
- Market research to facilitate the development of an effective strategy for national scale-up in Kenya started in June 2014 in four provinces. Data collection tools were developed and pretested, and the researchers have completed their training. Data collection in the four provinces will start in the beginning of October 2014.
- Provided technical assistance to Kenya. Met with the Ministry of Health (MOH) and the chlorhexidine technical working group to discuss and identify technical assistance that could be provided in support of their introduction and national scale-up of 7.1% chlorhexidine digluconate. Confirmed the MOH's interest in establishing a local production base, market research, formative research to identify a preferred dosage form, and pilot introduction.
- Completed a feasibility assessment in Kenya that indicated local production of 7.1% chlorhexidine digluconate is feasible in the country. Began manufacturer selection for local production of the

chlorhexidine product. Engaged with the Kenya Pharmaceutical Manufacturers Association to solicit interest from member companies, and an invitation for an expression of interest was posted in a newspaper. Onsite assessments of interested pharmaceutical manufacturers are planned for November 2014.

- Developed a document to show the cost for technical assistance in order to aid program implementers in identification of which activities are most critical for their situation. The document will be shared at the CWG meeting in October 2014 for finalization.
- Completed updates to the market sizing tool with the latest data and an additional country. The updated tool was posted on the Healthy Newborn Network website in August 2014.
- Completed a report on the rapid assessment of the feasibility of local production for the Democratic Republic of Congo and disseminated the report to the MOH and CWG members via email in May 2014.
- Developed the *Country Guidance for Implementation of Chlorhexidine for Umbilical Cord Care* document, which was released in conjunction with the World Health Organization's (WHO) recommendation on cord care. A supplementary country guidance document was also developed to assist countries with the implementation of the WHO recommendation on cord care.
- Developed instructions for dilution of 20% chlorhexidine digluconate solution at pharmacies for facility use.
- Finalized a CWG capacity statement which is intended to demonstrate the capabilities CWG partners can offer to ministries of health and other stakeholders.
- Finalized a CWG strategy document to help guide the CWG through future phases of planning and growth.
- Developed guidance for chlorhexidine procurement.
- Developed standard information on patient information leaflets.
- Developed a country status matrix to communicate the status of each country, including dosage forms and application regimens selected by each country.
- Updated the following CWG documents to maintain accuracy and relevancy: Technical Brief, Country Guidance, Supplementary Country Guidance, and Market Sizing Tool.
- Added French translations of Country Guidance and Supplementary Country Guidance.
- In October 2013, *BMC International Health & Human Rights* published: Coffey PS, Metzler M, Islam Z, Koehlmoos TP. Willingness to pay for a 4% chlorhexidine (7.1% chlorhexidine digluconate) product for umbilical cord care in rural Bangladesh: a contingency valuation study.

PATH achievements as members of the United Nations Commission on Life Saving Commodities (UNCoLSC) (not funded under HealthTech):

- PATH finalized a scope of work for staff in our Kampala office to support the Uganda MOH chlorhexidine implementation effort. The negotiation of the memorandum of understanding with Amref Health Africa that will disburse UNCoLSC funding was signed in August 2014.
- Completed a manufacturing assessment in Nigeria and provided technical assistance (gap analysis) to one pharmaceutical company (Drugfield). Drugfield has obtained regulatory approval for their gel chlorhexidine product and it is now on the market. Gap analyses are planned for two other

pharmaceutical companies (Emzor and Tuyil) in the near future. These companies are completing work on gel manufacturing facilities.

- Submitted the newborn commodities work plan to UNCoLSC at the end of May 2014. Approval of the work plan and the $320,000 budget were received in August 2014.
- Provided review and comment on the newborn health section of UNCoLSC's Advocacy Working Group toolkit.
- Provided technical assistance for Recommendation 7 (demand generation) in the chlorhexidine toolkit.
- Provided the final review and comments on the chlorhexidine section of the quantification tool developed by the Supply Chain and Local Market Shaping Technical Reference Team (formerly Recommendation 6).
- Completed a multiyear operational plan for chlorhexidine for umbilical cord care in Madagascar.
- Provided technical assistance to three countries/regions:
    1. Francophone West Africa (Burkina Faso, Côte d'Ivoire, Niger, and Senegal). Participated in the first stakeholder meeting on chlorhexidine for umbilical cord care and provided guidance to determine the next steps.
    2. Pakistan. Participated in a stakeholder meeting on chlorhexidine for umbilical cord care and provided input into development of the implementation strategy. Continue to guide decisions on an appropriate administration regimen for the chlorhexidine product and establishment of the supply-side strategy.
    3. Uganda. Participated in the first stakeholder meeting on chlorhexidine for umbilical cord care and provided guidance to determine the next steps.

Problems encountered and actions taken

The subagreement with the Promoting the Quality of Medicines in Developing Countries program of the USP was delayed for many months due to negotiations with the United Nations Children's Fund (UNICEF) regarding intellectual property issues. Although these issues were resolved in December 2013, negotiation on the subagreement with PQM/USP was prolonged due to disagreement on some clauses, including indemnification. In order to initiate immediate activities, the subagreement with USP under UNICEF funding was finalized by removing the development of a manufacturing guide for liquid chlorhexidine. PATH continued to negotiate with PQM/USP; however, it was decided not to develop the manufacturing guide since we could not reach agreement with PQM/USP on the aforementioned clauses and since value of developing a liquid chlorhexidine diminished as many countries chose the gel form.

A WHO representative attending a regional meeting in Kenya mentioned that the upcoming WHO recommendation on cord care supports the use of chlorhexidine for umbilical cord care only in communities. This created confusion among countries that planned to start using chlorhexidine for umbilical cord care at facilities. We accelerated the finalization of the guidance document that helps countries to make decisions on use of chlorhexidine based on their local settings and circulated this document to ministries of health and other in-country stakeholders. Both Kenya and Malawi eventually decided to use chlorhexidine for both home and institutional births.

Since 7.1% chlorhexidine digluconate is for use in countries outside the United States, it was originally planned that the product would be included in the medicine compendium. However, the medicine compendium has been discontinued. As a result, development of the chlorhexidine gel monograph has been significantly delayed. There has been prolonged discussion between the USP and US Food and Drug Administration as to whether 7.1% chlorhexidine digluconate can be included in the USP monograph (or USP-NF), which includes drug substances, dosage forms, and compound preparations that are used and regulated in the US market. If 7.1% chlorhexidine digluconate cannot be included in the USP-NF, there is need to seek another venue to disseminate the information.

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 will add to the evidence base by strengthening the application to the WHO Essential Medicines List and solidifying the strategy for global rollout by convening stakeholders. During Year 1, the CWG was formalized; this is an international collaboration of organizations committed to advancing the use of 7.1% chlorhexidine digluconate for umbilical cord care through advocacy and technical assistance. The CWG is jointly creating a strategy for chlorhexidine rollout globally. PATH, as the Secretariat of the CWG, will lead the group to identify and coordinate programmatic opportunities for chlorhexidine integration into global and regional platforms as well as build potential supplier bases for regional manufacturing and distribution. In Years 2 and 3, we will also provide leadership and technical support for both supply and demand initiatives in support of the UNCoLSC Year 1 implementation work plan. In Years 4 and 5, we will continue to lead this work by building on the knowledge and implementation base to scale the chlorhexidine product worldwide.

Cold Chain Equipment Inventories

Goal

Make collecting, updating, and using cold chain equipment inventory data a common and sustainable practice among Expanded Programme on Immunization (EPI) teams and their partners through the development and introduction of an appropriate inventory system that makes evidence-based equipment planning and management easier at all levels of the vaccine supply chain.

Status of the project as of September 30, 2014

In Year 3, the Microsoft® Access®-based Cold Chain Equipment Manager (CCEM) tool was implemented in five countries with World Health Organization (WHO) and United Nations Children's Fund (UNICEF) support. The importance of cold chain equipment inventories (CCEIs) was highlighted in several immunization supply chain strategy documents from WHO and the GAVI Alliance, and we hope that these references signal increased attention in the next year to the CCEI tools developed throughout this project, and that this attention will strengthen the global partnerships and the buy-in needed to ensure that long-term CCEI implementation resources and tools are available to EPI teams.

Working in close collaboration with EPI teams in Ghana and Laos, the web-based equipment inventory module—District Health Information System 2/Cold Chain Equipment Inventory (DHIS2/CCEI)—was extended by the Health Information Systems Programme (HISP) in India to enable valuable new equipment monitoring and maintenance functionality. However, to integrate this standalone DHIS2/CCEI module into the DHIS2 system used nationally in Ghana, Laos, and more than 20 other countries, in Year 4 it is critical that PATH identifies a modest amount of additional co-funding in order to finish this short-term development work. In Year 4 and Year 5, if additional funding is received, HealthTech is poised to demonstrate—in collaboration with the Ghana and Laos EPI teams, UNICEF, and WHO—how a web-based CCEI tool like DHIS2/CCEI can provide CCEI data to a wider cadre of staff and facilitate the management and performance of the national cold chain and logistics system.

