Envision FP

Transforming Contraception to Expand Access and Choice

Family Planning and Reproductive Health Methods to Address Unmet Need

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SUBMITTED TO:

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YEAR 6 SEMI-ANNUAL REPORT

OCTOBER 1, 2020 – MARCH 31, 2021

SUBMITTED BY:
Family Health International (FHI 360)

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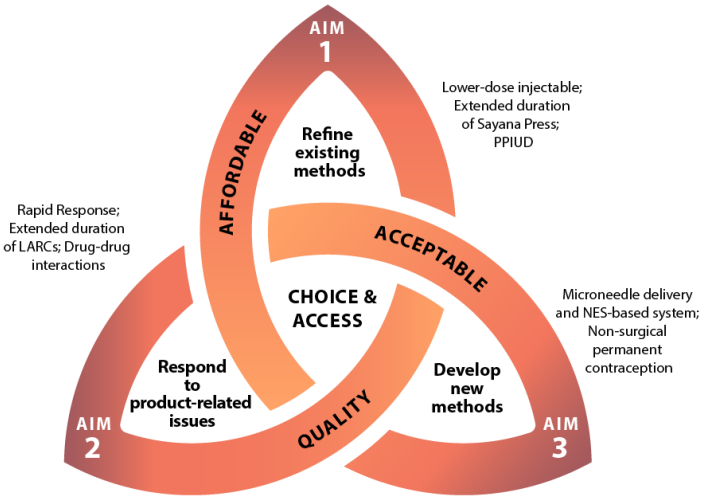
Introduction



The objective of *Envision FP* is to develop, introduce, and expand understanding of contraceptive technologies and approaches to enhance choice and reduce unmet need. The proposed research agenda aligns with the three specific aims outlined in the original USAID Annual Program Statement: 1) refine existing methods; 2) respond to product-related issues that arise from the field and impact provision; and 3) develop new methods to fill gaps. *Envision FP* focuses on key challenges and opportunities significant for users and programs in an effort to achieve the overall goal of broadening choice of and access to quality, affordable, and acceptable contraceptives to meet the changing needs and desires of women and girls throughout their reproductive lives.

The following sections define the activities, accomplishments and challenges for the first half of Year 6 (October 1, 2020 - March 31, 2021). Plans for the next six months are included, including updated simple Gantt charts for each activity. Year 6 budgets and expenditures through March 2021 are provided in Appendix 1.

AIM 1: REFINE EXISTING CONTRACEPTIVE METHODS

Lower-dose injectable contraception
Lead: Vera Halpern, MD

Goal: Develop and receive regulatory approval for a low-cost, lower-dose, three-month subcutaneous depot-medroxyprogesterone acetate (SQ DMPA) injectable contraceptive.

Significance and Impact: Over 40 million women worldwide use injectable contraceptives, particularly intramuscular (IM) DMPA (150 mg every 3 months). Despite its popularity, this dose is unnecessarily high. An alternative, Sayana Press (SP), provides 104 mg MPA subcutaneous (SQ) for 3 months, but also provides more drug than is likely needed. A lower-dose SQ DMPA product would offer a highly effective and safer contraceptive option for women. Reduced side effects would enhance acceptability and increase continuation.

Approach*:* The team will use a marketed DMPA IM formulation (Pfizer) to develop a lower-dose SQ product. A partially-blinded randomized trial will be conducted to assess pharmacokinetics (PK) and pharmacodynamics (PD) of three doses of Pfizer's current DMPA formulation (45 mg, 75 mg, and 105 mg) compared with Depo-subQ 104. MPA levels and ovarian activity will be evaluated after a single injection and all women will be followed for 7.5 months. The 105 mg

arm will provide a direct comparison with the marketed Depo-subQ 104, allowing the study to control for formulation differences between DMPA IM and SQ, with the possibility of pursuing a lower-cost generic SQ product. The team will leverage documentation from our ongoing PK/PD studies funded by the Gates Foundation to accelerate protocol development, investigational new drug (IND) preparation and study start-up.

Activities, accomplishments, and challenges in past 6 months: In Feb. 2021, the main manuscript was submitted to Contraception: X, the open access journal of Contraception.

Plans for the next 6 months: After publication of the main manuscript, we will post the study dataset on an open access platform. By Jun. 2021, an additional manuscript based on the PK/PD data from this study (in combination with PK/PD data from the ESS trial as described below) will be submitted for publication. We will also conduct a secondary analysis of the supportive PD data from this study to explore the role of secondary mechanisms of contraceptive action of MPA and provide information on potential biomarkers of contraceptive effectiveness (in addition to ovulation) for future contraceptive studies. A manuscript based on this secondary analysis of the supportive PD data will be submitted for publication by Aug. 2021.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Manuscript submission (main paper)					•							
Manuscript submission (secondary analysis of PD data)											•	
Manuscript submission (PK/PD data)									•			

Extending the reinjection interval of Sayana Press (SP)
Lead: Jennifer Deese, PhD

This study is being co-funded by the Bill & Melinda Gates Foundation, under the Contraceptive Technology Innovation Initiative (CTII) and Advancing priority CT leads to meet user needs (CTII-2). The return to ovulation sub-study is being co-funded by Envision FP and the Children's Investment Fund Foundation (CIFF).

Goal: Determine effectiveness, safety, and acceptability of extending the reinjection interval for Sayana Press (SP) and to determine the appropriate grace period for re-injection.

Significance: Evidence suggests that SP is effective for four months or longer but is currently indicated for three months. Extending SP duration by one month would reduce commodity costs for a year of protection by 25%. Given the same commodity budget, countries could serve 33% more women annually. Less frequent reinjections would also reduce drug exposure, provide greater convenience to women, and lower overall health system burdens.

Approach: The team will develop a 12-month, single-arm clinical trial to determine the effectiveness, safety, and acceptability of SP given every four months, and to determine the appropriate grace period for re-injection. Women will be enrolled in three countries to assess one-year pregnancy rates, adverse events and side effects, and discontinuation rates. Key

informant interviews will be conducted with FP providers and MOH decision-makers on the acceptability of extending SP intervals to four months. Should the resulting data support a 4-month reinjection interval, the team will seek changes in the WHO Selected Practice Recommendations (SPR) and country family planning guidelines.

Activities, accomplishments, and challenges in past 6 months: Data cleaning, coding, and assessment for the primary effectiveness analysis concluded in Oct. 2020. Draft tables, figures, and listings were generated in Nov. and Dec. 2020. Primary manuscript writing began in Jan. 2021. A results dissemination meeting was held with site investigators on Feb. 2, 2021. Participant follow-up in the extended follow-up (return to ovulation) sub-study was completed in Dec. 2020. The extended follow-up subset MPA data were received from PPD in Feb. 2021.

Plans for the next 6 months: Results will be presented to USAID in Apr. 2021. High-level results will be shared with CIFF and the Gates Foundation. Primary manuscript writing will continue through spring 2021 with the goal of submitting in May 2021.Open data submission activities will begin in the fourth quarter of 2021. Preparation of the clinical study report will occur with target completion by Oct. 2021.

