AWARD NUMBER: W81XWH-18-1-0672

TITLE: Phase 1/2b Testing of the *Sm*-TSP-2 Schistosomiasis Vaccine in Uganda

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REPORT DATE: October 2020

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2020	Annual Report	30Sep2019 – 29Sep2020

4. TITLE AND SUBTITLE
Phase 1/2b Testing of the *Sm*-TSP-2 Schistosomiasis Vaccine in Uganda

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-18-1-0672

5c. PROGRAM ELEMENT NUMBER

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5d. PROJECT NUMBER
0011192998

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES)
THE GEORGE WASHINGTON UNIVERSITY
1922 F Street NW
4th Floor
Washington, DC 20052

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
The Project goal is to perform a Phase I/IIb clinical trial to evaluate the safety and immunogenicity of the *Sm*-TSP-2/Alhydrogel® schistosomiasis vaccine in Ugandan adults and obtain preliminary data on proof-of-efficacy. Specific Aims are to: (1) Assess the safety and immunogenicity of the *Sm*-TSP-2/Alhydrogel® vaccine with or without AP 10-701 (a synthetic Toll-like Receptor-4 agonist) in individuals living in areas of Uganda endemic for S. *mansoni* and *S. haematobium*; (2) Compare the incidence and intensity of reinfection with *S. mansoni* at 12 and 18 months following vaccination with *Sm*-TSP-2/Alhydrogel® *vs*. the licensed Hepatitis B Virus (HBV) vaccine as a comparator; (3) Assess the cellular immune response to vaccination with *Sm*-TSP-2/Alhydrogel®. The study will be done in two parts. Part A will be a randomized, double-blind, controlled, dose escalation Phase I trial in 90 healthy Ugandan adults aged 18-45 years to test 3 doses (10 mcg, 30 mcg and 100 mcg) of the vaccine, with or without AP 10-701. In each cohort of 30 people, 12 will receive the *Sm*-TSP-2 vaccine alone, 12 will receive the *Sm*-TSP-2 vaccine mixed with AP 10-701, and 6 will receive the control HBV. Subjects will receive 3 intramuscular injections on Days 0, 56 and 112 and will be followed for 9 months after final injection. Part B will compare 100 people vaccinated with *Sm*-TSP-2 (dose/formulation determined in Part A) to 100 people vaccinated with HBV. Part B subjects will receive 3 intramuscular injections administered at 2-month intervals. After final vaccination, urine and stool samples will be collected at 12 and 18 months after the 3rd injection to determine rates of new schistosome infections. The primary endpoint is to determine if vaccination prevents infection with the schistosome worm as determined by schistosome worm eggs found in feces or urine. Additionally, other outcomes include studying the antibody responses to *Sm*-TSP-2.
The project will have significant impact on vaccine development for schistosomiasis that could protect U.S. Service members against infection by this parasite.
Progress to date in the current reporting period consists of initiation and completion of recruitment, screening, enrollment and vaccinations of Cohorts 1 and 2 in Part A of study; completion of recruitment and screening of Cohort 3 in Part A, and enrollment and vaccination of 27/30 participants in Cohort 3. Completion of enrollment and vaccinations in Cohort 3 in Part A will be in the beginning of Year 3 of the Project. Of note, enrollment in Cohort 3 was suspended from Mar-July2020 due to COVID-19 restrictions. An interim safety and immunogenicity analysis will occur once all Part A subjects have completed Day 140 of the study to determine which vaccine dose/formulation will be tested in Part B. The interim analysis will occur in Year 3 of the project. Initiation of recruitment, screening and enrollment in Part B of the study will be in Year 3 of the Project after the interim analysis is completed.

15. SUBJECT TERMS
Schistosomiasis; *Schistosoma mansoni*; Vaccine; *Sm*-TSP-2; Tetraspanin-2; Uganda

16. SECURITY CLASSIFICATION OF:			17. LIMITATION	18.NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified	29	

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1 INTRODUCTION

Schistosomiasis is the most important parasitic infection after malaria. Acute infection can result in significant illness and death in the form of Katayama fever, whereas chronic infection can lead to life-threatening complications such as portal hypertension (*S. mansoni*) or bladder obstruction, kidney failure, and bladder cancer (*S. haematobium*). The goal of this proposal is to perform a Phase I/IIb clinical trial to evaluate the safety and immunogenicity of the *Sm*-TSP-2/Alhydrogel® schistosomiasis vaccine in African adults for the first time and obtain preliminary data on proof-of-efficacy. *Sm*-TSP-2/Alhydrogel® has been tested in a first-in-human Phase I trial in schistosomiasis-unexposed adults in the U.S. In November 2017, a second Phase I trial was initiated in adults living in a region of Brazil where *S. mansoni* is endemic; this study was completed in March 2020 and analysis of safety and immunogenicity results from this trial are underway. *The next essential step in its clinical development is to test* Sm-*TSP-2/Alhydrogel*® in areas of Africa where both *S. mansoni* and S. haematobium *are endemic*.

2 KEYWORDS

Schistosomiasis; *Schistosoma mansoni*; Vaccine; *Sm*-TSP-2; Tetraspanin-2; Uganda

3 ACCOMPLISHMENTS

3.1 Major goals of the project

The **Specific Aims** of the project, as listed in the approved SOW for the grant, are to:

(1) Assess the safety and immunogenicity of the *Sm*-TSP-2/Alhydrogel® vaccine with or without AP 10-701 (a synthetic Toll-like Receptor-4 agonist) in individuals living in areas of Uganda endemic for S*. mansoni* and *S. haematobium*;
(2) Compare the incidence and intensity of reinfection with *S. mansoni* at 12 and 18 months following vaccination with *Sm*-TSP-2/Alhydrogel® *vs*. the licensed Hepatitis B Virus (HBV) vaccine as a comparator;
(3) Assess the cellular immune response to vaccination with *Sm*-TSP-2/Alhydrogel®.