Achievements in Year 3

HealthTech achievements:

- Completed a scope of work for HISP to finish the development of a DHIS2/CCEI module that captures some of the core functionality of CCEM, with the goal of having this web-based equipment inventory module as part of the ongoing global releases of DHIS2 managed by HISP. In April 2014, the final prototype of the core CCEI module in DHIS2 was made available at http://www.dhis2.org/downloads. The availability of the DHIS2/CCEI module and its development by HealthTech was announced on the DHIS2 user's global listserv with approximately 500 active members (https://launchpad.net/dhis2).
- Imported data on CCEIs from four regions in Ghana were used to configure a prototype of the DHIS2/CCEI module. The DHIS2 and EPI teams are committed to introducing this module as part of the national health management information system (HMIS) in Ghana; this effort is pending HISP's

completion of the integration of the DHIS2/CCEI module with the current DHIS2 software and the need to secure additional support for training and implementation.

- Throughout the development of a web-based decision support tool that can help national immunization programs calculate cold chain capacity requirements (funded by HISP), convened phone calls during the months of April, May, June, and July of 2014 with WHO staff to discuss the design of this web-based application and to ensure that it aligns with the WHO methodology.
- A draft CCEI Data Standard, developed by HealthTech in collaboration with the UNICEF Cold Chain and Logistics Taskforce in the previous fiscal year, was shared with the new GAVI Cold Chain Equipment Priority Working Group. This was shared as part of an active discussion by GAVI, WHO, UNICEF, and partners on the importance of data standards. We suggested that there might be a potential role for WHO in promoting data standardization, including advancing a CCEI reference standard that can be shared broadly with EPI teams and partners.
- Developed a draft cold chain assessment and planning report template and an outline of an equipment inventory implementation toolkit. Requested that GAVI develop this report template within the cold chain equipment task force as part of the GAVI Vaccine Supply Chain Strategy. HealthTech will leverage this GAVI initiative to refine and complete this report template and anticipates that CCEIs will become an expectation for GAVI funding in the future.
- Presented, in collaboration with the Partnership for Reviving Routine Immunisation in Northern Nigeria and the Northern States Maternal, Newborn, and Child Health Initiative, DHIS2/CCEI at the International Association of Public Health Logisticians Supply Chain Summit in November 2013. The presentation is available at: http://tinyurl.com/l4scear.
- The Kenya EPI technical team created an initial draft of a workflow diagram showing how monthly temperature alarms can be used to improve equipment maintenance systems. A prototype of the DHIS2/CCEI module configured with CCEM data for Nairobi County with Kenya Ministry of Health and the Clinton Health Access Initiative (CHAI) teams was also shared with the EPI and CHAI teams in Kenya.

Related PATH achievements (under other funding):

- Supported Pakistan's UNICEF polio team in the implementation of CCEM subnationally and developed a set of new custom reports that support a country-led vision for a vaccine cold chain that can deliver their polio program objectives. UNICEF plans to extend CCEM nationally in 2015. John Snow Inc.'s. USAID | DELIVER PROJECT team in Pakistan incorporated the CCEM data structure into the USAID-funded Vaccine Logistic Management Information System, which may provide a long-term, integrated *information and communications technology* solution to make collecting, updating, and using cold chain equipment inventory data a common and sustainable practice. The deployment of CCEM in Pakistan is described in *The International News* at: http://www.thenews.com.pk/Todays-News-6-232216-National-cold-chain-inventory-database-launched.
- In collaboration with UNICEF and the University of Washington, supported the Laos EPI staff at the national and district levels to design and prototype new DHIS2/CCEI functionality that allows health center staff to report monthly temperature alarms and vaccine stock data through short message

service to a centralized equipment inventory module; this new tool is seen by the EPI staff as a mechanism to increase support and communication between national, district, and health center-based staff. HISP set up a test instance of DHIS2/CCEI for Laos, which is functioning as of the second quarter of 2014. In September 2014, a multi-agency review of this system was conducted, with participants from WHO, UNICEF, and the World Bank; the outcome was a decision to continue toward a national deployment by the end of 2015.

- HISP and the University of Oslo sponsored a Google Summer of Code 2014 intern to work with the HealthTech team on the development of a web-based decision support tool that can help national immunization programs calculate cold chain capacity requirements. This new web-based tool is an advance prototype of a new application that can help EPI teams compare the impact of vaccine presentations and supply chain logistics on equipment capacity requirements.
- Attended the Effective Vaccine Management Assessment workshop in Tbilisi, Georgia, in November 2013. Presented CCEM to GAVI-eligible countries in the European Region as part of the tool set to support EPI improvement plans.
- Using funding from the Bill & Melinda Gates Foundation, further extended the DHIS2/CCEI module to track equipment preventative maintenance and repair services, according to functional requirements outlined by the Ghana EPI team. Accenture Development Partners and PATH, in collaboration with Ghana's EPI manager and the core EPI and HMIS technical teams, developed a final set of functional requirements to help track and report on equipment repair and maintenance services, which was successfully used to extend the DHIS2/CCEI module. This enhanced DHIS2/CCEI prototype was finalized in August 1, 2014.
- With support from WHO and UNICEF, CCEM was implemented in 2013-2014 in Cambodia, Georgia, Indonesia, Pakistan, and the Philippines, and in Uganda with support from CHAI.
- PATH contributed to submission of a manuscript entitled "Supporting immunization programs with improved vaccine cold chain information systems," which describes the DHIS2/CCEI deployment in Laos. The manuscript was accepted by the 2014 Institute of Electrical and Electronics Engineers Global Humanitarian Technology Conference (IEEE GHTC) committee. In October 2014, this paper will be delivered by a team from the University of Washington as an oral presentation during the annual IEEE GHT conference.

Problems encountered and actions taken

During the deployment of CCEM in Georgia, it became clear that additional testing was needed before releasing CCEM in Russian and that the deployment efforts introduced the use of Georgia script, which added complexity during technical support. These issues relate largely to script settings and number format settings on computers running in Georgia which produced a few error messages. With WHO Regional Office for Europe support, the CCEM developer worked on these issues and will remotely support the implementation of the Russian version of CCEM in Uzbekistan in late 2014, with the Georgia EPI team that implemented CCEM in 2013 providing in-country technical assistance.

Funding to support CCEM implementations in 2014 has largely been provided by WHO and UNICEF. However, it is important to note that it is when there are strong in-country partners such as CHAI in

Uganda, the UNICEF teams in Pakistan and Indonesia, and the WHO team in the Philippines that EPI teams are able to relatively quickly complete CCEM deployments and use these data for equipment planning and cold chain analysis. In Georgia, a strong but overworked EPI team was able to manage the entire process of CCEM implementation and report writing over the course of a year, but not without many delays due both to their existing heavy work burden and the need to overcome mistakes by the initial WHO consultant, who lacked the necessary experience to implement a highly structured, Access®-based equipment inventory solution. Furthermore, none of the five successful CCEM implementations in 2014 could have been completed without some minor support from HealthTech, most notably to provide rapid access to expert technical support from the CCEM developer to help teams address critical software deployment issues in advance of securing the necessary WHO or UNICEF funding. To help sustain successful deployments of CCEM, PATH will continue to recommend the CCEM developer for independent technical support contracts with WHO and UNICEF. The complex and laborious nature of these CCEM implementations highlights the importance of PATH and partners assembling the resources needed to develop a set of practical online resources that will facilitate and standardize the CCEM implementation process as new countries and new consultants seek to deliver successful cold chain equipment inventories and plans.

The most significant challenge to the CCEI project was unforeseen. In March 2014, HISP released a new DHIS2 global software platform (Version 2.16) that changed the core code on which the DHIS2/CCEI tool was built. This change in code suddenly meant that the current DHIS2/CCEI module can only be deployed as a standalone equipment inventory system and not as an integrated module in a national HMIS system built on DHIS2. On the positive side, this new DHIS2 version provides ministries of health with an open-source system that can track patients and health services. However, this change means that in order for DHIS2/CCEI to be released as an integrated module in DHIS2, and thereby maintained by HISP as a standard application in DHIS2, an additional $75,000 is needed to support the additional technical work to integrate the DHIS2/CCEI module. PATH has asked if HISP can support this additional programming work under its *Norwegian* Agency for Development Cooperation grant. PATH is also asking for support from UNICEF. Unfortunately, it is not yet clear how this final integration step will be funded.

The above technical development problem impacts the next steps in our collaboration with Ghana's EPI team to develop and implement DHIS2/CCEI with enhanced preventative maintenance and repair functionality. In order for DHIS2/CCEI to be integrated with the Ghana Health Service's (GHS) new version of DHIS2, the additional DHIS2 programming discussed above is needed. In addition, GHS asked for technical support from HISP to help them outline the steps needed for technical integration of the DHIS2/CCEI module with Ghana's successful national DHIS2 software instance. In hopes of securing additional resources to finish the integration of DHIS2/CCEI with the national DHIS2 instance, PATH has shared a final report with the Gates Foundation, outlining the support needed by GHS to successfully integrate the DHIS2/CCEI module with Ghana's DHIS2 system. PATH will continue to look for opportunities to support the potential at GHS to demonstrate its technical leadership in showing how data can be used for routine management decisions within the immunization program.

Due to a change in leadership and shifting of UNICEF priorities, PATH has not yet established a collaborative project agreement with UNICEF to support introduction of the DHIS2/CCEI tool in Ghana and Laos. PATH is in the process of proposing a new collaborative project with UNICEF that will focus on supporting the introduction of DHIS2/CCEI in Ghana and Laos and stronger documentation of end-user feedback captured during these activities and during the UNICEF/WHO-supported CCEM introductions in Indonesia, Malawi, and Pakistan.