The extended follow-up subset EE/ENG/norgestrel data are expected to be available from PPD in May 2021. Data cleaning and statistical analyses of the extended follow-up dataset will be completed in the third quarter of 2021. A paper on return to ovulation based on the SPE clinical data and PK/PD modeling, co-funded by CIFF and *Envision FP*, will be written and submitted for publication in the fourth quarter of 2021.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Data cleaning	•											
Primary data analysis		•	•	•	•							
Primary manuscript writing				•	•	•	•	•				
Clinical study report preparation							•	•	•	•	•	•
Open data submission											•	•
Extended follow-up cohort follow-up	•	•	•									
Extended follow-up specimen shipment and MPA/EE/ENG/norg analysis				•	•	•	•	•				
Extended follow-up data cleaning and statistical analysis							•	•	•			

Phase I Clinical PK/PD study of DMPA XT
Lead: Vera Halpern, MD

This study is being co-funded by two grants from the Bill & Melinda Gates Foundation: the Contraceptive Technology Innovation Initiative (CTII) and Advancing Priority CT Leads to Meet User Needs (CTII-2). Envision FP funds are not being used for any site activities.

Goal: Develop and receive regulatory approval for a low-cost, 6-month subcutaneous depot-medroxyprogesterone acetate (SQ DMPA) injectable contraceptive.

***Significance and Impact*:** Over 40 million women worldwide use injectable contraceptives to prevent pregnancy. In sub-Saharan Africa, more than one-third of modern method contraceptive users rely on injectable contraceptives. Depending on the formulation, currently available injectables are effective for one to three months, requiring women to return to their provider monthly, every other month or quarterly. A longer-acting injectable would facilitate use, improve continuation, possibly increase effectiveness, and provide women with greater choice. Adaptation of existing methods for novel uses is an appealing, cost-efficient approach to expedite availability of new contraceptive options.

Approach: The team will use a marketed DMPA IM formulation (Pfizer) to develop a 6-month SQ product. A partially-blinded randomized trial will be conducted to assess pharmacokinetics (PK) and pharmacodynamics (PD) of one injection of either 150mg/mL or 300mg/2mL of Pfizer's current DMPA formulation compared with two cycles of Depo-subQ 104. MPA levels and ovarian activity will be evaluated and women will be followed for up to 18 months.

Activities, accomplishments, and challenges in past 6 months: In Jan. 2021, the main study manuscript titled, "Clinical trial to evaluate pharmacokinetics and pharmacodynamics of medroxyprogesterone acetate after subcutaneous administration of Depo-Provera," was published in Fertility and Sterility. We have started drafting a secondary manuscript describing the relationship between the dose of subcutaneous of DMPA and duration of ovulation suppression, as well as the distribution of serum MPA concentrations when ovulation returns. This paper also includes PK/PD data from the Lower Dose trial, as described above.

Plans for the next 6 months: By Jun. 2021, we will submit the secondary manuscript regarding the PK/PD analysis for publication.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Main study manuscript published				•								
Secondary manuscript submission									•			

Transforming postpartum IUD (PPIUD) insertion
Lead: Markus J. Steiner, PhD

Goal: Stimulate interest and facilitate sustained postpartum IUD (PPIUD) services through registration, introduction, and evaluation of an easy-to-use PPIUD inserter.

Significance and Impact: Many women in the extended postpartum period have unmet need for contraception. Postpartum IUD insertion is safe and effective, and USAID has made investments in expanding access to such services across Africa. However, PPIUD insertion can be technically challenging, and the current copper IUD inserter cannot be used postpartum. Pregna International, Ltd. has developed and is testing a simple, inexpensive, easy-to-use pre-

loaded, pre-sterilized PPIUD inserter that could increase convenience, simplify insertion, reduce expulsions, and enhance safety. In countries where access to PPIUD services is limited, this new inserter has the potential to spark sustained interest and dramatically increase uptake.

***Approach**:* FHI 360 will provide technical assistance to Pregna in preparation for submission to obtain CE Marking, achieve UNFPA/WHO Prequalification, and qualify for USAID procurement. In discussion with USAID, after learning that over 60,000 units have been distributed to 13 countries, we have expanded the approach to include an assessment of initial experiences with the device.

Activities, accomplishments, and challenges in past 6 months: We worked with the Pregna regulatory team and Dr. Blumenthal on the UNFPA reviewer comments received Dec. 30, 2020. Pregna's written response was submitted Feb. 15, 2021 and given the wording of the questions, the team is cautiously optimistic this will be the last round of review.

When Pregna checked on the status of the UNFPA review on Mar. 23, 2021, they learned that the review would be delayed due to lack of funding to pay the external reviewers.

Plans for the next 6 months: On April 28, 2021, Pregna learned that funding has been identified and the review is proceeding. We are waiting for the final decision regarding prequalification before making further plans.

AIM 2: RESPOND TO PRODUCT-RELATED ISSUES WITH EXISTING CONTRACEPTIVE METHODS

Rapid response and proactive risk mitigation for contraceptive programs
Lead: Elena Lebetkin, MPH

This activity closed under *Envision FP* as of Sep. 2020 and further work will be implemented under Innovate FP.

Access to implant removal study
Lead: Rebecca Callahan, PhD

This activity was completed under *Envision FP* as of Sep. 2020.

Contraceptive drug-drug interactions (DDIs)
Lead: Kavita Nanda, MD

Hormonal contraceptives (HCs), when used with antiretroviral (ARV) or anti-TB drugs, may be subject to PK interactions that could lead to decreases in efficacy or increases in toxicity. WHO's updated guidance on HCs and HIV note that women taking ARVs can use all HC methods, but special consideration may be needed (Category 2) for those who use progestin-only contraceptives with certain ARVs. Since then, more data have become available and the knowledge base is rapidly changing.

Technical leadership

***Goal**:* Support efficient, consistent, and thorough study of issues related to contraceptive DDIs that will inform global and local policies.

Significance and Impact: Engaging partners working in the rapidly emerging area of contraceptive DDI research will support efficient research design and evaluation while facilitating a faster application of results to policy and practice in the field. USAID is supporting other activities in this field, and our experienced and knowledgeable technical team can provide input and technical feedback, as needed.

Approach: FHI 360 staff will engage groups currently conducting research around this topic, providing technical assistance as needed.

Activities, accomplishments, and challenges in past 6 months: All data abstraction for the systematic review paper on interactions between hormonal contraceptives and ARVs has been completed with confirmation by two reviewers.

Plans for the next 6 months: A manuscript draft will be completed by end of May 2021. We anticipate internal and USAID review in Jun. and submission for publication in Jul.

DDI Database

***Goal**:* Develop a comprehensive, evidence-based, up-to-date, publicly available online database of information on contraceptive DDIs, to be housed on FHI 360's Contraceptive Technology Innovation Exchange platform (ctiexchange.org).

***Significance and Impact**:* A centralized resource to inform clinical practice and policy specifically related to contraceptive DDIs is lacking. Such a tool would improve clinical practice across FP and disease areas, enable policy makers to strengthen guidelines to ensure that women can use the best contraceptive options given other needed treatments, and offer guidance for the design of new contraceptive and multipurpose prevention technologies.