The **Major Tasks** and **Subtasks** of the project are as follows:

Major Task 1: Obtain IRB and Regulatory Approvals for Phase I/II Clinical Trial
Subtask 1: Prepare & Submit Clinical Protocol and Associated Documents for Ethical Committee Review
Subtask 2: Submit Clinical Protocol and Associated Documents for Regulatory Review
Subtask 3: Import Study Vaccine Supplies into Uganda from U.S.

Major Task 2: Train MUWRP Study Staff for Clinical Trial
Subtask 1: Coordinate with MUWRP for Training of Study Staff

Major Task 3: Study Part A (Phase I) Participant Recruitment, Vaccination, and Follow-up
Subtask 1: Conduct Part A of Clinical Trial
Subtask 2: Determine *Sm*-TSP-2/Alhydrogel dose and formulation to be tested in Phase II
Subtask 3: Complete follow-up assessments up to 9 months post-final vaccination

Major Task 4: Study Part B (Phase II) Participant Recruitment, Vaccination, and Follow-up
Subtask 1: Conduct Part B of Clinical Trial

Major Task 5: Laboratory and Data Analyses (Product Stability Testing)
Subtask 1: Conduct stability testing of *Sm*-TSP-2 Drug Substance & *Sm*-TSP-2/Alhydrogel vaccine

Major Task 6: Laboratory and Data Analyses

Subtask 1: Complete resolution of database queries
Subtask 2: Ship biological specimens from MUWRP to GWU for analysis
Subtask 3: Conduct immunological analyses
Subtask 4: Conduct parasitological analyses on biological specimens collected from study subjects
Subtask 5: Conduct data and statistical analyses

Major Task 7: Report Findings
Subtask 1: Complete Clinical Study Report
Subtask 2: Disseminate findings (abstracts, presentations, publications)

3.2 Accomplishments under these goals

Overall, by the end of the project Year 2 annual reporting period, enrollment and vaccinations had been completed for Cohorts 1 and 2 of study Part A. Enrollment of Cohort 3 of study Part A had been initiated in March 2020 but had to be suspended after only 3 of 30 participants were enrolled due to restrictions on clinical trial activities imposed by the Ugandan government due to COVID-19. Enrollment was re-started in July 2020 after easing of these restrictions, but screening had to be re-opened due to some previously screened volunteers no longer being available for the study. This required shipping additional screening serum samples from the study site in Kampala to George Washington University, Washington, DC, for anti-*Sm*-TSP-2 IgE antibody testing (completed in September 2020). Screening for the remainder of Cohort 3 enrollment was completed in September 2020, with planned completion of enrollment into Part A of the study planned for 08OCT2020.

The following were the specific accomplishments under each task during this reporting period:

Major Task 1:
- Revision of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) to incorporate minor changes based on feedback from site in Uganda as well as administrative changes noted by George Washington University (GW)
- Submission of version 4.0 of the clinical trial protocol to the GW IRB (October 2019)
- Approval of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) by the GW IRB (November 2019)
- Submission and approval of version 1.0 of the clinic appointment cards to the GW IRB (November 2019)
- Revision of the informed consents and assessment of understanding form for study TSP-18-03 (updated to version 2.0) to incorporate minor changes based on feedback from site in Uganda
- Submission of informed consents (including translations) and assessment of understanding form to the GW IRB (December 2019)
- Approval of the amended study Part A data collection forms (version 8.0), clinic appointment cards (version 1.0) by the local Ugandan IRB (Makerere University School of Public Health - MUSPH) (October 2019)
- Submission of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) by the MUSPH IRB (November 2019)
- Approval of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) by the MUSPH IRB (December 2019)
- Submission of informed consents (including translations) and assessment of understanding form (updated to version 2.0) to the MUSPH IRB (December 2019)
- Submission of the version 1.0 of the clinic appointment cards to the national Ugandan IRB (the Uganda National Council for Science and Technology – UNCST) (October 2019)
- Submission of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) to the national Ugandan IRB (UNCST) (December 2019)
- Importation of first shipment of investigational study product from the USA into Uganda (Oct 2019)

- Submission and approval of the study Part A and B informed consent forms (including translations into Luganda) and Assessment of Understanding forms (updated to version 2.0) to incorporate minor changes based on feedback from site in Uganda by the GW IRB (January 2020)
- Submission and approval of the continuing review by the GW IRB (January 2020)
- Submission and approval of the continuing review by the MUSPH IRB (February 2020)
- Submission of the study Part A and B informed consent forms (including translations into Luganda) and Assessment of Understanding forms by the MUSPH IRB (March 2020); verbal notification of approval has been received but the official approval letter is still pending
- Acknowledgement of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) by the Ugandan national IRB (UNCST) (January 2020)
- Approval of the clinical trial protocol for study TSP-18-03 (updated to version 4.0) by the Ugandan NDA (January 2020)
- Importation of second shipment of investigational study product from the USA into Uganda (February 2020); temperature monitoring during shipment indicated a major temperature excursion to -0.2^{o}C, therefore this shipment was quarantined and disposed of according to site standard operating procedure (as directed by the sponsor)
- Submission and approval of study product importation permit by the Ugandan NDA for importation of third shipment of investigational study product from the USA into Uganda (March 2020)
- Submission of annual reporting for IND 017791 (*Sm*-TSP-2/Alhydrogel with GLA-AF by Baylor College of Medicine to the Food and Drug Administration (FDA) (January 2020)
- Submission of administrative changes to the study Part A and B informed consent forms (including translations into Luganda) and assessment of understanding forms V.2 dated 03DEC 2019 to the UNCST (national Ugandan IRB) (June 2020)
- Submission and acknowledgement of administrative changes to the study Part A and B informed consent forms (including translations into Luganda) and assessment of understanding forms V.2 dated 03 DEC 2019 to the Ugandan NDA (June 2020)
- Submission and approval of the manufacturer's (GSK) assessment on the temperature excursion of Engerix B by the Ugandan NDA (May-June 2020)
- Approval of administrative changes to the study Part A and B informed consent forms (including translations into Luganda) and assessment of understanding forms V.2 dated 03 DEC 2019 by the MUSPH IRB (May 2020)
- Submission and acknowledgement of the notification of modified participant schedules and procedures due to COVID-19 and justification for continued study activities by the UNCST (April 2020)
- Importation of third shipment of investigational study product from the USA into Uganda (May 2020); temperature monitoring during shipment indicated two temperature excursions above 8°C. These were considered minor and the Sponsor provided permission to continue using this shipment of IP.
- Importation of fourth shipment of investigational study product from the USA into Uganda (June 2020); temperature monitoring during shipment indicated two temperature excursions above 8^{o}C (11.8^{o}C and 11.4^{o}C). These were considered minor and the Sponsor provided permission to continue using this shipment of IP.
- Submission of a risk management plan for resumption of participant recruitment during the COVID-19 pandemic, which was in line with the Ugandan NDA guidelines (July 2020).
- Continuing review approval/certificate for study TSP-18-03 by the Ugandan NDA (August 2020)