Pathway from research to field implementation and use

The current CCEM software tool supports EPI and partners in the management of a national CCEI and functions as an equipment planning tool for national-level EPI managers and global immunization experts. However, to make implementation and use of CCEI data a common and sustainable practice by EPI staff at all levels of the vaccine supply chain, we must assess how inventory data and tools can make the work of staff at lower levels easier and more effective. In Year 2, we will engage in a set of focused needs assessments to identify the information requirements of cold chain managers at subnational supply chain levels. In Years 2 to 3, we will use the assessment outputs to help develop, test, and demonstrate simple and appropriate tools that can integrate with the current CCEM tool but make CCEI data available to inform decisions by lower-level cold chain managers. We will also continue to refine the existing CCEM tool to make it simpler to use as a national-level planning and management tool. Throughout Years 1 through 5, we will continue to support EPI teams in CCEI data collection and use for decision-making at all levels of the vaccine cold chain. As part of ongoing CCEM implementations, we will develop, test, and refine a set of training materials and develop regional CCEM expertise, in collaboration with partners, to create a sustainable set of technical resources that can increasingly support CCEM use beyond this project.

Initiative for 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, 2014

In Fiscal Year (FY) 3, the Initiative for Multipurpose Prevention Technologies (IMPT) expanded its funding base with additional support provided to CAMI Health from the Bill & Melinda Gates Foundation. Two key components of the IMPT strategy are being funded: (1) to support CAMI Health as Secretariat of the IMPT, and (2) to facilitate the MPT scientific agenda. The activities under the third IMPT strategy, conduct MPT communications and advocacy, are not supported under the Gates Foundation funding. These activities are carried out by HealthTech, the Guttmacher Institute, and the Association of Reproductive Health Professionals (ARHP) in conjunction with CAMI Health and IMPT partners.

CAMI Health, in collaboration with IMPT partners, made substantial advances in all three of the strategic areas in FY3. As noted below, CAMI Health and partners highlighted MPTs at a number of important conferences and forums around the world; CAMI Health also responded to requests from IMPT partners for the development of new MPT online resources and materials. Under CAMI Health/IMPT, the Scientific Agenda Working Group (SAWG) made updated recommendations on MPT product priorities and gaps after an iterative development and vetting process. The SAWG also updated the MPT Product Pipeline Database, and in conjunction with the IMPT Steering Committee and Supporting Agency Collaboration Committee, identified and strategized around other priority issues for the MPT scientific agenda. Lastly, the Communications and Advocacy Working Group expanded outreach with key stakeholders in the United States, developed key communications messages in Kenya and South Africa, and developed outreach efforts to reach a broad array of experts and stakeholders across the family planning, STI, and HIV arenas.

Achievements in Year 3

- CAMI Health established a subgroup of the SAWG to address STI-specific issues for MPT development in October 2013, and organized an in-person meeting of this STI working group (STI WG) in Washington, DC, in February 2014. Since its inception, the STI WG has held conference calls quarterly to identify potential active pharmaceutical ingredients for both bacterial and viral STIs and reach consensus on a framework and priority next steps.

- In November 2013, CAMI Health collaborated with ARHP to co-host a live webinar: "Developing Technologies for Preventing Unintended Pregnancy and STIs." A recording of the webinar is available on the CAMI Health website.
- CAMI Health hosted a booth at the International Conference on Family Planning in Addis Ababa, Ethiopia, in November 2013 and collaborated with stakeholders in the preparation of MPT-related presentations for the conference.
- CAMI Health staff collaborated with the Guttmacher Institute to create an infographic in December 2013. This was a three-month process, including vetting the infographic with the IMPT Steering Committee. The infographic can be found on the CAMI Health website.
- CAMI Health launched a dedicated MPTs website on behalf of the IMPT in December 2013.
- In December 2013, MPTs were featured in the San Francisco Chronicle in a co-authored article by CAMI Health's executive director and Manjula Lusti-Narasimhan of the World Health Organization (WHO), and Entre Nous published a co-authored article by Manjula Lusti-Narasimhan, Mario Merialdi, and CAMI Health's executive director. CAMI Health's executive director also wrote a blog on MPTs, which was featured in the Gates Foundation blog, Impatient Optimists.
- In January 2014, MPTs were featured in the *BJOG: An International Journal of Obstetrics & Gynaecology*; "Multipurpose prevention technologies: maximising positive synergies" was co-authored by CAMI Health's executive director.
- In January 2014, CAMI Health hosted the live webinar, "MPT Product Development and Regulatory Issues 101." A recording of the webinar is available on the CAMI Health website.
- CAMI Health organized and convened the IMPT Steering Committee for an in-person strategy meeting in Washington, DC, in April 2014. The outcome was a revision of the strategic plan for the IMPT developed in March 2013, including guidance for IMPT next steps and priorities. The report from this meeting outlines this plan and was circulated among Steering Committee members.
- In April 2014 in Washington, DC, CAMI Health held the first in-person convening of MPT supporting agency members, called the "Supporting Agency Collaboration Planning Meeting," during which the Supporting Agency Collaboration Committee (SACC) was officially established. The meeting report outlined action items and consensus discussed at the meeting, and was distributed to SACC members. The executive summary is available on the CAMI Health website.
- CAMI Health and STI WG members presented a poster entitled "MPTs: A game changer for STI prevention" at the June 2014 Sexually Transmitted Diseases Prevention Conference in Atlanta, GA.
- In June 2014, the US foreign operations bill included language urging increased support and funding for and coordination around research and development of new contraceptive technologies, including those that may also prevent STIs.
- CAMI Health organized an outreach event in Oakland, CA, in July 2014 aimed at raising awareness about and support for MPTs from the sexual and reproductive health community.
- CAMI Health completed initial data collection for MPT product investments made in 2013 and began drafting a report in August 2014. A final report is anticipated by January 2015. This activity included tracking requests for applications (RFAs) that support MPTs and their funding levels. As part of CAMI Health's MPT pipeline database update, a broader review of RFAs that support MPTs in the pipeline data was simultaneously conducted. In February 2014, CAMI Health convened the SAWG to

discuss simultaneous RFA tracking in the pipeline database. Additionally, CAMI Health and AVAC staff discussed how to harmonize tracking of MPT product investments and agreed to work together to ensure that tracking of MPT investments and the products is harmonized. AVAC's focus will be on products with HIV indications, and CAMI Health will focus more on non-HIV and contraceptive MPTs.

- In August 2014, the Guttmacher Institute held an educational briefing on MPTs with staff from the offices of Rep. Eliot Engel (D-NY) and Rep. Albio Sires (D-NJ) that included discussions of implications for the development of MPTs.
- CAMI Health staff and key advisors developed and administered a provider survey to gauge MPT acceptability and demand in various settings, collecting data from conferences, including Reproductive Health 2013, the International Congress on AIDS in Asia and the Pacific, the International Conference on Family Planning, and two California Family Health Council Women's Health Update conferences. The data were collected from more than 300 health care providers globally. CAMI Health completed data entry and development of the data analysis protocol for this pilot study in August 2014, and preliminary analysis is underway.
- In July 2014, CAMI Health convened an in-person meeting in San Francisco, CA, with a SAWG subcommittee and a socio-behavioral technical expert to develop a framework for the integration of commercialization and social-behavioral attributes into the MPT target product profiles (TPPs). A draft of this framework was finalized in September 2014 and CAMI Health has distributed it to nearly 30 social-behavioral and commercialization experts for review and comment through an iterative process.
- CAMI Health launched its redesigned website and updated MPT Product Pipeline Database in September 2014. In preparation for this launch, CAMI Health staff, the web designer, and the communications consultant redeveloped the resource center, database, and other web pages for ease of use and clarity of information. In addition, the newly launched STI MPT listing, developed by the STI WG, was integrated into the updated MPT Product Pipeline Database. Overall, CAMI Health produced biweekly updates for the CAMI Health website and modified the MPT web page on a monthly basis.
- In September 2014, CAMI Health organized and presented a panel on MPTs at the Social Capital Markets conference in San Francisco, CA, in collaboration with other IMPT members. This conference targeted entrepreneurs, private investors, major foundations, governments, and others dedicated to increasing the flow of capital toward social good. Outcomes included outreach from private investors and an online media article.
- With support from the National Institute of Child Health and Development, the Gates Foundation, and the US Agency for International Development (USAID), CAMI Health co-hosted a two-day technical meeting, "Hormonal Contraceptives in MPTs," in Washington, DC, in September 2014. This meeting brought together contraceptive experts, HIV prevention experts, MPT developers, and funders. An executive summary of the meeting has been completed and a more in-depth meeting report is forthcoming.
- CAMI Health developed a preliminary draft of an MPT funding optimization and enhancement strategy in September 2014, including a strategy to engage European supporting agencies. In the

process of drafting this strategy, CAMI Health conducted donor prospect research for funders in support of MPTs. This strategy is currently under review.