Approach: FHI 360 has led reviews of HC DDIs for the WHO MEC for over a decade. The team's existing review of current HC products and ARVs will be updated and supplemented with other reviews of HCs interactions with anti-TB drugs, antibiotics, and anticonvulsants. Information on PK DDIs, relevant clinical data, and current guidance will be compiled into a custom online database that will allow users to easily obtain information on interactions between HC methods and non-HC drugs. Efforts to inform and update global guidelines will continue and use of guidelines will be encouraged by engaging in-country staff to promote and solicit feedback on DDI evidence and recommendations.

Activities, accomplishments, and challenges in past 6 months: The database has been maintained. No updates have been made pending completion of the HC-ARV systematic review.

Plans for the next 6 months: We will update the ARV data once the new HC DDIs with ARVs systematic review is completed.

Supporting scale-up of the hormonal IUD
Lead: Kate Rademacher, MHA

Goal: Implement and evaluate best practices in the global introduction and scale-up of the levonorgestrel intrauterine system (LNG IUS) as a highly effective method of contraception.

Significance and Impact*:* The LNG IUS is one of the most effective forms of reversible contraception available and is increasingly popular among women worldwide. The LNG IUS offers a number of advantages including reduction of menstrual cramps and blood loss, fewer side effects compared to some other hormonal methods, and possible alleviation of anemia in some populations. All of these characteristics could provide substantial benefits to women in developing countries. Recent assessments have indicated that in settings where unmet need for family planning is high, the LNG IUS could play an important role in helping to reduce unintended pregnancies and improve maternal health. To date, the high cost of the method has been a barrier to making it widely available; however, the approval of a lower cost LNG IUS by the FDA in 2015 has revitalized discussions around expanding access to this method in developing countries.

Approach*:* The team will engage in global technical leadership activities to promote the evaluation, introduction and scale-up of the LNG IUS. Note: In 2021, the nomenclature for the LNG IUS was changed to hormonal IUD to align with WHO guidance. This new term is used in the activity title and below.

Activities, accomplishments, and challenges in past 6 months: During the past six months, we made substantial progress with work related to (1) the hormonal IUD and (2) contraceptive induced menstrual changes as summarized below.

1. **Global- and country-level updates regarding the hormonal IUD**

FHI 360 continued to serve as co-Secretariat of the Hormonal IUD Access Group and supported meetings of both the Steering Committee and the Partners Group. Key activities included:

- Two Roundtable discussions were convened with Bayer and Medicines360 to discuss training resources/approaches with service delivery partners and donors. Both calls were successful and plans for future roundtable discussions are underway.
- FHI 360 continued to partner with CHAI and the PSM-GHSC on the ongoing hormonal IUD supplier landscape assessment. A Pugh matrix was completed, and five suppliers were identified to move forward for further due diligence. A progress report was provided to the Steering Committee in March.
- A global e-newsletter was launched with over 900 subscribers. FHI 360 also worked with PSM-GHSC to support the development of draft news announcements about the inclusion of the hormonal IUD in the USAID and UNFPA Catalogues; drafts are being reviewed internally.
- A national introduction and scale-up plan for the hormonal IUD for Nigeria was finalized and is currently being validated by the Federal Ministry of Health (FMOH).
- FHI 360 continued to manage content on the Access Portal website including expanding the resource library and helping co-develop a new method introduction guide.
- A draft of a refreshed global learning agenda for the hormonal IUD was developed and circulated to partners and donors for input. An outline of a draft manuscript was developed that is tentatively entitled, “Five Years Later, What Have We Learned? Implementation of a

Global Learning Agenda for the Levonorgestrel Intrauterine System" and shared with potential co-authors.

- FHI 360 co-authored a Concept Note for a new High Impact Practices (HIP) Strategic Planning Guides (SPG) focused on contraceptive product introduction and scale-up that was accepted. The HIP brief will be developed in collaboration with the EECO project and several other partners.

2. **Contraceptive-induced menstrual changes**

Approval was granted by FHI 360's IRB and the Kenya IRB (KEMRI) for the study entitled, "Pretesting of a community health worker job aid for counseling clients on changes in menstrual bleeding associated with hormonal contraception and copper IUD use," and Phase 1 of the study was completed in partnership with the Afya Uzazi project. In-depth interviewers were conducted with community health volunteers (CHVs) in Nakuru and Baringo counties, and the feedback obtained was used to revise the NORMAL tool.

With funding from *Envision FP* and R4S, FHI 360 sponsored a 2-day technical consultation on contraceptive-induced menstrual changes (CIMCs) on Nov. 17-18, 2020. Over 550 people registered from 266 organizations in 67 countries with approximately 200 participants each day. Following the meeting, a "Call to Action" was drafted and shared with USAID for review. This document includes draft research agendas for CIMCs focused on 1) measurement and indicators, 2) contraceptive R&D and biomedical research, 3) social-behavioral research related to user preferences, and 4) programmatic research. Moving forward, activities will be co-funded through Innovate FP and R4S.

A new video, "Exploring Potential 'Side Benefits' of Contraceptive Methods," was developed by FHI 360 and the John's Hopkins Center for Communication Programs. The video was co-developed by Knowledge SUCCESS and the Contraceptive Technology Innovation (CTI) Exchange and disseminated through multiple channels (including at the CIMC technical consultation and through the RHSC, FP2020, Knowledge SUCCESS, and FHI 360's global e-newsletters).

Plans for the next 6 months: FHI 360 will continue to serve as co-Secretariat of the Hormonal IUD Access Group. This will include supporting global-level and country-level coordination through both the Steering Committee and Partners Group, as well as support for hormonal IUD introduction in "first mover" countries in collaboration with CHAI and the PSM-GHSC project. FHI 360 will revise the Hormonal IUD Access Portal and related materials to reflect the new "hormonal IUD" nomenclature (note new URL: http://www.hormonaliud.org) and lead development and distribution of the quarterly e-newsletter with updates for global- and country stakeholders. The refreshed learning agenda for the hormonal IUD will be completed with input from in-country stakeholders, and a synthesis manuscript about the work of the Hormonal IUD Access Group will be written and submitted for publication (target journal is Global Health: Science and Practice). Note: it is anticipated that ongoing work on the hormonal IUD supplier landscape assessment will be supported starting later this year.

Phase 2 of the study testing the community-based NORMAL tool in Kenya will be completed. Results will be disseminated and a manuscript will be drafted and submitted for publication.