Major Task 3:

- Initiation/completion of recruitment and screening for Cohort 1 of study Part A (October-November 2019)
- Initiation of enrollment for Cohort 1 of study Part A (November 2019)
- Completion of enrollment for Cohort 1 of study Part A (December 2019)

- Initiation of recruitment and screening for Cohort 2 of study Part A (December 2019)
- Finalization of Safety Monitoring Committee (SMC) charter and completion of organizing teleconference with SMC members (October 2019)
- An interim monitoring visit was completed (November 2019)
- Shipment of Investigational Product from GW to MUWRP (October 2019)
- Two oversight visits by GW project personnel were completed (October and November 2019)
- Build and release of the electronic data capture (EDC) database for Part A of the study (October-December 2019)
- Finalization of Safety Monitoring Committee (SMC) blinded interim safety summary report #1 (safety data for 7 days post-dose 1) for Cohort 1 (10 mcg dose), and completion of teleconference with SMC members (January 2020)
- SMC recommendation to continue the trial without modification and permission granted to dose escalate to Cohort 2 (30 mcg dose) (January 2020)
- Initiation and completion of Cohort 2 first vaccinations (30 subjects) (January-February 2020)
- Finalization of SMC interim blinded safety summary report #2 (safety data for 7 days post-dose 1) for Cohort 2 (February 2020)
- Completion of teleconference with SMC members (March 2020)
- SMC recommendation to continue the trial without modification and permission granted to dose escalate to Cohort 3 (March 2020)
- Initiation of enrollment for Cohort 3 (100 mcg) of study Part A; three of 30 subjects received vaccination #1 before COVID-19 restrictions were enforced in Uganda (March 2020)
- Completion of Cohort 1 second vaccinations (January 2020) and initiation of Cohort 1 third vaccinations (March 2020)
- Initiation of Cohort 2 second vaccinations (March 2020)
- An interim monitoring visit was completed (March 2020)
- Completion of configuration and test programming edit checks for study Part A EDC database (January-March 2020)
- Discrepancy management and data query resolution for study Part A database (January-September 2020)
- Continuation of recruitment and screening for study Part A – Cohort 3 (paused temporarily in mid-March due to the COVID-19 pandemic)
- Completion of Cohort 1 third vaccinations (April 2020); one of 30 subjects did not receive their third vaccination because they were two months out of window due to COVID-19 lockdown. Subject will be followed for safety.
- Completion of Cohort 2 second vaccinations (April 2020); three of 30 subjects did not receive their second vaccinations because two were incarcerated and one was more than 1 month out of window – they will not receive further vaccinations but will continue safety follow-up.
- Initiation of Cohort 2 third vaccinations (May 2020)
- Completion of Cohort 2 third vaccinations (June 2020)
- Initiation of Cohort 3 first vaccinations for three of 30 subjects that received vaccination #1 before COVID-19 restrictions were enforced in Uganda (April 2020)
- Completion of Cohort 3 second vaccinations for three of 30 subjects that received vaccination #1 before COVID-19 restrictions were enforced in Uganda (June 2020)
- An interim monitoring visit was completed (June 2020)
- Completion of the coding to export OpenClinica data extracts into separate datasets for each study form, which are ready data query checks, and data analyses (April–June 2020)
- Completion of the coding for delinquency reports (checking the completeness of a form as a whole, whether an eCRF is marked as complete in OpenClinica database), generation of reports, and review and hard coding of the site's responses (April–June 2020)
- Continuation of the coding for offline data queries for all study forms (April–September 2020)
- Completion of Cohort 3 third vaccinations for three of 30 subjects that received vaccination #1 before COVID-19 restrictions were enforced in Uganda (August 2020)
- Initiation and Completion of Cohort 3 first vaccinations for 25 of the remaining 27 subjects following easing of COVID-19 restrictions (August 2020)

- Resumption of screening to complete the identification of the remaining 3 participants for Cohort 3 following easing of COVID-19 restrictions (September 2020)

Major Task 5:

- Conduct stability testing of *Sm*-TSP-2/Alhydrogel vaccine lot 1975: M48, analysis of results, and release of results (January-March 2020)
- Conduct stability testing of *Sm*-TSP-2 Bulk Drug Substance Lot #11-69D-002: M96, analysis of results, and release of results (April-June 2020)
- Conduct stability testing of *Sm*-TSP-2/Alhydrogel Schistosomiasis Vaccine Lot #11-69F-003: M96, analysis of results, and release of results (July-September 2020)

Major Task 6:

- Shipment from MUWRP to GW of screening serum samples for Cohort 1 volunteers, for anti-*Sm*-TSP-2 IgE testing to determine eligibility (November 2019)
- Completion of anti-*Sm*-TSP-2 IgE testing/release of results for Cohort 1 eligibility determination (November 2019)
- Completion of fecal and urine microscopy testing for ova and parasites as part of screening for study Part A (October 2019 – Sept 2020)
- Completion of the laboratory manual of procedures (version 1.0) by GW (October 2019)
- Shipment from MUWRP to GW of screening serum samples from potential Cohort 2 participants for IgE against the vaccine antigen *Sm*-TSP-2 to determine eligibility (January 2020).
- Anti-*Sm*-TSP-2 IgE testing at GW, analysis of assay results, and release of results for Cohort 2 eligibility determination (January 2020).
- Shipment from MUWRP to GW of screening serum samples from potential Cohort 3 participants for IgE against the vaccine antigen *Sm*-TSP-2 (see above) to determine eligibility (March 2020).
- Anti-*Sm*-TSP-2 IgE testing at GW, analysis of assay results, and release of results for Cohort 3 eligibility determination (March 2020).
- Cryopreservation of whole blood derivatives (serum, plasma, and PBMCs) from Cohorts 1-3 at protocol-designated time points (October 2019-September 2020).
- Shipment from MUWRP to GW of screening serum samples for final Cohort 3 volunteers following easing of COVID-19 restrictions, for anti-*Sm*-TSP-2 IgE testing to determine eligibility (September 2020)
- Completion of anti-*Sm*-TSP-2 IgE testing/release of results for remaining Cohort 3 eligibility determination (September 2020)

Additional accomplishments:

- Weekly conference calls were conducted between the GW and MUWRP project teams to coordinate execution of the clinical trial.
- Renewal of local clinical trials insurance policy with Ugandan insurance company, as per Uganda NDA stipulation (June 2020).

3.3 What opportunities for training and professional development has the project provided?

Nothing to report.

3.4 How were the results disseminated to communities of interest?

Nothing to report.

3.5 What do you plan to do during the next reporting period to accomplish the goals?

Since all recruitment, screening and enrollment in Cohorts 1, 2 and 3 have been completed during this reporting period, safety follow-up of all enrolled subjects will continue. Part A of the clinical trial is now fully enrolled (n=90); all remaining vaccinations in Cohort 3 will be completed

in this part of the study by the end of February 2021. Following completion of all study Day 140 visits for Part A participants, serum samples will be tested for IgG antibodies to *Sm*-TSP-2. A report on the interim analysis of safety and immunogenicity data through Day 140 of Part A, will be prepared in March/April 2021 and will be submitted to the Safety Monitoring Committee for review and discussion to determine the dose and formulation to be tested in Part B of the study. This will be also shared with the Ugandan local IRB for their review prior to initiation of Part B of the study. Recruitment and enrollment of Part B of the trial will be initiated immediately thereafter.

Recruitment into Part B of the trial will first be initiated via "briefing sessions" with interested prospective adult volunteers after advertising the study in neighborhoods and communities in and around Kampala by means of radio advertisements, posters, brochures, and word of mouth. Following these briefing sessions, adult volunteers who are interested will be invited for individual consenting and screening appointments. A sufficient number of screened and eligible participants will be identified prior to enrolling, randomizing and vaccinating in Part B of the study. Study visits and procedures will proceed as per the approved study protocol.

4 IMPACT

Nothing to report to date. However, the expected short- and long-term impact of the project are as follows:

Short-term Impact. The short term impact is to provide proof-of-concept for the safety and immunogenicity of one of the first schistosomiasis vaccines tested in Africa. Specifically, the goal of this proposal is to perform a **Phase I/IIb clinical trial** to evaluate the safety and immunogenicity of the ***Sm*-TSP-2/Alhydrogel** schistosomiasis vaccine in African adults for the first time, and to obtain preliminary data on proof-of-efficacy. *Sm*-TSP-2/Alhydrogel has recently been tested in a first-in-human Phase I trial in schistosomiasis-unexposed adults in the U.S. In November 2017, a second Phase I trial was initiated in adults living in a region of Brazil where *S. mansoni* is endemic. The next essential step in its clinical development is to test it in areas of Africa where both *S. mansoni* and *S. haematobium* are endemic.

Long-term impact. The proposed clinical trial is critical to the development of the first successful preventative vaccine for schistosomiasis. The vaccine represents an essential technology to prevent acute schistosomiasis, a mission-abortive health threat to the US military deployed to Africa and the Middle East. The vaccine would be used alongside praziquantel in programs of "vaccine linked chemotherapy" to prevent post-treatment re-infection and chronic schistosomiasis. Achieving this goal would provide as a deliverable a key global health biotechnology that would accelerate the global elimination of schistosomiasis.

5 CHANGES/PROBLEMS

5.1 Changes in approach and reasons for change

No changes in approach, design or objectives were made during the reporting period.

5.2 Actual or anticipated problems or delays and actions or plans to resolve them

1. As stated in previous reports, the proposed start date listed on the grant application for this project was Nov. 1, 2018, the grant was unexpectedly awarded with a start date of Sept. 30, 2018, earlier than anticipated. Therefore, finalization of the study protocol, informed consent form and related clinical trial documents, and initial submission of the clinical trial protocol to the local Ugandan IRB and the George Washington University IRB, did not occur until October 2018. The Statement of Work for this grant had indicated that submission of the protocol to the Ugandan IRB would occur prior to initiation of the grant; however, given the earlier than expected grant start date, this was not possible. Furthermore, the Ugandan local IRB (Makerere University School of Public Health IRB) would not review the protocol until the notice of grant award had been received. Therefore, initial

submission of the study to the local Ugandan and US ethical review bodies did not occur as early in the project period as originally anticipated. However, both submissions did occur in Month 1 of the project (October 2018), stipulations were received from both IRBs, and responses to the stipulations were submitted in December 2018. Therefore, the delay in receiving initial IRB approval was only a few months and has not significantly impacted the initiation or timelines of the trial.