- IMPT SAWG co-chairs reviewed and sanitized the existing MPT dosage-form TPPs (on-demand, intravaginal ring, and injectable). Presentations on updated TPPs were given at the USAID Cooperating Agencies meeting, IMPT Steering Committee meeting, and SACC meetings. After sending requests for review to more than 75 IMPT network members, CAMI Health received and catalogued 24 responses to the MPT dosage-form TPPs in September 2014.
- After sending requests for review to more than 75 MPT technical experts, including funders, product developers, and non-developers, CAMI Health received and catalogued 21 responses to the annual FY3 MPT Product Prioritization Survey in September 2014.
- CAMI Health hosted the MPT Manufacturing Issues live webinar in September 2014. The presentation can be found on the CAMI Health website.
- Based on extensive consultation with the Communication Advisory Committees (CACs), key MPT messages were developed for Kenyan and South African target audiences. HealthTech developed and vetted a Microsoft® PowerPoint® presentation on MPTs with the Kenya CAC and an MPT factsheet with the South Africa CAC.
- The Guttmacher Institute reached out to eight members of Congress to educate them on MPT research and development at USAID, as well as three members of Congress to educate them on MPT research and development at the US National Institutes of Health. MPTs were mentioned in several request letters circulated by the community and members of Congress, and the Global Health Technologies Coalition included MPTs in their request for the FY15 spending bill for foreign operations.
- CAMI Health produced a three-minute video on MPTs, entitled "MPTs for a Better World," that was launched in September 2014 and can be found on the CAMI Health website. WHO also highlights MPTs and the CAMI Health MPT video on the home page of their website.
- In September 2014, the Guttmacher Institute held a meeting with Dr. Deborah Birx, Ambassador at Large and US Global AIDS Coordinator, to discuss the US President's Emergency Plan for AIDS Relief's new initiative on adolescent girls and young women, including the potential role of MPTs. Also in September, the Guttmacher Institute helped organize a meeting with CAMI Health at the Office of the US Global AIDS Coordinator, along with a representative from the Planned Parenthood Federation of America, to inform them of MPTs.

Problems encountered and actions taken

No problems to report.

Pathway from research to field implementation and use

IMPT is a global coalition with the goal of advancing the development of MPTs for reproductive health. The IMPT will advance development of MPTs over the next five years through the following key initiatives: developing a scientific agenda for MPT research and development, including a socio-behavioral research component that will guide prioritization of investment and product development; expanding global support for MPT development, including among supporting agencies, researchers, and advocates both within and outside of the United States; and fostering greater coordination and

collaboration among key stakeholders involved in MPT development. These activities will be carried out simultaneously in Years 1 through 5, with the goal of increasing the global MPT product development pipeline by Years 4 and 5.

Injectable Antibiotics for Newborn Sepsis Treatment

Goal

Contribute to efforts to accelerate availability, accessibility, and correct use of injectable antibiotics for newborn sepsis treatment in key countries by the year 2016.

Status of the project as of September 30, 2014

PATH continues to participate in the United Nations Commission on Life-Saving Commodities (UNCoLSC) Injectable Antibiotics Working Group, responding to expressed project needs, providing feedback, and sharing information with UNCoLSC and other partners and stakeholders. Several activities have been completed, and others await further decision-making from the World Health Organization (WHO)/UNCoLSC Injectable Antibiotic Technical Resource Team (IA TRT). More detailed information can be found below.

Achievements in Year 3

- The Manufacturing Subgroup (consisting of the Clinton Health Access Initiative [CHAI], PATH, and the US Agency for International Development [USAID]) presented an update of their activities and recommendations to the IA TRT meeting in January 2014 in Washington, DC. The update included reporting on a discussion with the Recommendation 5 committee on regulatory barriers as well as an overview of the Subgroup's findings. The findings included showing that manufacture of four generic IAs is competitive and potential barriers to production are registration requirements and lack of concrete, funded demand. The Subgroup's recommendations for next steps included finalizing the country bottleneck analysis and conducting a quality study.
- Collaborated with CHAI and USAID to complete a manufacturing landscape for drugs of interest. Shared a list of gentamicin manufacturers with the IA TRT in May 2014 (they in turn shared it with the United Nations Children's Fund Supply Division).
- Provided detailed feedback to the IA TRT on the work plan and budget for Phase II of UNCoLSC, as well as the Nigeria bottleneck report.
- As part of the IA Quality Subgroup, conducted a literature review to locate reports and evidence of counterfeit/substandard antimicrobials in African countries, with a focus on gentamicin, oral amoxicillin, and procaine penicillin. This report was shared with the IA TRT and USAID. A manuscript is being drafted based on the literature review.
- Developed a first draft of frequently asked questions regarding the simplified antibiotic regimen for outpatient treatment of neonatal sepsis. This document awaits further decision-making from WHO and input from the IA TRT.

Problems encountered and actions taken

HealthTech's activities surrounding the identification of information regarding the quality of IAs in focus countries and monitoring gaps related to new delivery systems and formulations of IAs for management of neonatal sepsis in low-resource settings are dependent on decisions made by the IA TRT. This

decision-making process has been slow and, therefore, has delayed the initiation of many activities. We are only able to begin our activities as they are sanctioned by the IA TRT.

Pathway from research to field implementation and use

The project activities will focus on increasing availability and access to appropriate IAs over the course of three years. In Year 1 (HealthTech Year 3), we will align with the IA TRT to characterize the manufacturing, use, and quality of the drugs. Concurrently, HealthTech will complement UNCoLSC work by assisting in the planning of strategies to address bottleneck analysis recommendations and updated treatment guidelines. In Years 2 and 3 (HealthTech Years 4 and 5), we will continue supporting the IA TRT, drive innovative technology and market shaping approaches related to IAs, and support implementation needs.

Microbicide Delivery

Goal

Facilitate adoption and use of low-cost delivery methods for tenofovir (TFV) in clinical trials and for broader commercial introduction and use in South Africa and elsewhere.

Status of the project as of September 30, 2014

There were three key activities underway in 2013-2014, all of which were in support of the low-cost delivery of TFV gel. First, CONRAD was awarded an APS, which included support to conduct an acceptability study of the TEKPAK paper applicator for delivery of TFV gel among women in South Africa. In the last 12 months, PATH, CONRAD, and CAPRISA have jointly developed this study, which has been designed as a follow-on to CAPRISA 008, whereby a subsample of women exiting CAPRISA 008 would be recruited into this study. As of September 2014, the study was submitted for ethical and regulatory review in South Africa. Pending all necessary approvals, including those in the United States, it is projected to start in the second quarter of 2015.

An applicator manufacturer scan was conducted in China, India, and South Africa with the goal of identifying applicator manufacturers in these countries that could serve as future suppliers/manufacturers for low-cost applicators for TFV delivery. As of September 2014, Phase 1 of the scan was completed in all countries. This phase included identification of existing applicator manufacturers and collecting preliminary information about their business and manufacturing capabilities via desk research and manufacture contact. Based on the information collected, leading facilities were selected for participation in Phase 2 of the scan, which included onsite visits and assessments. A final phase of the scan will include bench testing of selected applicators with TFV gel at the PATH facility in Seattle, WA, to assess dose delivery and performance.

A third activity, a collaboration between PATH and CONRAD, was to evaluate the feasibility of formulating fast-dissolving tablets (FDTs) for TFV delivery, using a novel formulation approach developed at PATH. As of September 2014, several TFV FDTs were developed and are undergoing physical characterization. In collaboration with CONRAD, leading formulations will be advanced for preclinical evaluation by CONRAD.

Achievements in Year 3

- HealthTech, in collaboration with CONRAD and CAPRISA, completed the development of all study documents for "Evaluation of a user-filled, paper applicator for delivery of Tenofovir 1% gel among women in rural Kwazulu-Natal, South Africa." The study received conditional approval from the University of KwaZulu Natal's Institutional Review Board (IRB) and was also submitted to the South African Medicines Control Council (MCC) for approval. HealthTech also executed an IRB authorization agreement with CONRAD/Eastern Virginia Medical School (EVMS) for the delegation of IRB review from PATH to CONRAD/EVMS.

- Completed Phase 1 of a manufacturing scan to identify applicator manufacturers in China, India, and South Africa. Phase 2, which includes manufacturer visits and assessments, was completed in India and South Africa and is underway in China.
- HealthTech and CONRAD held a half-day meeting at PATH to discuss the FDT project, including agreement on strategy and timelines.
- Agreements were established between PATH and CONRAD for TFV FDT work, including provision of TFV to PATH for formulation activity.
- HealthTech designed five placebo FDT formulations, conducted physical characterization and stability studies on placebo FDTs, and sent them to CONRAD for evaluation and feedback. Based on feedback from CONRAD, HealthTech designed three formulations of TFV FDTs, which are currently undergoing physical characterization at PATH. Feedback from CONRAD on these formulations will identify lead formulation candidates to be taken forward for preclinical evaluation by CONRAD.

Problems encountered and actions taken

All study materials were submitted by CAPRISA to the University of Kwa-Zulu Natal IRB and MCC in July 2014. However, CAPRISA was notified by the MCC in September 2014 that the study submission did not include a required document. This document had not been required at the time of the MCC submission; thus, it was not originally included in the study packet. However, CAPRISA immediately resubmitted the packet with the required documentation. As of September 2014, the team was waiting to hear when the MCC review would take place.

Regarding the FDT activities, the PATH-CONRAD research and development agreement (no transfer of funds between the organizations) was not fully executed until May 15, 2014. This caused a delay in initiating the proposed activities as per the originally proposed timeline.