FHI 360 will also contribute to development of a HIP SPG brief focused on contraceptive product introduction and scale-up.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Serve as co-Secretariat of Hormonal IUD Access Group	•	•	•	•	•	•	•	•	•	•	•	•
Contribute to next phase of strategic options / supplier analysis in collaboration with CHAI and PSM; lead engagement with several suppliers	•	•	•	•	•	•	•	•	•			
Coordinate country-level activities related to the hormonal IUD in priority countries	•	•	•	•	•	•	•	•	•	•	•	•
Pre-test community-based version of NORMAL in Kenya; analyze and disseminate data	•	•	•	•	•	•	•	•	•	•	•	
Plan and convene a technical consultation on contraceptive-induced menstrual bleeding changes in partnership with R4S and develop/disseminate meeting report	•	•	•	•								
Contribute to development of a HIP SPG brief focused on contraceptive product introduction and scale-up							•	•	•	•	•	•

AIM 3: DEVELOP NEW METHODS TO ADDRESS METHOD-RELATED NONUSE OR FILL GAPS

Contraceptive microneedle patch

Biodegradable microneedle patch intradermal delivery (ID) systems, which are being investigated for a variety of uses, including contraception, allow for self-administration without generating sharps waste. Unlike current contraceptive patches, which remain in place, the microneedle patch is applied and quickly removed. A contraceptive microneedle patch would offer women a truly innovative, discreet option allowing simple and safe self-administration.

Development of an intradermal (ID) biodegradable microneedle patch loaded with LNG/ENG/NES *(IAA-NICHD FY17 $84,091, FY18 $50,000 & Additional funding transferred from completed projects $40,834)*

Lead: Jennifer Ayres, PhD

This activity is co-funded by core funds from USAID's Office of Population and Reproductive Health and Interagency Agreement funds from the NICHD.

Goal: Develop innovative longer-acting delivery systems, including user-initiated options, for established and alternative progestins to expand contraceptive choices.

Significance and Impact: Given the increasing popularity of progestin-only contraceptives worldwide, additional innovative options could expand choice, improve continuation, and reduce unmet need. Potential improvements include fewer side effects, health benefits, and options for self-administration of a longer-acting formulation. Biodegradable microneedle patch intradermal delivery (ID) systems, which are being investigated for a variety of uses, allow for self-administration.

***Approach**:* We are exploring several approaches to develop microneedle delivery systems to deliver different progestins over an extended duration. With *Envision FP* funds, we are exploring direct delivery of three different progestins (NES, LNG, and ENG) using modifications to Dr. Mark Prausnitz's (Georgia Tech) existing microneedle patch platform. This research is complemented by our research funded by the Gates Foundation where we are exploring the feasibility of a delivery platform for progestins that involves incorporating ENG-loaded biodegradable microspheres or polymer-coated drug particles into biodegradable microneedle patches. The focus of our *Envision FP* work to date has been on the delivery of LNG. A variety of polymer compositions for the microneedles will also be explored to control release and optimize duration. We will select microneedle patch formulations to advance into *in vivo* testing in rats under *Envision FP* to characterize release, refine the formulation and provide proof-of-concept; preliminary results for LNG-loaded microneedles have been obtained.

Activities, accomplishments, and challenges in past 6 months: Georgia Tech analyzed data collected during a placebo study that evaluated 18 patch designs of varied needle size, needle density, and patch size. The manuscript for this study is in progress and has been delayed as the author is no longer working at Georgia Tech. Georgia Tech continued the development and optimization of a 1-month ENG patch, which will be evaluated in a rat PK study after formulation optimization to improve detachment efficiency and increase drug loading. Georgia Tech also improved the process for making core-shell microneedles to reduce the initial burst, designed larger patches to increase drug loading, designed experiments to evaluate the effects of gamma sterilization on MNPs, and continued optimization of rapid detachment mechanisms to support the development of prototype roller patch designs. In addition, they began developing and optimizing processes for casting MNPs by nano-dispensing precise quantities of the casting solution into each microneedle tip individually.

Plans for the next 6 months: Georgia Tech will finish the manuscript summarizing the results of the placebo study. They will continue optimization of the 1-month ENG patch to increase drug loading and detachment efficiency before evaluating formulations in a 1-month rat PK study. Although LNG is the lead candidate for future development, ENG is being considered as a back-up, and ongoing activities with ENG will provide information on how API structure and solubility affect microneedle properties and release characteristics. Efforts to reduce the initial burst and increase the duration of release will continue with a focus on the core-shell design that has yielded promising results. Georgia Tech will also continue optimization of larger patch designs and rapid detachment mechanisms and initiate experiments to evaluate the effects of gamma sterilization on prototype MNPs.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Analyze data from placebo study and draft manuscript	•	•	•	•	•	•	•	•				
Optimize 1-month ENG patch	•	•	•	•	•	•	•	•				
Rat PK study to evaluate 1-month ENG patch								•	•			
Optimize 3-6 month LNG patch to reduce initial burst and increase duration of release	•	•	•	•	•	•	•	•	•			
Conduct *in vitro* release studies for 3-6 month LNG patch	•	•	•	•	•	•	•	•	•			
Optimize 3-6 month LNG patch for human dosing	•	•	•	•	•	•	•	•	•			
Develop processes for nano-dispensing into MN molds				•	•	•	•	•	•			
Evaluate the effects of gamma sterilization on MNPs							•	•	•			

Assessing user preferences for the design of a contraceptive microneedle patch *(IAA-NICHD FY16 $159,090)*

Leads: Rebecca Callahan, PhD and Aurelie Brunie, PhD

This activity was co-funded by core funds from USAID's Office of Population and Reproductive Health and Interagency Agreement funds from the NICHD.

Goal: Assess potential user acceptability of and design preferences for contraception administered by microneedle patch technology.

Significance and Impact: To date, microneedle patches have been primarily studied in the context of vaccine administration, drug/blood chemistry level monitoring, and for pediatric use. A series of acceptability studies with potential end-users including adults, health care providers, and children indicate that this technology is largely acceptable based on the microneedle patch characteristics of minimal pain, ease of use, reduced risk of needle stick, and potential for self-administration. There are also potential cost-efficiencies if microneedle patches are widely produced, used, and effective. Microneedle patches have been described as an attractive option for use in remote and low-resource settings worldwide, given low provider training requirements and reduced need for refrigeration.

To complement *Envision FP*'s work to develop a contraceptive microneedle patch, FHI 360 will also conduct research to understand preferences of users – both contraceptive clients and providers – for key product attributes (e.g., usability, size, wear time, pain, disposal). The technical specifications of a contraceptive microneedle patch are still to be determined, which makes this an ideal time to explore user preference and to incorporate these into the product design. The primary objective of this study is to assess acceptability of a microneedle patch for contraception, particularly in resource-poor settings, to ensure uptake of the technology. The data generated through this study will provide critical, end-user input to guide the development of a microneedle patch technology for relatively painless, easy, and cost-effective delivery of contraception.

Approach: We will use a mixed methods approach to assess the feasibility and acceptability of using microneedle patch technology for delivery of contraceptive agents. This will involve using qualitative research methods and use a discrete choice experiment survey to: (1) explore initial acceptability of the microneedle patch for contraceptive delivery and potential barriers to use among prospective end-users and providers; (2) define desired qualities or characteristics of a microneedle patch for contraceptive use; and to (3) quantify the relative importance of various contraceptive microneedle patch attributes to potential end-users of.