2. When the grant was originally proposed, the Ugandan collaborators on this project at the Makerere University Walter Reed Project indicated that submission to the national Ugandan IRB (UNCST) could occur in parallel to the local IRB submission. However, at the time of the grant initiation, the project team was informed that the current UNCST regulations required approval by the local Ugandan IRB first, before submission could be made to the national IRB. Therefore, submission to UNCST could not occur in Month 1 of Year 1 of the project as originally intended, and had to wait until final approval by the Makerere University School of Public Health IRB, which was received in January 2019. Submission to UNCST occurred immediately upon receipt of local IRB approval and full approval for the trial was received in May 2019, Month 8 of Year 1 of the project).
3. The novel coronavirus (COVID-19) was declared a global pandemic by the WHO on 11 March 2020 and this has impacted the study in several ways. Importantly, the Ugandan government limited activity country-wide to promote social distancing and this impacted the study team's ability to conduct study visits with participants at the study site. The president of Uganda banned all public transportation, and in short order, all transportation (including private vehicles) until approximately the first week of May 2020. Enrollment into Cohorts 1 and 2 were completed before the emergence of COVID-19. The country lockdown and limitations on public transport affected both study staff's ability to get to work and study subjects' ability to come into the study site. Subjects in Cohort 1 were in the process of receiving their third and final vaccinations just prior to the country lockdown and subjects in Cohort 2 were in the process of receiving their second vaccination. Therefore, some vaccinations and in-person follow up visits were delayed and occurred slightly out of window (not more than a week). Luckily, MUWRP was able to obtain some vehicle stickers from the Ugandan Ministry of Health in early April 2020 and they therefore were able to re-initiate in-person study visits and vaccinations by driving participants from their homes to the study clinic. Third vaccinations of Cohort 1 and second vaccinations of Cohort 2 were therefore completed with a few exceptions (e.g., participants who were stuck outside of Kampala due to the sudden travel restrictions). Teleconferences were held with the site to discuss contingency planning during this time and accommodations were made in accordance with local and GW regulatory recommendations to continue safety follow-up of enrolled subjects. Enrollment into Cohort 3 was temporarily paused in March 2020 due to the COVID-19 restrictions and but was resumed when restrictions were lifted in July 2020. Unfortunately, not all individuals who had previously been screened in February/March 2020 and been deemed eligible, were still available for study participation, and therefore recruitment and screening activities had to be re-opened in August 2020 to complete enrollment of Cohort 3 of Part A. This necessitated another shipment of serum samples from screened participants to GW in Washington, DC, for IgE testing against the *Sm*-TSP-2 vaccine antigen. This was completed in September 2020 and enrollment of the final Cohort 3 participants was done on 08OCT2020.
4. MUWRP received a second shipment of IP from GW in February 2020 but there was a temperature excursion below 0^{o}C while the shipment was in transit, rendering the IP unusable. The site's inventory of IP was therefore low in March 2020. GW was unable to ship additional IP at that time due to COVID-19 transportation restrictions and limited air travel (including cargo) into Uganda. A shipment to replace IP supplies was finally sent in April 2020 once restrictions were partially lifted. This resulted in some participants receiving their second or third doses of vaccine slightly out of window; these out-of-window deviations were approved by the study sponsor (Baylor College of Medicine).

5.3 Changes that had a significant impact on expenditures

Given the COVID-19 pandemic, the site intends to make changes to the recruitment strategy for Part B of the study as necessary to ensure compliance with COVID-19 preventive measures

instituted by the government of Uganda (e.g., a ban on gatherings and need for social distancing). There are limitations in the number of passengers per public vehicle resulting in increased costs of public transportation. Additionally, there is increased risk of exposure to COVID-19 as the majority of passengers are not following the recommended prevention guidelines and the vehicles are not sanitized. To that end, these issues may impact the number of participants that can be safely seen at the site particularly for screening activities. Therefore, MUWRP plans to conduct field activities at two landing sites (Ggaba and Kasenyi) and perform stool analysis as a prescreening activity so that only eligible participants (stool positive for Schistosoma ova) are invited over to the Kampala site for full screening. The expenditures related to initiation of Part B of the clinical trial (e.g., recruitment and advertising expenses, transportation costs, participant compensation, clinical and laboratory personnel salary expenses, clinical supplies, etc.) will pick up significantly in Year 3 of the project as recruitment, enrollment, vaccinations and study visits are initiated.

5.4 Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Protocol version 4.0 was submitted and approved by both the GW and MUSPH IRBs. The changes from version 3.0 to 4.0 consisted primarily of the following:

- Minor grammatical and editorial corrections.
- Clarification that urine testing for *Schistosoma haematobium* will also be performed at all timepoints when fecal testing for *Schistosoma mansoni* will be conducted (i.e., urine samples will be collected whenever fecal samples are collected for endpoint testing). This was an oversight that had always been intended and is necessary in order to meet the study objectives as listed in the protocol.
- Change of blood volume collected for CBC, ALT, and Creatinine

6 PRODUCTS

6.1 Publications, conference papers, and presentations

Nothing to report.

6.2 Website(s) or other Internet site(s)

The clinical trial was registered on the Clinicaltrials.gov website during the previous reporting period (https://clinicaltrials.gov/ct2/show/NCT03910972?term=TSP-2&draw=2&rank=1). The progress of the trial will be updated periodically on this website, at a minimum every six months. Results will also be posted to this site when they become available.

6.3 Technologies or techniques

Nothing to report.

6.4 Inventions, patent applications, and/or licenses

Nothing to report.

6.5 Other Products

Nothing to report.

7 PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

7.1 Individuals who worked on the project during the reporting period

George Washington University (GW) Participants:

Name: David Diemert, MD
Project Role: Grant PI; Protocol Chair
Researcher Identifier: 0000-0002-2789-0512 (Orcid ID)
Nearest person month worked: 1 person month per year
Contribution to Project: No change.