CONRAD suggested developing an oval-shaped TFV FDT for vaginal administration. HealthTech is working with the tool engineering partner (Applied Engineering, Garfield, New Jersey) to design new oval-shaped tooling to form oval blisters. After several rounds of iteration based on feedback from HealthTech, the tooling is almost finalized. We are expecting the oval tooling to arrive at the end of October 2014, following which oval-shaped TFV FDTs will be shipped to CONRAD.

Pathway from research to field implementation and use

The project activities over five years are designed to lead to low-cost delivery methods for TFV that will be appropriate for developing-country settings, including a single-use paper applicator and FDTs. In Years 1 and 2, we will establish support for the paper applicator with key stakeholders, including ProPreven, the South African joint venture responsible for registration, manufacture, and distribution of TFV 1% gel. We will also facilitate discussions with TEKPAK, the applicator manufacturer, and ProPreven to plan for future supply of applicators to Africa. In parallel, we will provide bench data to support user instructions. In Years 2 through 5, we will work with CONRAD and CAPRISA to ensure appropriate acceptability data are collected to inform introduction of TFV with the paper applicator in South Africa. In Year 3, with input from CONRAD and CAPRISA, we will focus on evaluating the FDT

technology and work on the formulation of a TFV FDT for vaginal route delivery. Pending future support, in Year 4 we will continue to refine the FDT formulation and conduct a regulatory analysis. In Year 5, we will conduct an assessment of pharmaceutical manufacturers to determine which might be appropriate to manufacture FDTs for developing countries.

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, 2014

PATH continues to participate as an implementing partner of the HBB GDA and in the United Nations Commission on Life-Saving Commodities (UNCoLSC) Neonatal Resuscitation Working Group, responding to expressed project needs, providing feedback, and sharing information with HBB GDA, UNCoLSC, and other partners and stakeholders. Several reports/tools have been completed and shared with key stakeholders. During this year, one research study was completed and disseminated and in the coming year two others will be submitted for ethical review. More detailed information can be found below.

Achievements in Year 3

- Helped plan and participated in the Resuscitation Working Group in-person meeting in Washington, DC, in January 2014, and planned the next in-person meeting, scheduled for October 2014. Participated in the HBB GDA in-person meeting held in February 2014 in Chicago, IL.
- Finalized the *Quantification Tool for Neonatal Resuscitation Devices* based on country findings and feedback from Tanzania and Uganda. We initially shared the tool with the Ministries of Health of Tanzania and Uganda. Next, we completed two versions of the quantification tool (standard and enhanced versions) to meet users' needs. Both versions are available on the PATH website, and also linked on the Healthy Newborn Network (HNN) and HBB websites:
  - PATH: http://www.path.org/publications/detail.php?i=2401.
  - HNN: http://www.healthynewbornnetwork.org/resource/quantification-tool-neonatal-resuscitation-devices-version-1.
  - HBB: http://www.helpingbabiesbreathe.org/Quantification%20Tool.html.

  Shared the quantification tool and its links with the US Agency for International Development (USAID), the HBB GDA, Neonatal Resuscitation Working Group members, and the UNCoLSC Recommendation 6 team.
- Completed market sizing for the eight priority UNCoLSC countries. Findings were shared with USAID and Neonatal Resuscitation Working Group members in the report, *Market Sizing Estimates for Neonatal Resuscitation Equipment*, which has been posted on the PATH, HNN, and HBB websites:
  - PATH: http://www.path.org/publications/detail.php?i=2408.
  - HNN: http://www.healthynewbornnetwork.org/resource/market-sizing-estimates-neonatal-resuscitation-equipment.
  - HBB: http://www.helpingbabiesbreathe.org/resources.html.

- Completed an update on HealthTech's market shaping activities for neonatal resuscitation equipment. The report, *Shaping the Market for Neonatal Resuscitation Equipment*, has been posted on the PATH and HNN websites:
  - PATH: http://www.path.org/publications/detail.php?i=2409.
  - HNN: http://www.healthynewbornnetwork.org/resource/path-update-shaping-market-neonatal-resuscitation-equipment.
- After review by neonatologists, finalized the following guides on commercially available technologies related to the Survive and Thrive GDA: continuous positive airway pressure devices, thermoregulation devices, rechargeable lighting, cesarean section/birth simulators, and portable ultrasound. The purchasing guide for fetal monitors is in the process of being finalized.
- Finalized the landscape report, *Neonatal Airway Interfaces*, which will be shared with USAID.
- Completed the final report of user evaluation of the Upright Resuscitator at Seattle Children's Hospital and disseminated it to both USAID and Laerdal Medical AS. Submitted a manuscript on the evaluation to *Respiratory Care*, the official science journal of the American Association for Respiratory Care.
- In collaboration with Save the Children, developed the protocol and study forms for the Upright Resuscitator user evaluation to be conducted by Save the Children in Uttar Pradesh, India. A HealthTech consultant completed the first field visit to meet and help prepare the team in India for the study. The protocol is in the process of being submitted to PATH's institutional review board (IRB) and a local Indian IRB.
- Conducted a literature review, and drafted and submitted the study protocol, "Assessment of reprocessing practices for neonatal resuscitation equipment," to PATH's Research Determination Committee, which determined the study to be non-research. Data collection tools have been completed, and Uganda has been identified as the country in which we will conduct the assessment.
- In the process of finalizing a report on the estimated adequacy of supply of required resuscitation commodities to meet the estimated market size. To do this, we designed an online survey and collected responses from manufacturers. More in-depth interviews were conducted with Laerdal and Ambu to obtain their insights.

Problems encountered and actions taken

The planned evaluation of a new device (NeoBreathe, from Windmill Health Technologies™) was not initiated due to delays on the part of the device developer. We followed up with the developer and will wait for the device to be ready for evaluation.

We had planned to conduct the assessment of reprocessing practices in Tanzania given previous HBB and PATH work there. When our country office contacted the Tanzania Ministry of Health (MOH), they thought our work overlapped with the work of another nongovernmental organization (NGO). We had several calls with that NGO and confirmed that our work would actually complement their work and they were supportive of this. We shared this information with the MOH, but they still preferred that we work elsewhere. The Uganda MOH has confirmed that they will support the conduct of the study in their country. We will proceed with our activities there.

Pathway from research to field implementation and use

Project activities will focus on identifying and evaluating any innovation in this product category over the course of five years. Of immediate interest are the simplified resuscitator designs being developed by Laerdal. In Year 1, we will evaluate the Laerdal devices in bench testing. In Years 1 and 2, we will seek funding to conduct independent evaluations of these devices in developed- and developing-country settings. In Years 3 through 5, provided we see favorable results from the independent user evaluations in various settings, we anticipate joining a wider group of partners in integration of the new devices into the existing HBB programmatic platform to achieve global scale. We anticipate that any other product innovation in this category will follow a similar pathway from discovery to field implementation and use. Simultaneously, we will determine the market size and adequacy of supply through development and dissemination of an estimation model and quantification tool that can be applied generically to resuscitation equipment. Data from this model will be shared with manufacturers to encourage them to engage in further product innovation in this space.

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, 2014

In Year 3, we successfully completed the study to assess the performance of two noninvasive hemoglobin (Hb) measurement devices, the Pronto and the Pronto-7, in close collaboration with the Kintampo Health Research Center (KHRC) in Ghana. The results were shared with the product developer (Masimo Corporation) and other key stakeholders. A follow-up study to collect waveform raw data, to confirm performance, was designed by Masimo and conducted by the research team at KHRC. Both studies indicated that the devices are precise, show high within patient repeatability, but continue to exhibit a consistent upward bias. When the devices are used for spot checks at the point of care, this bias would have to be taken into account when interpreting readings. The team of engineers at Masimo believe that the higher than normal level of blood perfusion in pregnant women might be interfering with the infrared signal, leading to the consistently higher Hb values recorded by the noninvasive devices. Measurement techniques, such as paying particular attention to proper placement of the probe and the position of the woman during the measurement, might improve the performance of the devices. Further evaluation of improved measurement techniques might be warranted to test these assumptions. Masimo is also exploring software and hardware updates that may improve device performance (both bias and precision). In September 2014, Masimo released a new sensor designed for infants and children ranging in age from 9 to 59 months. Masimo is investigating whether the new sensor is better suited for use with pregnant women, possibly addressing the problem of bias that was documented in Ghana. The availability of a noninvasive Hb measurement device for infants and children would be a huge advantage for child health programs. The HealthTech team is planning to conduct a study to evaluate the new technology among infants and children 9 to 59 months of age in Guatemala and Rwanda. Planning and discussions with in-country partners are underway.

In addition, under other funding, PATH is working closely with Masimo to transfer the technology to Thinta Diagnostics (a technology development group in Cape Town, South Africa) to develop an affordable noninvasive technology, designed more specifically to address the needs of low-resource settings. Key end-user design feedback has been collected to help understand use cases and user profiles, and to identify critical design attributes and features of the physical product. The HealthTech team is coordinating efforts with the PATH product development team to ensure that a low-cost and optimal product will be available as soon as possible for use in developing-country health settings.