Activities, accomplishments, and challenges in past 6 months: The second study manuscript was published in BMC Reproductive Health in Mar. 2021, Optimizing the design of a contraceptive microarray patch: a discrete choice experiment on women's preferences in India and Nigeria. Quantitative data have been posted as planned to the Harvard Dataverse and USAID DDL. This activity is complete.

Development of biodegradable contraceptive implants
Lead: Jennifer Ayres, PhD

This activity is currently being co-funded by a grant from the Bill & Melinda Gates Foundation: Advancing Priority CT Leads to Meet User Needs (CTII-2). The prior Gates Foundation Contraceptive Technology Innovation Initiative (CTII) grant provided funding as well. There was a funding shortfall for the Biodegradable Implant (BDI) program which slowed project progress. USAID support leveraged primary Gates funding and helped to bridge select activities between the CTII and CTII-2 grants. In Year 5 of Envision FP, USAID provided additional funds to continue support for ongoing BDI activities, supplementing activities funded by the current CTII-2 grant.

Goal: Advance the development of a biodegradable contraceptive implant (BDI).

Significance and Impact*:* Contraceptive implants are ever more popular in countries where they have been made increasingly available because of the Implant Access Program and the 2012 volume guarantee. However, currently available implants require removal either at the end of their efficacy period, or when a user decides to stop using the method. A biodegradable implant would not require removal thus reducing the burden for users, avoiding any access to removal issues, and potentially contributing to lower healthcare infrastructure costs, an important advantage in resource-constrained settings.

The biodegradable implants we are designing will be of intermediate duration (18 to 24 months), longer than contraceptive injectables, but shorter than other long-acting methods such as IUDs and current implants, be removable for up to 12 months, and have a short (<6 months) period at the end of the efficacy period until fertility returns (the tail). The design and intermediate duration of efficacy will provide a new and innovative contraceptive option for women. Biodegradability will obviate the burden of seeking and undergoing implant removal, while the option for removability up to 12 months after insertion would allow women the flexibility to remove the implant early due to side effects or a desire to become pregnant.

Approach: FHI 360 is collaborating with Dr. Mark Saltzman at Yale University to develop a LNG-containing implant using a novel copolymer comprised of two

monomers, pentadecalactone (PDL) and dioxanone (DO). This approach was previously initiated under funding from USAID APS (AID-GPO-A-00-10-0060) and transferred to CTII once the USAID funding ended. Year 5 activities focused on continued development of the biodegradable implant with the novel copolymer developed by Yale.

Activities, accomplishments, and challenges in past 6 months: With CTII-2 funding, we initiated a 2-year rat PK study to evaluate release kinetics for both coated and uncoated core-shell implants. The final BDI formulation will have a biodegradable core; however, due to limitations in the prototype manufacturing methods, the prototypes in this PK study have a core of medical grade stainless steel. As such, the team at Yale has also continued efforts to adapt their manufacturing methods to accommodate a biodegradable core. They also evaluated the mechanical properties of monolithic BDI prototypes as a function of time in dissolution media. They have designed and started manufacturing implants for studies to evaluate the effects of polymer molecular weight, exposure to gamma radiation and storage at 40 °C on implant properties and release characteristics. The timeline for manufacturing implants for these studies was extended due to delays in procurement of LNG. With support from Envision FP, the team at Yale optimized the synthesis of poly(PDL-co-DO) and synthesized polymers of varying molecular weight. They also designed a study to characterize implant degradation in vitro and in vivo. FHI 360 began drafting the pre-IND briefing package to request feedback on the planned toxicology studies. The briefing package is based on a preliminary toxicology assessment performed for poly(PDL-co-DO) with CTII-2 funding. Revisions made to the toxicology assessment extended the timeline for submission of the pre-IND package, which is now scheduled for May 2021.

Plans for the next 6 months: With CTII-2 funding, we will continue ongoing studies to characterize *in vivo* PK, *in vitro* release, polymer degradation and mechanical properties of implant formulations. The team at Yale will complete manufacture of implants and initiate studies to evaluate terminal sterilization (radiation), stability, and accelerated dissolution conditions. With support from *Envision FP*, we will finish preparing and submit the pre-IND briefing package and then establish plans for IND-enabling toxicology studies based on FDA feedback. Yale will also initiate activities to characterize implant degradation, *in vitro* and *in vivo*. Under FHI 360's new Innovate FP award from USAID, we will initiate activities intended to accelerate the ongoing work funded by the BMGF and *Envision FP*. Please refer to the Innovate FP Year 1 Workplan for details.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Funded by CTII-2												
• Complete manufacture of implants for rat PK study	•	•										
• Conduct rat PK study		•	•	•	•	•	•	•	•	•	•	•
• Characterize *in vitro* release, polymer degradation and mechanical strength for implant formulations	•	•	•	•	•	•	•	•	•	•	•	•
• Evaluate multiple accelerated dissolution assays								•	•	•	•	•
• Evaluate effects of terminal sterilization (radiation) on implant formulations							•	•	•	•	•	•
• Initiate preliminary stability evaluation							•	•	•	•	•	•
Funded by *Envision FP*												
• Prepare and submit briefing package to the FDA	•	•	•	•	•	•	•	•				
• Establish plans for IND-enabling toxicology studies										•	•	
• Optimize polymer synthesis				•	•	•	•	•	•	•		
• Characterize implant degradation, *in* vitro and *in* vivo									•	•		

PROJECT MANAGEMENT AND MONITORING & EVALUATION

In an effort to ensure that *Envision FP* project activities are completed on time and within budget, FHI 360 has a centralized hub of operations for project management as well as monitoring & evaluation. These functions work together to serve as a feedback loop for the status of individual activities in support of project planning and reporting requirements as well as to identify opportunities for learning and project efficiency.

Project management
Lead: Amanda Troxler, BA

Project management support is provided at both the specific activity and overall project levels. *Envision FP* project management staff are responsible for ensuring that all reporting requirements to USAID are met and serves as a liaison between USAID and the activity-level project managers, communicating issues related to timeline and budget.

Monitoring and evaluation
Lead: Amanda Troxler, BA

The monitoring and evaluation (M&E) staff focus on implementing the Performance Monitoring Plan (PMP) in close collaboration with project management, the full team, and USAID. The M&E approaches include the indicators, outcome mapping, learning, and evaluation, and builds on

what was developed and implemented for the CTI Initiative. M&E staff also assist with the Key Results Reporting, Management Reviews and regular reporting, coordinating closely with the project management team.

OTHER ACTIVITIES AND INTERAGENCY AGREEMENTS (IAAS)

The *Envision FP* team also manages the following portfolio of activities supported through additionally obligated funds and Interagency Agreements:

Technical Assistance for FP-HIV Integration (GH-C-POP FY15 $90,000)
Lead: Irina Yacobson, MPH

Activities, accomplishments, and challenges in past 6 months:

FP/PrEP integration job aid

- We have revised the job aid based on the comments from both providers in Kenya USAID experts. Based on the feedback from Kenya, we split the tool in two distinct parts to accommodate different models of FP/PrEP integration (the one where FP providers counsel about PrEP and help women to make informed choice to use PrEP, but refer to another provider for PrEP initiation, and one where FP providers can offer a full range of PrEP services).
- The revised draft was provided to USAID; currently, USAID is seeking WHO input/approval of the job aid.
- One of the challenges was that it took longer than expected to get comments back from all the experts due to the competing priorities they had because of the COVID-19 pandemic.