Name: Jeffrey Bethony, PhD
Project Role: GW Clinical Immunology Laboratory (CIL) Director
Researcher Identifier: 0000-0002-7901-2113 (Orcid ID)
Nearest person month worked: 1 person month per year
Contribution to Project: No change.

Name: Elissa Malkin, DO
Project Role: Sub-Investigator
Researcher Identifier: 0000-0003-0943-5433 (Orcid ID)
Nearest person month worked: 1 person month per year
Contribution to Project: No change.

Name: Kelly Thomas, MBA
Project Role: Clinical Research Manager
Researcher Identifier: n/a
Nearest person month worked: 3 person month per year
Contribution to Project: No change.

Name: Samantha Daaka, MPH
Project Role: Clinical Research Coordinator
Researcher Identifier: n/a
Nearest person month worked: 3 person months per year
Contribution to Project: No change.

Name: Guangzhao Li, MS
Project Role: Biostatistician II, GW CIL
Researcher Identifier: n/a
Nearest person month worked: 1 person month per year
Contribution to Project: No change.

Name: Lara Hoeweler
Project Role: Research Assistant, GW CIL
Researcher Identifier: n/a
Nearest person month worked: 2 person month per year
Contribution to Project: No change.

7.2 Changes in active other support of the PD/PI or senior/key personnel since the last reporting period

The following lists the changes to Other Support for Drs. Diemert and Bethony since the previous reporting period.

7.2.1 David Diemert (Grant PI)

Other Support that started in reporting period:

a) **Title of the project:** A randomized, double-blinded, placebo-controlled, dose-escalation phase 1 clinical trial to evaluate the safety and immunogenicity of recombinant HIV-1 envelope protein BG505 SOSIP.GT1.1gp140 Vaccine, Adjuvanted in healthy, HIV-1 uninfected adults
   1. Funding Agency: Bill & Melinda Gates Foundation (subaward from Rockefeller University, the prime awardee)
   2. Goal: The goal of this project is to conduct a Phase 1 clinical trial to test the safety and immunogenicity of the BG505 SOSIP.GT1.1gp140 Vaccine, Adjuvanted that is being developed to protect against infection with HIV.
   3. Specific Aims:
      i. Primary Endpoint (Safety): To evaluate the safety and tolerability of the HIV-1 envelope protein BG505 SOSIP.GT1.1 gp140 vaccine, Adjuvanted, in HIV-uninfected adults
      ii. Secondary Endpoint (Immunogenicity): To assess the frequency and magnitude of binding antibody responses to GT1.1 trimer in HIV-uninfected adults
      iii. Exploratory Endpoints (Immunogenicity):
         a. To assess the frequency of GT1.1-specific CD4 binding site (CD4bs)-class B cells and antibody responses
         b. To assess the frequency of GT1.1-specific V2-apex class B cells and antibody responses
         c. To assess the frequency and magnitude of off target B-cell and antibody responses
         d. To assess the frequency and magnitude of IP induced T-cell responses
   4. Start and end date (month/day/year – month/day/year): 11/11/2019 – 11/30/2023
   5. Level of Funding:
   6. Level (%) of effort in the project: 10%

b) **Title of the project:** Controlled Infection for Testing Efficacy of Hookworm Vaccines in Brazil
   1. Funding Agency: Wellcome Trust (GW is a subawardee of the project prime awardee, the Fundação da Desenvolvimento da Pesquisa [FUNDEP])
   2. Goal: Implement a new paradigm for the early assessment of novel hookworm vaccines by transferring the Hookworm Vaccine Challenge Model to *Necator* endemic areas of Brazil in order to tests *Na*-GST-1/Alhydrogel® and *Na*-APR-1/Alhydrogel® with or without GLA-AF as follows:
   3. Specific Aims:
      i. Establish the Controlled Human Hookworm Infection (CHHI) model in Brazil.
      ii. Conduct a dose-escalation study evaluating CHHI in individuals infected with *N. americanus*.
      iii. Assess the efficacy and safety of *Na*-GST-1/Alhydrogel® and *Na*-APR-1/Alhydrogel® in a double-blind Phase 2 HVCM trial in adults resident in a *Necator*-endemic area.
   4. Start and end date (month/day/year – month/day/year): 02/01/2020 – 01/31/2025

5. Level of Funding:
6. Level (%) of effort in the project: 10%

c) **Title of the project:** Coronavirus Prevention Network (CoVPN) Site Preparedness
1. Funding Agency: NIAID/NIH
2. Goal: to conduct start-up activities to prepare for and initiate Phase 3 randomized, placebo-controlled vaccine trials to evaluate the safety, efficacy, and immunogenicity of SARS-CoV-2 vaccines in adult volunteers aged 18 years and older.
3. Specific Aim: Initiate preparations for conducting Phase 3 clinical trials of experimental COVID-19 vaccines as part of the CoVPN.
4. Start and end date (month/day/year – month/day/year): 07/01/2020 – 11/30/2020
5. Level of Funding:
6. Level (%) of effort in the project: 20%