Achievements in Year 3

- With the KHRC, enrolled 238 participants, and conducted testing at the KHRC district hospital using the two noninvasive devices, the HemoCue®, and a reference method. Shared the technical report with the US Agency for International Development (USAID). Conducted additional data analysis in April 2014. Shared a draft version of the report on the additional findings with USAID in May 2014.
- Completed a Ghana market analysis cost assessment report and disseminated preliminary cost analysis findings to Masimo and USAID.
- Conducted two rounds of expert consultations regarding the noninvasive devices with maternal health providers in South Africa. Collected feedback on need, scenarios of use, and feasibility in three areas around Johannesburg, Cape Town, and East London.
- Held a meeting in July 2014 with members of the Association of Rural Doctors in South Africa to gather input and assess interest in the tool.
- In preparation for the Demographic and Health *Surveys* in Rwanda in 2016, HealthTech and USAID discussed the opportunity to assess the noninvasive device for use with infants and children 12 to 59 months of age. Submitted a concept note for a clinical evaluation in Rwanda to USAID and initiated preliminary planning for the study.
- Discussions with Masimo for the technology transfer to South Africa (not with HealthTech funding) were finalized and a plan set in place. Agreements between Masimo and Thinta Diagnostics were signed to launch the technology transfer in South Africa. This could have implications on the availability of a low-cost device for Africa. In collaboration with Thinta, PATH is developing user requirements, a business plan, and a go-to-market strategy.

Problems encountered and actions taken

No problems encountered.

Pathway from research to field implementation and use

The project activities will follow a progression over the course of five years. In Years 1 and 2, we will conduct a performance study, a cost analysis, and an operational feasibility study. Starting in Year 3, we will follow with implementation pilots to generate demand and create sustainable 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 Maternal and Child Health Integrated Program, the Global Alliance for Improved Nutrition, MEASURE DHS, and others in developing countries will inform and support plans for scale-up.

Planning for Introduction and Scale: Synthesizing Best Practices and Lessons Learned

Goal

Support the US Agency for International Development's (USAID) Center for Accelerating Innovation and Impact (CII) in achieving its goal of developing and disseminating a comprehensive toolkit for effective planning for introduction and scale-up of global health innovations during the first half of 2014.

Status of the project as of September 30, 2014

The content and layout of the guide have been oscillating between HealthTech and USAID's CII in various reviews from June 2014 to present. USAID CII is reviewing the final content in a designed layout and will provide specific feedback to the layout, case studies, overall look and feel, and specific text for consideration as HealthTech finalizes the version for publication in 2014. In parallel, photos and additional content have been collected for adding variety and illustration to case studies and examples. Once all changes have been made and agreed upon, the entire publication will go through a final proofreading process (in layout) and then be sent to the printer for a test print before final printing.

Achievements in Year 3

- Conducted a literature review on best practices in planning for introduction and scale-up, including existing case studies. Shared the literature review with USAID in February 2014.
- Conducted targeted outreach and interviews with PATH staff and external experts to gain feedback on the introduction and scale-up framework and collect comments on experiences for quotations within the publication.
- Based on the literature review and stakeholder feedback collected, HealthTech proposed and wrote case studies and examples of best practices for the examples section of the User's Guide.
- Created sample outputs of the User's Guide for USAID review.
- Drafted and refined best practices, lessons learned, and critical success factors for each of the four sections of the toolkit.
- Generated a creative brief for USAID to review. Incorporated feedback into the plan.
- Co-wrote draft narrative content for the introduction, framework overview, and description of phases and key activities and shared it with USAID for review.
- Presented two design directions for the toolkit to USAID to select from.
- Delivered the first fully complete layout of the document to USAID in September 2014.

Problems encountered and actions taken

The USAID CII review and edit of the complete narrative text of the document took much longer than we had anticipated in our original schedule.

We advised USAID CII of the schedule and budget impact of this delay (final document delivery pushed out until November 2014 and an additional $30,000 in funding would be required). USAID CII agreed with the revised schedule and stated they would provide the additional funds in the next fiscal year (October 1, 2014–September 30, 2015).

Pathway from research to field implementation and use

In Year 3, HealthTech will collect and synthesize examples of best practices and lessons learned and will design and produce a key component of CII's guide for planning introduction and scale-up, which CII will then disseminate within USAID and to the broader global health community.

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

Goal

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

Status of the project as of September 30, 2014

Over the past year, the SILCS Diaphragm team registered many successes, including product launch in ten countries based on the 2013 European regulatory approval, and regulatory approval/market clearance in Canada and from the US Food and Drug Administration (USFDA). Regulatory approval and market introduction in developed countries—where diaphragms are still marketed—has been used to raise awareness about this new product and generate interest and awareness among stakeholders in developing countries. HealthTech and Kessel are evaluating requests from potential distribution partners in multiple countries. In addition, the product is now registered in Malawi and Zambia through the Effective Contraceptive Options (EECO) project.

Some of our activities in the coming year include: CONRAD implementing two clinical studies to validate an alternative contraceptive gel; conducting economic health impact modeling work to evaluate the SILCS Diaphragm as a microbicide delivery system compared to other HIV prevention strategies; following up on a key recommendation from the health systems assessment in South Africa; and continuing work with Kessel to improve quality in order to facilitate production scale-up.

Achievements in Year 3

- Received approval from Profamilia's institutional review board (IRB) and the national IRB review committee in the Dominican Republic on the protocol for the Phase 1 postcoital test study of barrier effectiveness of the SILCS Diaphragm when used with Contragel. After the two ethics approvals in the Dominican Republic were received, the study documents were submitted and approved by the Chesapeake IRB on behalf of Eastern Virginia Medical School. An Interagency Agreement allowing the PATH Research Ethics Committee to defer their review to the Chesapeake IRB was approved by both parties in September 2014.
- HealthTech implemented a Materials Transfer Agreement between Kessel and CONRAD for transfer of Contragel for the clinical studies. HealthTech arranged for shipment of additional Contragel inventory sent by Kessel. CONRAD received the study product in August 2014.
- In preparation for the Phase 1 safety study of SILCS and Contragel, CONRAD submitted a pre-Investigational Device Exemption (IDE) package to the USFDA outlining the safety study and requesting determination as to whether a full IDE would be required before this study could be implemented. In July 2014, the USFDA responded that this study meets the requirements of a non-

significant risk study; now the study can move forward once approvals are granted by the local ethics review committees or IRB.

- HealthTech staff presented a poster summarizing a health systems assessment in India at the 13th Congress of the European Society of Contraception and Reproductive Health in Lisbon, Portugal, in June 2014.
- The subagreement between HealthTech and CONRAD for the two SILCS Diaphragm/Contragel clinical studies, and the regulatory work associated with these, was approved by the US Agency for International Development (USAID) in May 2014.
- The qualitative and quantitative market research reports on IMRB International's evaluations of country preparedness, market segments, and distribution channels in India were finalized and submitted to USAID in August 2014. These reports have been shared with other organizations working to introduce reproductive health products in India.
- Completed the Phase 1 modeling activity evaluating the cost-effectiveness of the SILCS Diaphragm as a barrier contraceptive in South Africa. A manuscript describing this model was submitted to the journal *BMC Public Health* in August 2014.
- Completed the field portion of the SILCS health systems assessment in South Africa in December 2013.
- HealthTech and MatCH finalized Africa for distribution desk research of policies and guidelines for introduction of the SILCS Diaphragm in South Africa. MatCH shared the report at the March 2014 Stakeholder Consultation on Priority Implementation Research to Inform Development of World Health Organization Normative Guidance on Topical Pre-Exposure Prophylaxis meeting in Durban, South Africa. This report has been shared with other nongovernmental organizations evaluating policies for microbicide introduction.
- Dr. Jenni Smit of MatCH presented preliminary findings from the health systems assessment of the SILCS Diaphragm in South Africa at the International Conference on Family Planning in Addis Ababa, Ethiopia, in November 2013, as part of the panel, "Innovation to Introduction: Planning for introduction of MPTs."
- Results from the health systems assessment of the SILCS Diaphragm in South Africa also were accepted for presentation at the HIV Research for Prevention conference in Cape Town, South Africa, in October 2014. MatCH will present their findings at the conference.
- Added Value completed market research in South Africa in December 2013 and presented findings to HealthTech staff. HealthTech sent the market research results to USAID in January 2014.
- HealthTech shared results from the market research in South Africa and India with the Expanding EECO project and other organizations working to introduce reproductive health products in sub-Saharan Africa.
- Obtained ethics review approvals from both PATH and University of the Witwatersrand for the implementation of an acceptability study in South Africa of the SILCS Diaphragm when used with gel. Launched the study in July 2014. As of September 2014, the study had achieved full enrollment.
- Submitted to the USFDA the 510(k) market submission for the Caya™ diaphragm in February 2014, and responded to several requests for additional information. The USFDA completed their review of the 510(k) submission and granted market clearance in late August 2014.