FP/HIV integration tool

- An informal desk review of the provider tools in support of integration, which are mostly limited to counseling flipcharts, was conducted.
- A series of discussions with FP/HIV integration experts at USAID was held to better understand the needs among HIV providers in the field (based on the experiences USAID missions had). The process was also informed by the results of our FP/HIV integration assessment in Namibia.
- The first draft of the tool is being conceptualized based on USAID expressed need to have a tool that addresses the needs of clients based on their life stage and in various HIV settings (HIV counseling and testing services, HIV treatment and care services, PMTCT, etc.)
- Rapid assessment in the field was not possible due to the COVID-19 restrictions.

Plans for the next 6 months:

FP/PrEP integration job aid

- Incorporate WHO comments (and any additional comments from USAID staff and finalize the FP/PrEP integration job aid

FP/HIV integration tool

- Compete the first draft of the FP/HIV integration tool and circulate to USAID (and possibly other experts for review.
- If situation with COVID-19 will allow, solicit the feedback from selected providers in the field (scaled down version of field-testing).
- Incorporate the feedback from all the reviewers and finalize the tool (this may require more than one round of revisions).

Longitudinal study of LARC acceptors in Senegal
Lead: Marga Eichleay, MPH

Goal: To better understand the factors related to LARC continuation in low resource settings in order to provide guidance that will improve routine family planning service delivery.

Significance and Impact: Long-acting, reversible contraceptives (LARCs) including subdermal implants and intrauterine devices (IUDs) have begun to show their potential to radically change voluntary family planning (FP) in Africa. LARCs have taken on greater importance in the contraceptive method mix in many countries, with implants in particular seeing marked increases in users. While failure rates of LARCs are low, discontinuation is an important concern that can leave women vulnerable to pregnancy if they do not adopt another method. Effectively meeting the current (and increasing) demand for LARCs requires responsive and effective strategies to ensure expanded access as part of a broad method mix that also includes related services such as follow-up, management of side effects and removals. There is a dearth of information--from the client's point of view—on how to help women effectively manage side effects associated with LARCs and on how service delivery factors may affect a decision to continue or discontinue the method. Enhanced understanding of these factors and their interplay is important, as it could inform guidelines and approaches to routine service delivery.

Approach: This longitudinal study of long-acting, reversible contraceptive users began as part of a five-year, USAID-funded project implemented by Marie Stopes International (MSI) and its partners, one of whom was FHI 360. Referred to as the SIFPO (Support for International Family Planning and Health Organizations) 2 project, the goal was to deliver high quality family planning services at scale by providing access to and expanding method choice globally. Funding from MSI was discontinued prior to project completion; however, the project received funding through *Envision FP* beginning in March 2018. Under *Envision FP*, the study goal and focus remained the same as the initial SIFPO2 funding. The quantitative component consists of surveys of LARC acceptors who will be interviewed at service delivery sites, then re-interviewed 1, 3, 6 and 12 months after accepting an implant or an IUD. The qualitative component will include formative cognitive interviews and mid-term in-depth interviews (IDIs) with a subset of survey participants reporting experiences with side effects. The formative cognitive interviews will be conducted prior to the beginning of the survey activities to refine the latter's content and development. This process is expected to result in surveys that not only capture the information needed, but in a way that reflects participants' understanding and experiences with LARC methods. The mid-term interviews will be conducted after the six-month survey

follow-up to provide richer details and a deeper understanding of women's experiences coping with side effects.

Activities, accomplishments, and challenges in past 6 months: The manuscript was submitted to the Journal of International Perspectives on Sexual and Reproductive Health. However, the journal closed Dec. 2020 and the manuscript was withdrawn.

Plans for the next 6 months: The team will submit the manuscript to Frontiers in Global Women's Health by Jun. 2021.

ECHO continuation
Lead: Rebecca Callahan, PhD

Goal: To assess contraceptive experience, including method continuation and access to removal services, among a subset of women exiting the ECHO trial.

Significance and Impact*:* The ECHO study offers a rare opportunity to follow a relatively large cohort of women using long-acting reversible contraceptive (LARC) methods and DMPA in Sub-Saharan Africa, for which continuation rates are extremely limited, especially beyond one year of use. Similarly, little is known about LARC users' access to and experiences with method removal. Most of the women exiting ECHO will have been using their method for 12-18 months in the context of the trial. Following them after study exit will allow for documentation of method experience beyond one year.

Approach*:* This is a prospective observational longitudinal study including a phone survey at 6 and 12 months with a sample of women who have exited the ECHO trial in South Africa and Zambia. The study will be conducted in collaboration with MatCH Research Unit (MRU) of the University of the Witwatersrand in South Africa and the University of North Carolina (UNC) Kamwala Research Clinic in Zambia. The primary study objective is to document contraceptive status over at least 12 months following exit from the ECHO trial and measure method-specific and overall continuation rates. Secondary objectives are to describe reasons for contraceptive discontinuation and to describe implant and IUD removal outcomes, including success or failure at obtaining removal and number of removal attempts. Additionally, to delve deeper into decisions around continuation/discontinuation and experience accessing LARC removal, sites will conduct 12-15 in-depth interviews during the second year of data collection.

Activities, accomplishments, and challenges in past 6 months: The two South African sites and the UNC Kamwala site in Zambia have completed participant follow-up through 24 months as well as an additional survey module assessing the effect of the COVID-19 pandemic on contraceptive access and use. Follow-up was largely successful with a few unreachable due to phone number changes or no response. The South African sites have completed all stakeholder and participant qualitative interviews, which included questions on access and challenges to removal, and questions on how the COVID pandemic impacted family planning and contraceptive services. The Zambia site has completed the stakeholder interviews, and participant interviews will be complete by the end of Apr. 2021. Data analysis is in progress for both the survey and qualitative components. During the reporting period the study team

presented a poster at the R4P conference describing HIV testing frequency by contraceptive method. The team also prepared and submitted an abstract describing the main study findings to the Society of Family Planning Annual Meeting to be held in Sep. 2021.

Plans for the next 6 months: From now until end of Year 6, we will complete data collection and all analyses. We will prepare two manuscripts for publication, one describing the results of the 24-month follow-up and one describing the effects of the COVID-19 pandemic on FP access and use. We will complete all study close-out activities.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 – September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Final Month 24 interviews	•	•										
COVID-19 survey data collection	•	•	•	•	•	•						
COVID-19 qualitative interviews with women and providers	•	•	•	•	•	•	•					
Survey data cleaning and analysis				•	•	•	•	•				
Qualitative analysis				•	•	•	•	•				
Study site close-out activities								•	•			
Report/manuscript writing								•	•	•	•	•

Evidence for contraceptive options and HIV outcomes (ECHO) Study *(GH-C-POP FY16 $1,250,000, FY17 $3,850,000; OHA FY16 $2,500,000, FY16 $280,000 (transfer), FY17 $1,250,000)*

Lead: Tim Mastro, MD, DTM&H (as co-PI)

This study was co-funded by the Bill & Melinda Gates Foundation.