ci) **Title of the project:** CoVPN 3001: Phase 3, SARS-CoV-2 Vaccine (ModernaTX, Inc.)
1. Funding Agency: NIAID/NIH
2. Goal: The primary efficacy objective of this trial is to evaluate the ability of the mRNA-1273 SARS-CoV-2 vaccine to prevent first occurrence of COVID-19 disease starting at 14 days after the second study injection. Eligible participants will be randomized to receive either the mRNA-1273 SARS-CoV-2 vaccine or inactive placebo via intramuscular injection on study Day 1 and Day 29. Participants will undergo a variety of visits and procedures to assess safety, immunogenicity, and efficacy of the vaccine. Efficacy and safety assessments will continue for 24 months after the second vaccination.
3. Specific Aims:
    i. Primary:
        a. To demonstrate the efficacy of mRNA-1273 to prevent COVID-19.
        b. To evaluate the safety and reactogenicity of 2 injections of mRNA-1273 given 28 days apart.
    ii. Secondary:
        a. To evaluate the efficacy of mRNA-1273 to prevent severe COVID-19.
        b. To evaluate the efficacy of mRNA-1273 to prevent serologically confirmed SARS-CoV-2 infection or COVID-19 regardless of symptomatology or severity.
        c. To evaluate vaccine efficacy (VE) against a secondary definition of COVID-19.
        d. To evaluate VE to prevent death caused by COVID-19.
        e. To evaluate the efficacy of mRNA-1273 to prevent COVID-19
        f. after the first dose of investigational product (IP).
        g. To evaluate the efficacy of mRNA-1273 to prevent COVID-19 in all study participants, regardless of evidence of prior SARS-CoV-2 infection.
        h. To evaluate the efficacy of mRNA-1273 to prevent asymptomatic SARS-CoV-2 infection.
4. Start and end date (month/day/year – month/day/year): 07/01/2020 – 06/30/2022
5. Level of Funding:
6. Level (%) of effort in the project: 29%

cii) **Title of the project:** A Master Protocol Assessing the Safety, Tolerability, and Efficacy of Anti-Spike (S) SARS-COV-2 Monoclonal Antibodies for the Treatment of Ambulatory Patients with COVID-19
1. Funding Agency: Regeneron Pharmaceuticals, Inc.

2. Goal: This is an adaptive, phase 1/2/3, randomized, double-blinded, placebo-controlled master protocol to evaluate the efficacy, safety, and tolerability of REGN10933+REGN10987 monoclonal anti-SARS-CoV-2 antibody combination therapy in adult outpatients (i.e., ambulatory patients) with COVID-19.
3. Specific Aims:
    i. To evaluate the safety and tolerability of REGN10933+REGN10987 compared to placebo.
    ii. To evaluate the virologic efficacy of REGN10933+REGN10987 compared to placebo in reducing viral shedding of SARS-CoV-2.
    iii. To evaluate the clinical efficacy of REGN10933+REGN10987 and REGN10989 compared to placebo.
4. Start and end date (month/day/year – month/day/year): 06/14/2020 – 09/12/2021
5. Level of Funding: Per participant
6. Level (%) of effort in the project: 4%

Other Support that <u>ended</u> in reporting period:

Nothing to report.

7.2.2 Jeffrey Bethony (GW Clinical Immunology Laboratory Director)

Other Support that <u>started</u> in reporting period:

a) **<u>Title of the project</u>:** AIDS and Cancer Specimen Resource (ACSR)
    1. Funding Agency: National Institutes of Health
    2. Goal: The goals of this project are to biobank material from individuals who have a malignancy and are positive for Human Immune Deficiency (HIV) virus. The materials in the ASCR are banked according to NCI Best Practices.
    3. Specific Aims:
        i. Specific Aim 1: Develop and maintain an ACSR infrastructure that allows efficient translation of the overall ACSR mission into a functional program with clear lines of administrative and fiscal oversight and ongoing quality management and program evaluation.
        ii. Specific Aim 2: Provide scientific leadership, implement organizational function and expand utilization and relevance of the ACSR that allow HIV-malignancy investigators to achieve their research agenda.
        iii. Specific Aim 3: Acquire, maintain and distribute a diverse collection of high quality well-annotated biospecimens that support current and future trends in HIV and AIDS malignancy research.
        iv. Specific Aim 4: Support NCI funded initiatives, international collections, collaborative projects and affiliated programs by providing ACSR biorepository services in response to the evolving research trends in the HIV and AIDS malignancy epidemic
    4. Start and end date: 09/01/2019 - 08/31/2024
    5. Level of Funding:
    6. Level (%) of effort in the project: 35%

b) **Title of the project:** Controlled Infection for Testing Efficacy of Hookworm Vaccines in Brazil
    1. Funding Agency: Wellcome Trust (GW is a subawardee of the project prime awardee, the Fundação da Desenvolvimento da Pesquisa [FUNDEP])
    2. Goal: Implement a new paradigm for the early assessment of novel hookworm vaccines by transferring the Hookworm Vaccine Challenge Model to *Necator* endemic areas of

Brazil in order to tests *Na*-GST-1/Alhydrogel® and *Na*-APR-1/Alhydrogel® with or without GLA-AF as follows:

3. Specific Aims:
    i. Establish the Controlled Human Hookworm Infection (CHHI) model in Brazil.
    ii. Conduct a dose-escalation study evaluating CHHI in individuals infected with *N. americanus*.
    iii. Assess the efficacy and safety of *Na*-GST-1/Alhydrogel® and *Na*-APR-1/Alhydrogel® in a double-blind Phase 2 HVCM trial in adults resident in a *Necator*-endemic area.
4. Start and end date (month/day/year – month/day/year): 02/01/2020 – 01/31/2025
5. Level of Funding:
6. Level (%) of effort in the project: 10%

b) **Title of the project:** Methotrexate treatment of Arthritis caused by Chikungunya virus (MARCH): A randomized controlled trial of methotrexate versus placebo in the treatment of chronic arthritis after chikungunya infection
    1. Funding Agency: National Institutes of Health
    2. Goal: We propose the first randomized, double-blind, placebo-controlled evaluation of the efficacy and pathologic mechanism determined by synovial biopsy of 6 months of MTX (n=134) vs. placebo (n=67) therapy for chronic Chikungunya virus (CHIKV) arthritis in Colombia with the option for open-label MTX use for up to one year for all participants.
    3. Specific Aims:
        i. Specific Aim 1: Methotrexate (MTX) vs. placebo for 6 months will significantly decrease ACR20/50/70, DAS-28, pain, stiffness, mobility, disability, inflammatory cytokines, and CHIKDAS at year 1 and 2 follow-ups.
        ii. Specific Aim 2: MTX vs. placebo treatment will decrease activation of synovial macrophages and FLS via inhibition of pathogenic cytokines such as IL-1 and IL-6.
        iii. Specific Aim 3: In patients with COVID19 infection, low-dose MTX vs. placebo will be safe and is associated with decreased disease severity and decreased levels of CRP, IL-6 and TNF.
    4. Start and end date (month/day/year – month/day/year): 04/01/2020 – 02/28/2021
    5. Level of Funding:
    6. Level (%) of effort in the project: 2.25%