- HealthTech commercialization staff implemented a desk research analysis of country-level information regarding the feasibility of regulatory approval, unmet needs for family planning, and indicators for commercial viability. The spreadsheet analysis was shared with Kessel in August 2014; it will serve to help assess opportunities for future introduction planning.
- Kessel successfully completed a factory audit by the regulatory representative of WomanCare Global in July 2014, with no findings or recommendations.
- Kessel and HealthTech worked closely with WomanCare Global staff on product registration in Malawi and Zambia, both of which were received by August 2014. HealthTech and Kessel contributed to development of instructions and provider materials to support the introduction of the Caya™ diaphragm in Malawi and Zambia through the EECO project.
- In August 2014, HealthTech arranged for additional Contragel inventory to be shipped from Kessel to CONRAD, to replace the inventory sent in 2013. The delays in getting the agreement in place for this study meant that the first shipment of Contragel would expire before the study was implemented, so Kessel agreed to replace the 50 tubes of Contragel for this study.
- Implementation of the SILCS Diaphragm Phase 2 economic modeling was delayed as we negotiated the scope and budget with USAID for this activity. Initial funding was allocated from the Fiscal Year (FY) 2013 Microbicide Account obligation (September 2013). After an amended budget request was submitted, HealthTech was notified in April 2014 that an additional $77,000 was approved. HealthTech began working on the subagreements with the London School of Hygiene and Tropical Medicine and the University of Bristol in May 2014. In July 2014, HealthTech requested an additional $26,000 from FY14 funds for this SILCS Phase 2 economic modeling to allow the London School to incorporate analysis into this model from a discrete choice experiment (DCE) they are conducting with separate funds in South Africa (evaluating uptake of HIV prevention strategies). Funding the London School to conduct the analysis required to incorporate the new DCE data into our model will strengthen the model's validity. HealthTech received confirmation in September 2014 that the additional allocation was approved. HealthTech has moved forward on getting the subagreements for this Phase 2 activity in place.
- The WEFO-tec factory is still encountering unacceptably high in-process reject rates within and across production batches, primarily due to streaking of the colorant molecules during the injection molding process. WEFO-tec will try reducing the amount of colorant slightly to see if this improves the yield. They will also conduct a manufacturing run using pre-mixed colorant and silicone. Results of these production runs are expected to be available in October 2014/November 2014.

Pathway from research to field implementation and use

The project activities will focus on advancing the commercialization of the SILCS Diaphragm over five years by validating a contraceptive gel for use with the diaphragm in developing countries (Contragel, reformulated tenofovir, or other gel); 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; and then building strategies for market introduction, developing regulatory submissions, and scaling up production to bring the SILCS Diaphragm to key developing-country markets.

Skunkworks

Diagnostic for Preeclampsia and Eclampsia

Skunkworks funding contributed to the identification of novel biomarkers for the detection of preeclampsia and eclampsia. This opportunity helped us to pursue the objective to create rugged, low-cost solutions suited for distribution and use with the global poor.

Activities funded included the work of an Israeli consultant to develop a relationship between PATH and a potentially interesting Israeli start-up with technology for an early-term preeclampsia diagnosis. This initial work facilitated due diligence by PATH and provided introduction and a nondisclosure agreement (NDA) with the Israeli start-up. This first stage of work laid the foundation for collaboration. The NDA was negotiated with the academic technology transfer office holding title to the technology and with the technology inventor's start-up, which holds existing licensing agreements. The consultant provided introductions, assisted in negotiating the NDA with the technology transfer office and inventors, and provided translational services (Hebrew/English).

These activities resulted in the identified biomarker being included in an awarded PATH Saving Lives at Birth submission, with the Israeli academic partner submitting a letter of support. With Saving Lives at Birth funding, the product team will evaluate the opportunity and advantages of this particular marker versus others in the development of future assays.

Magnesium Sulfate Dilution Bottle

PATH has adapted the concept of a dilution bottle to simplify the process of magnesium sulfate ($MgSO_4$) administration. The dilution bottle contains a 50% $MgSO_4$ solution and is pre-marked with a fill line. When a 50% $MgSO_4$ solution is required, the necessary amount can be withdrawn directly from the bottle. When 20% $MgSO_4$ is required, a health care worker can simply add sterile water (diluent) to the bottle up to the pre-marked fill line to make a 20% $MgSO_4$ solution. This $MgSO_4$ dilution bottle can facilitate the safe calculation of required doses by obviating the need to remember complex equations for dilution, thus minimizing the chance that the wrong dilution might be administered. The bottle could also reduce the burden associated with procurement and inventory control since only one type of dilution bottle must be procured and stocked for the treatment of preeclampsia and eclampsia. We aim to evaluate technical feasibly and commercial viability of such a $MgSO_4$ dilution bottle to ascertain how we should best proceed with this concept.

To date, we have achieved the following:

- Scanned national essential medicines lists of countries in sub-Saharan Africa to understand how $MgSO_4$ is listed.
- Determined that either glass or plastic (high-density polyethylene) is appropriate for the dilution bottle based on a literature review. Also, based on laboratory testing as well as a literature review, identified that a minimum of 75mL is required in order to have sufficient headspace in a sealed bottle to allow for the smooth withdrawal of $MgSO_4$.

- Engaged with one of the largest manufacturers of $MgSO_4$ to understand the pros and cons of manufacturing such a dilution bottle. This discussion led to an alternative concept for the $MgSO_4$ dilution bottle: a dilution bottle that contains water for injection (WFI), instead of $MgSO_4$, with a pre-marked fill line so that 50% $MgSO_4$ can be added to make a 20% $MgSO_4$ solution.
- Commenced preparation for a concept evaluation with policymakers, procurement officials, and service providers in two countries. We will leverage the existing activity for the ready-to-use pack under the United Nations Commission on Life-Saving Commodities for this concept evaluation. The concept of both the $MgSO_4$ and WFI dilution bottles will be evaluated as components of this ready-to-use pack using prototypes created by the 3D printer at PATH.

Magnesium Sulfate Job Aid

PATH, in collaboration with the University of Washington, developed a mobile application for magnesium sulfate ($MgSO_4$) administration which includes a dosing calculator and detailed checklist based on the World Health Organization's protocol. This application is a job aid designed specifically to address the challenges with correctly calculating $MgSO_4$ dosage. Using a smart phone or tablet, health care providers enter the dosing stage and route (e.g., loading intravenous or intramuscular maintenance) and the concentration of the $MgSO_4$ being used into the application and it calculates the amount of $MgSO_4$ that should be administered, provides the proper steps for dilution (if needed), reminds providers to check vital signs, and includes safe parameters for continued administration.

In December 2013, PATH conducted a small-scale, design-stage user evaluation in Kenya in collaboration with the APHIAplus Western Program. The application was validated by health care providers in Kenya; health workers felt it was an easy-to-use valuable tool, and overall were enthusiastic about the use of mobile devices. With Skunkworks funding, HealthTech updated the content of the $MgSO_4$ application, incorporating the feedback received from users in Kenya. A final prototype was developed and the project was included as a Saving Lives at Birth 2014 finalist but not an awardee. PATH is continuing to work with partners to integrate this tool into existing projects and make this mobile application available for download at no-cost from the Google play store.

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 the 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 and a small pilot study in Africa, the team will assess the feasibility, acceptability, and usability of the mPneumonia application.

Skunkworks funding supplements a larger effort being funded by the United Nations Commission on Life-Saving Commodities. Ghana was selected as the country setting and Kintampo Health Research Center as the implementing partner. We created an initial version of the mPneumonia application for field

testing (Phase 1) conducted in Ghana in March 2014. Based on usability testing among end users conducted in Phase 1, refinements were made and an improved iteration of the mPneumonia application was produced for the pilot study (Phase 2). The mPneumonia team developed the study protocol and obtained ethical approvals to conduct the pilot. Work on the mPneumonia pilot project is currently in progress.

Participation in an Expert Consultation Meeting: Consultation on Uterine Balloon Tamponade Research

In July 2014, two maternal health experts from PATH attended a meeting in New York, NY, organized by Gynuity Health Projects and Massachusetts General Hospital. The meeting convened experts on management of postpartum hemorrhage (PPH) and research design to discuss appropriate research strategies for evaluating the effectiveness and safety of using a uterine balloon tamponade (UBT) in the management of cases of PPH. While the UBT has proven to be successful in pilot studies, this was an opportunity to explore strategies to evaluate the impact of the device before this method is rolled out on a larger scale. Our team gave a presentation, titled "Brief history of the uterine balloon tamponade for the management of postpartum hemorrhage." The focus of the presentation was on the work PATH has done to date to assess and advance an appropriate and affordable UBT device for use in low-resource areas. Feedback from the experts on product design and key requirements was sought. Most experts stressed the need to keep the device simple and low cost. Since the meeting's main agenda was to discuss research needs to build a strong evidence base for the technology, it was suggested we consider assessing "new" PATH devices against the Bakri balloon and the standard of care, when it becomes available.

Sickle Cell Disease Technology Landscape

HealthTech supported a literature review of prevention, diagnosis, management, and treatment of sickle cell disease (SCD) in newborns and produced a landscape of technologies associated with the continuum of care. These results were used to identify technology innovation ideas for potential future development. In sum, across the continuum of care of SCD, there are many opportunities for technology innovation. Specifically, technologies appropriate for low-resource settings would be very useful for preventive genetic testing of adults before conception as well as pregnant women. Diagnostics for early detection, especially for newborns and young children, are key to identifying individuals with the disorder and initiating them into care, as well as differentiating from those who are carriers. While a number of diagnostics are currently used in developed countries, technologies that can be applied in low-resource settings—where most individuals with SCD live—are desperately needed; this means diagnostic tools that are low cost, do not need trained personnel, produce rapid and accurate results, and require minimal equipment and regents. For individuals diagnosed with SCD, tools for detecting and managing complications of SCD as well as treatment and potentially curative measures are largely inaccessible in low-resource settings due to cost, complicated equipment, and the need for trained personnel to administer. Innovations in these tools could extend survival of individuals with SCD by improving

management and prevention of SCD complications. Due to the extent of the disease, the impact any one of these technology innovations could make on morbidity and mortality—especially in the geographic regions most affected—is significant.