***Goal*:** To evaluate whether there is a link between use of hormonal contraception and increased risk of acquiring HIV infection.

***Significance & Impact*:** As the HIV epidemic spread, it became important to explore risk factors for HIV, and particularly whether there was an association between use of specific contraceptives and HIV acquisition. A number of observational studies have examined this issue. Some of these studies suggest that injectable methods, particularly DMPA, might increase a woman's risk of acquiring HIV infection, while other studies show no association. The lack of definitive data from observational studies makes it difficult to offer guidance on contraceptive use in settings where women have a high risk of acquiring HIV and where many women use progestin-only injectable methods such as DMPA, often due to limited options for contraception.

***Approach*:** Designed to address this critical evidence gap, the ECHO Study randomized women to DMPA, the copper IUD, and Jadelle to evaluate whether there is any difference in the risk of acquiring HIV infection among users of these methods. The study also compared side effects, pregnancy rates, and how well women stayed on each of the three contraceptive methods. A

total of 7,830 sexually active HIV-negative women ages 16 to 35 were enrolled across 12 study sites in four countries (Kenya, South Africa, Swaziland, and Zambia). The first participant enrolled on Dec. 9, 2015, and enrollment was completed on Sep. 12, 2017. The total duration of the study in the field was almost 35 months, and the results were published and presented on Jul. 13, 2019.

Activities, accomplishments, and challenges in past 6 months: The following four manuscripts, including one primary paper and three ancillary papers, were published:

Sexually transmitted infections among women randomised to depot medroxyprogesterone acetate, a copper intrauterine device or a levonorgestrel implant in the Journal of Sexually Transmitted Infections,

Exploring the use of pre-exposure prophylaxis among women from Durban, South Africa, as part of the HIV prevention package in a clinical trial in AIDS and Behavior,

Effects of three contraceptive methods on depression and sexual function: an ancillary study of the ECHO randomized trial in the International Journal of Gynecology & Obstetrics, and

Weight change among women using intramuscular depot medroxyprogesterone acetate, a copper intrauterine device, or a levonorgestrel implant for contraception: findings from a randomised, multicentre, open-label trial in Lancet EClinical Medicine.

Plans for the next 6 months: As manuscripts are published, they will be added to future reports.

WHO's continuous identification of research evidence (CIRE) *(IAA-NICHD FY16 $68,182, FY17 $75,000, FY18 $79,120, FY19 $77,273)*

Support is being provided to the WHO for CIRE, which facilitates the evidence gathering for the updating of WHO guidance on contraceptive use. An agreement was executed with WHO in January 2017.

Activities, accomplishments, and challenges in past 6 months: This activity ended as of Sep. 30, 2020. Agreement closeout paperwork was completed and sent to WHO.

Southern Africa method mix technical assistance (*OHA FY17 $500,000)*
Lead: Elena Lebetkin, MPH

Goal: Provide technical assistance to up to five Southern African countries to support method choice analysis and technical/advocacy efforts to foster method choice expansion.

Significance and Impact*:* In many countries with high HIV prevalence, the family planning method mix is heavily skewed to the injectable contraceptive, DMPA. In Southern Africa, namely South Africa, Namibia, Botswana, Swaziland, and Lesotho, both HIV prevalence and the use of DMPA is high. As the international community awaits the ECHO trial results, working with countries in Southern Africa to expand the method mix is important not just in terms of method choice, but also in the event that there is a link between HIV acquisition and DMPA use.

This funding presents the unique opportunity to work in Southern Africa, where family planning funding is minimal, but the need to foster method choice expansion is present.

***Approach**:* FHI 360 will work in collaboration with USAID to conduct individual country assessments in order to identify country-specific gaps in method choice and develop and implement a technical assistance plan in order to help the target countries expand method choice.

Activities, accomplishments, and challenges in past 6 months:

Botswana: After consulting with USAID/Botswana and MOH point people to determine local needs, the team provided a technical review of the existing family planning guidelines to ensure that the guidelines are up-to-date and accurate. The MOH point people reviewed and accepted changes to the guidelines and requested additional assistance formatting the document and adding provider tools as appendices. The team is currently reviewing the feasibility of formatting the document as the file was provided in a corrupt state and we need to explore our ability to complete this additional work with the budget remaining.

Lesotho: The assessment was approved by the Lesotho IRB in Nov. 2020 and the Johns Hopkins School of Public Health IRB in Jan. 2021. Data collection started in Jan. and was finalized in Mar. 2021. In Feb., the situation in Lesotho with COVID became concerning and all data collection was moved to a virtual format. Additionally, due to COVID, the timeline for the activity needed to be extended, so the contract with Jhpiego was extended until the end of Sep. to allow additional time to complete tasks safely. During data collection, the Jhpiego and FHI 360 team had weekly calls to discuss the data and FHI 360 provided real-time updates to USAID/Washington to report to the Mission.

Plans for the next 6 months: The assessment results will be presented at a local Lesotho dissemination meeting in person, COVID permitting. If an in-person meeting is not possible, a virtual dissemination event will be held. The team will develop a report of the assessment findings and potentially a manuscript for publication.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 - September 30, 2021	2020			2021								
	Q1			Q2			Q3			Q4		
	O	N	D	J	F	M	A	M	J	J	A	S
Namibia TOT		•										
Botswana – Update FP training materials and guidelines as per MOH request			•	•	•	•	•					
Lesotho – in-country assessment			•	•	•	•						
Lesotho – data analysis							•	•				
Lesotho - Country workshops/stakeholder meetings								•	•			
Lesotho - Country assessment report & manuscript								•	•	•	•	
Lesotho – Continued TA as requested			•	•	•	•	•	•	•	•	•	•

Preparing for Ring Opportunities through Market Introduction Support and knowledge Exchange (PROMISE)

Lead: Kristine Torjesen, MD/MPH

Goal: To shape the market and establish a family planning service delivery platform for future multipurpose vaginal rings (VR) through the provision of early product introduction support for the dapivirine vaginal ring (DVR). The intent is for this work to create an enabling environment for the introduction and sustainability of VR products for pregnancy and HIV prevention, such as segesterone acetate-ethinyl estradiol VR (Annovera), 90-day DVR, and dapivirine-levonorgestrel VR.

Significance: Given the high burden of unintended pregnancies and sexually transmitted infections, including HIV, among women in sub-Saharan Africa, research efforts have focused on the development and implementation of female-initiated drug-delivery methods, such as the VR, particularly for low- and middle-income countries (LMIC). Improving options for prevention products in sexual and reproductive health is critical to address women's diverse and dynamic preferences. Yet access to currently approved VRs is limited in LMIC, primarily due to high product cost and lack of investment in their market introduction in these countries. VRs remain a relatively unfamiliar formulation to most women in LMIC. Pending regulatory approval, IPM's dapivirine ring for HIV prevention will be the first VR to be primarily marketed in sub-Saharan Africa. This presents a market shaping opportunity to build awareness, acceptance, and demand for VRs as an additional method choice to meet women's sexual and reproductive health needs, as well as a health systems opportunity to strengthen family planning services to support VR delivery. Successful market introduction of the DVR will pave the path for accelerated introduction and uptake of future VR products in sub-Saharan Africa, including longer-acting and MPT VRs for both contraception and HIV prevention.

Approach: Work will be conducted over 18 months by a consortium of partners, across five countries prioritized for regulatory approvals and early introduction efforts. Partners may include: AVAC, Avenir Health, LVCT Health, Afton Bloom, University of Washington and Wits RHI. The geographic focus of this work will be in South Africa, Kenya, Uganda, and Malawi. The work will be conducted in close collaboration and coordination with the International Partnership for Microbicides (IPM), who are the market authorization holder for the DVR, as well as the product developers of the dapivirine-levonorgestrel VR currently in Phase 2 trials.

Activities, Accomplishments, and Challenges in past 6 months:

Activity 1: PROMISE finalized the Dapivirine Ring Global Action Plan in Dec. 2020 and is currently carrying out an update to reflect progress over the past quarter. Key informant interviews were conducted to complete the value chain situation analysis for integrated and differentiated delivery models for the ring in South Africa and Kenya (final analyses to be generated in April 2021) and the Ring Introduction Matrix (produced in 2019 under OPTIONS) was updated. A Willingness to Pay/Normative Costing study protocol (for implementation in Kenya) was developed, received ethical approval, and data collectors trained. The goal of the study is to provide information to key decision-makers about the costs that will be associated with the introduction and scale-up of the ring. Global stakeholder interviews were conducted to help shape the costed rollout plan resource guide, which will provide a framework to

countries as they move forward with creating implementation plans for the ring. Work on converting PrEP-it from an excel- based tool to a web-based tool and incorporating multiple delivery modalities ("method mix") continues. PrEP-it has been beta tested by several users throughout the period of performance to ensure optimal functionality. Finally, a manuscript was developed highlighting how learnings from oral PrEP introduction and scale-up can be leveraged to prepare for ring delivery (to be submitted in May).

Activity 2: Mission concurrence to work in Zambia was received in Dec. 2020 and conversations about the ring with national technical working groups (TWGs) and the MOH were carried out in each PROMISE country. The first Ring Learning Collaborative (RLC) regional meeting was launched (virtually) with over 65 participants. The RLC brings together key global and national stakeholders such as government policymakers, implementers, civil society, and donors from South Africa, Kenya, Zimbabwe (via CHOICE, a sister project to PROMISE), and Zambia. The RLC provides a space for the co-creation of policy language and implementation plans, the identification of cross-cutting issues, and a discussion of implementation needs and service delivery mechanisms appropriate for the dapivirine vaginal ring. A concept and discussion guides to conduct stakeholder dialogues (with AGYW, health care providers and community members) across the PROMISE countries was submitted for a non-research determination with the FHI 360 ethics board. These dialogues aim to provide an in-depth understanding of the stakeholder perspective on what is needed to introduce the ring alongside oral PrEP, with an eye toward inclusion of additional prevention methods such as CAB-LA for women. An expert panel was convened to review evidence on simultaneous use of the ring and oral PrEP to inform future implementation studies and messaging and guideline recommendations on simultaneous use (a report out of this consultation was produced in Dec. 2020). National guideline template language for the dapivirine ring has been drafted in collaboration with USAID and IPM.

Activity 3: A demand creation desk review has been conducted in South Africa and Kenya exploring the national HIV prevention and FP demand creation strategies, programs and tools used by stakeholders in each country. Content modifications for the adaptation of the HIV Prevention Ambassador Training and the development of the standard framework and tools to support countries to integrate new HIV prevention products into FP and HIV prevention demand creation activities are underway. Advocacy workshops were held in Zimbabwe and Kenya to inform the advocacy messaging framework and advocacy tools/materials that will be designed for local adaptation. Finally, a concept for story mapping project (to be carried out in collaboration with IMPT) is in development and has preliminary USAID approval. This activity will support an enabling environment for female-initiated HIV prevention and FP choices.

Activity 4: PrEPWatch has been updated fully integrate the dapivirine ring content throughout the PrEPWatch site. In addition, the first two quarterly ring newsletters have been released. The PROMISE team completed the PROMISE Learning Session Experience brief which succinctly summarized the impact and outputs of the PROMISE-hosted capacity building sessions on the dapivirine ring.

Challenges the PROMISE team have faced this period have largely been due to the COVID-19 pandemic, resulting in difficulty setting up key informant interviews (due to MOH priorities and time limitations) and having in-person interactions for the Ring Learning Collaborative and other activities that would benefit from face-to-face collaboration. In addition, lack of

regulatory approval for the ring in PROMISE countries has slowed movement on ring introduction overall.

Plans for the next 6 months:

Activity 1:

- Value chain situation analyses for all PROMISE countries will be finalized, and carried out in additional, to be determined, countries.
- Costed rollout guide will be developed, applied in 2-3 PROMISE countries and application report out produced.
- PrEP-it 2.0 will be finalized and launched.
- Willingness to Pay/Normative Costing data collection will be completed. Data analysis in progress.
- Dapivirine Vaginal Ring Global Action Plan will be updated, as needed.

Activity 2:

- Two additional Ring Learning Collaborative regional meetings will be conducted with learning collaborative participants engaged throughout the period of performance via virtual mechanisms.
- Stakeholder dialogues will be conducted in the PROMISE countries and data analyzed.
- Dapivirine ring national guideline template will be finalized.
- Manuscript on how to leverage oral PrEP for ring introduction will be submitted to *Current HIV/AIDS* Report for review.

Activity 3:

- Demand creation framework and tools to support countries to integrate new HIV prevention products into FP and HIV prevention demand creation activities will be completed.
- Advocacy messaging framework and package of advocacy tools will be produced for local adaptation.
- Plan 4 Ring Toolkit will be developed and fully integrated into PrEPWatch.
- Ring adaptation of the HIV Prevention Ambassador Training will be finalized.
- South Africa story mapping project (in collaboration with IMPT) will move forward once approved by USAID.
- PrEP Journey Tool (to support PrEP decision-making) will be developed and launched for national adaptation.

Activity 4:

- Research/resource utilization plans for completed tools and resources will be developed and implemented.

Year 6 Implementation Timeline

Envision FP Year Six Work Plan October 1, 2020 - September 30, 2021	2020			2021								
	Q5			Q1			Q2			Q3		
	O	N	D	J	F	M	A	M	J	J	A	S
Service delivery channels strategy	•	•	•	•	•	•	•	•	•	•	•	•
National planning and programming	•	•	•	•	•	•	•	•	•	•	•	•
Demand creation and market shaping	•	•	•	•	•	•	•	•	•	•	•	•
Knowledge management	•	•	•	•	•	•	•	•	•	•	•	•

Appendix 1: Year 6 Budget and Expenditures through March 2021

See attached.