The literature review was completed and submitted to the US Agency for International Development (USAID) on May 15, 2014. We await an opportunity to discuss with USAID the most likely areas for investment in technology innovation in this space.

Upright Resuscitator Video Analysis

This study is being undertaken to determine if there are any specific clinical criteria in the manner in which bag and mask (resuscitator) ventilation was provided by the participants in the Seattle user evaluation of the conventional and upright resuscitator that could be correlated with lung function results, such as the tidal volume and peak inspiratory pressure. These criteria, if identified, may be useful in training programs. The objectives of this effort are to (1) review the key components in the method of providing bag and mask ventilation that are likely to influence ventilation and correlate these with key lung function parameters, such as tidal volume and peak inspiratory pressure; and (2) identify components, if any, that may be useful in training programs to promote adequate ventilation without producing excessive tidal volumes and peak inspiratory pressures.

Initially, ten criteria were developed to analyze the videos during the period of ventilation, partly based on the criteria used during direct observation of the method of ventilation at the time of the evaluation. Next, the videos of eight participants were analyzed. Based on this preliminary analysis, the criteria for further analysis were classified into three major factors: (1) mask hold, (2) method of squeezing the bag, and (3) chest rise. The number of videos analyzed to date is too few to draw any conclusions. Evaluating the other videos taken during the Seattle study will increase the sample size, hopefully to provide adequate data for analysis. This additional evaluation will be conducted during Year 4 of the HealthTech project.

Performance and Monitoring

Performance and Monitoring

A majority of HealthTech performance and monitoring data are reported yearly in aggregate across all projects, some data will be compiled at the project's end. Table 1 below shows the data collected as of Year 3. Table 2, on page 44 describes the indicators in detail.

Table 1. HealthTech Performance and Monitoring Data

Indicator	Y1 Data	Y2 Data	Y3 Data	Y4 Data	Y5 Data
Number of high potential technologies identified	4	15	**6**		
Number of technologies or components evaluated in a lab/bench or controlled setting	6	8	**4**		
Number of technologies being designed with user input	4	3	**2**		
Number of technologies in the introduction phase	0	3	**1**		
Number of technologies evaluated in the field implementation phase	1	1	**0**		
Number of suppliers/manufacturers with assessed capacity to enter the market with a technology that appropriately meets product specifications	5	13	**8**		
Number of technologies with potential for sustainable supply	4	6	**3**		
Unit cost/price of each technology compared to existing technologies *(reported at project end)*	-	-	**-**	-	
Number of successful technology transfers *(reported at project end)*	-	-	**-**	-	
Number of research/development partnerships formalized	6	14	**8**		
Level of use of HealthTech V information about product category or technology by external groups	Downloads/views from the PATH website: 7,691 Conferences where information was disseminated: 10	Downloads/views from the PATH website: 18,884 Conferences where information was disseminated: 26	**Downloads/views from the PATH website: 29,766** **Conferences where information was disseminated: 12**		
Number of products that are registered for use in developed or developing countries	1	4	**2**		
Use rates of new technologies *(reported at project end)*	-	-	**-**	-	
Amount of outside funds used to support HealthTech V	$522,925	$2,733,098	**$671,250**		

Indicator	Y1 Data	Y2 Data	Y3 Data	Y4 Data	Y5 Data
Coverage of new technologies at facility/district level *(reported at project end)*	-	-	-	-	
Availability of supply of new product *(reported at project end)*	-	-	-	-	
Number of guidelines/policies and decisions approved that support broader scale-up of product use at a global, national, or subnational level *(reported at project end)*	-	-	-	-	

Table 2. HealthTech Performance and Monitoring Matrix

Indicator	Indicator Definition	Indicator Measurement	Source of Data	Method of Data Collection	Schedule of Data Collection	Type of Indicator
Intermediate Result 1: Increased availability of innovative and affordable health technologies						
IR 1.1: Identification and prioritization of new and promising technologies to address health development challenges						
Number of high potential technologies identified	Program's contribution to identification of high potential technologies through landscape analyses that explore acceptability, potential markets, technical feasibility, barriers, intellectual property (IP) issues, costs, financial factors, and stakeholder views.	Number of target product profiles (TPP) for high potential technologies completed	Project records	Landscape reviews and stakeholder feedback	As needed	Output
IR 1.2: Development of viable health technologies that are appropriate, affordable, and acceptable for distribution and use in low-resource settings and show promise for sustainable market development						
Number of technologies or components evaluated in a lab/bench or controlled setting	Number of products reaching validation phase. Tracks outcomes and recommendations to discontinue, improve existing design, or move to field evaluation.	Number of products disaggregated by stage completed	Evaluation report	Lab/bench-based protocols and studies	As needed per technology	Output
Number of technologies being designed with user input	Number of user assessments per technology. Tracks outcomes and recommendations to discontinue, improve existing design, or move to field evaluation.	Number of products disaggregated by stage completed	Evaluation report	User assessment studies, expert consultations	As needed, per technology	Output
Number of technologies in the introduction phase	Number of technologies that progress to introduction phase.	Number of technologies evaluated through pilot testing	Record review—evaluation reports	Special studies: using mixed methods	Annually	Output
Number of technologies evaluated in the field implementation phase	Number of technologies that progress to field implementation phase.	Number of technologies introduced at regional, subnational, or national level	Project records	Special studies: using mixed methods	TBD by technology	Output
Number of suppliers/manufacturers with assessed capacity to enter the market with a technology that appropriately meets product specifications	Number of suppliers who have the necessary capacity to supply a product meeting established product requirements.	Number of identified suppliers/ manufacturers with substantial supply capability of the technology	Project records	Supplier assessments	TBD by technology	Output
Number of technologies with potential for sustainable supply	Number of technologies that have been analyzed in terms of value proposition/business case/building toward sustainable supply.	Number of technologies with market requirements established	Project records	Project reports	TBD by technology	Output
Unit cost/price of each technology compared to existing technologies	Unit cost/price of new technology compared to existing technologies at comparable stage of production.	Dollars per unit at prototype stages; initial manufacturing; and/or projected cost at various levels of scale-up	Project records	Project reports	Project end	Output
Number of successful technology transfers	Number of entities receiving knowledge, expertise, or technology capacity to enable them to produce product according to established specifications. Will solicit feedback on quality of transfer and actions beyond the initial transfer of knowledge/resources.	Evidence of product manufactured to product specifications; increase in knowledge levels; increase in technical capacity	Project and manufacturing records—technology transfer partner survey	Project reports; follow-up survey to possibly include interviews	Project end	Output
IR 1.2a: Innovation fostered to identify new concepts and opportunities for technology development						
Number of research/development partnerships formalized	Total number/type of partnerships between US, international, private, and research or manufacturing institutions.	Number of partnerships formed	Project records	Routine data collection through project reporting	Annually	Process
Level of use of HealthTech V information about product category or technology by external groups	Total number of instances that information about technology opportunities is accessed by external groups.	Number of technology update reports downloaded from PATH website; number of times technology information disseminated at conferences/meetings	Project records	Records review	Annually	Outcome

Indicator	Indicator Definition	Indicator Measurement	Source of Data	Method of Data Collection	Schedule of Data Collection	Type of Indicator
Intermediate Result 2: Increased use of new health technologies in developing countries						
IR 2.1: Introduction of innovative health technologies in developing country settings, bridging the "research to use" gap						
Number of products that are registered for use in developed or developing countries	Evidence of regulatory approval in developed/developing countries including international quality assurance schemes such as World Health Organization prequalification and/or product registration.	Number of regulatory approvals per product	Approval from authorizing agencies	Routine data collection through project reporting	Annually	Output
Use rates of new technologies	Rates will be calculated differently for each given technology, (i.e., estimations of sales/procurement; facility, private sector, or household data).	Number of users disaggregated per technology	Project and partner records	Special studies	Project end	Outcome
Amount of outside funds used to support HealthTech V	Funds leveraged through commercial partnerships. Identifies new partners, catalyzed by commitment, competition from the private sector. Total co-investments disaggregated by private, public, and nonprofit partners and by project.	Dollars allocated	Project and partner records	Total amounts disaggregated by partner, sector, and project	Annually	Outcome
IR 2.2: Scale-up to global access and use of health technologies						
Coverage of new technologies at facility/district level	Rates of coverage for technologies in use. Depending on the technology, coverage rates would be measured differently.	Portion of the population with access to the technology	Population records	Special studies	Project end	Outcome
Availability of supply of new product	Number of units that manufacturers are producing.	Number of product units produced (absolute and as percentage of total market estimate (if possible) TBD by product type	Partner records	Record review	Project end	Outcome
Number of guidelines/policies and decisions approved that support broader scale-up of product use at a global, national, or subnational level	Support from global and national policy/decision-making bodies to create enabling environment for technology introduction.	Number of guidelines or policies created that support scale-up of specific technologies	Policy review and partner records	Routine data collection through project reporting	Project end	Outcome