c) **Title of the project:** AIDS Malignancy Consortium (AMC)
    1. Funding Agency: National Institutes of Health (sub from Montefiore)
    2. Goals The overall vision of AMC is to reduce incidence, morbidity, and mortality of cancers occurring in People Living With HIV (PLWH), largely through clinical trials testing hypothesis- driven, pathogenesis-directed novel agents for the treatment of invasive cancers and precancerous lesions, especially AIDS-associated KS and lymphoma, and including PK interaction studies with Anti-RetroVirals (ARVs). In the last funding period, the scope of the AMC research agenda expanded significantly with the conception, planning, launching, and successful implementation of the Anal Cancer HSIL Outcomes Research (ANCHOR) trial, and broadened therapeutic emphasis including non-AIDS defining cancers and immunotherapy, and inclusion of HIV-negative individuals with virally-mediated cancers in selected trials when their inclusion would inform the independent contributions of the virus mediating the cancer in the setting of HIV infection. In the next funding period, AMC will substantially expand the scope of its research agenda and network. Some of these new efforts have already been initiated in the current funding period, whereas others are being planned and will be launched in the first year of the next funding period. These new scientific priorities have been enabled by careful strategic planning, including: (1) identification and vetting of new Latin American

(LATAM) sites by the International Resource Committee (IRC); (2) expanding the leadership team providing oversight of international sites through recruitment of Associate Chairs for Africa (initially S. Gopal, then W. Phipps) and LATAM (V. Fink), as well as international Vice-Chairs of each Scientific Working Groups; (2) recruitment of an Associate Chair for Cancer Control/Prevention (P. Castle); (3) development and expansion of the AMC Career Enhancement Program, which has been highly successful in engaging new junior investigators at AMC domestic and international sites, and strengthening management of the program; (4) recruitment of an Executive Officer (to provide oversight in streamlining protocol development process, an important step given the diversity and complexity of AMC trials, and the expanding number of new investigators.

3. Start and end date (month/day/year – month/day/year): 09/01/2020 – 08/31/2025
4. Level of Funding:
5. Level (%) of effort in the project: 5%

d) **Title of the project:** A randomized, double-blinded, placebo-controlled, dose-escalation phase 1 clinical trial to evaluate the safety and immunogenicity of recombinant HIV-1 envelope protein BG505 SOSIP.GT1.1gp140 Vaccine, Adjuvanted in healthy, HIV-1 uninfected adults
   1. Funding Agency: Bill & Melinda Gates Foundation (subaward from Rockefeller University, the prime awardee)
   2. Goal: The goal of this project is to conduct a Phase 1 clinical trial to test the safety and immunogenicity of the BG505 SOSIP.GT1.1gp140 Vaccine, Adjuvanted that is being developed to protect against infection with HIV.
   3. Specific Aims:
      i. Primary Endpoint (Safety): To evaluate the safety and tolerability of the HIV-1 envelope protein BG505 SOSIP.GT1.1 gp140 vaccine, Adjuvanted, in HIV-uninfected adults
      ii. Secondary Endpoint (Immunogenicity): To assess the frequency and magnitude of binding antibody responses to GT1.1 trimer in HIV-uninfected adults
      iii. Exploratory Endpoints (Immunogenicity):
         a. To assess the frequency of GT1.1-specific CD4 binding site (CD4bs)-class B cells and antibody responses
         b. To assess the frequency of GT1.1-specific V2-apex class B cells and antibody responses
         c. To assess the frequency and magnitude of off target B-cell and antibody responses
         d. To assess the frequency and magnitude of IP induced T-cell responses
   4. Start and end date (month/day/year – month/day/year): 11/11/2019 – 11/30/2023
   5. Level of Funding:
   6. Level (%) of effort in the project: 2.5%

Other Support that <u>ended</u> in reporting period:

Nothing to report.

7.3 Other organizations involved as partners

7.3.1 **Organization Name: Makerere University Walter Reed Project (MUWRP)**

Location of Organization: *Kampala, Uganda*

Partner's contribution to the project:

- Facilities (clinical trial site)
- Collaboration

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Hannah Kibuuka, MD
Project Role:	Trial PI; Subaward PI
Researcher Identifier:	0000-0002-2293-1944 (Orcid ID)
Nearest person month worked:	1 person month per year
Contribution to Project:	No change.
Name:	Proscovia Naluyima, PhD
Project Role:	MUWRP Laboratory Director
Researcher Identifier:	n/a
Nearest person month worked:	3 person months per year
Contribution to Project:	No change.
Name:	Francis Kiweewa, MBChB, MMed, MPH
Project Role:	Head of Research and Scientific Affairs at MUWRP
Researcher Identifier:	0000-0003-4938-9558 (Orcid ID)
Nearest person month worked:	3 person month per year
Contribution to Project:	No change.
Name:	Monica Millard, BSN, MPH
Project Role:	MHRP Country Director in Uganda
Researcher Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	No change.
Name:	Nicholas Tamale MD
Project Role:	Medical Officer and Study Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	No change.
Name:	Douglas Makumbi MD
Project Role:	Medical Officer and Study Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	No change.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Musabe Chrispus Bakunda MD
Project Role:	Medical Officer and Study Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	9 person months per year
Contribution to Project:	Dr. Bakunda replaced Dr. Makumbi on this project in October 2020. He has performed work in leading the coordination of the actual implementation of the study at the MUWRP site in Uganda, and helping the trial PI in supervising the clinical trials staff. Upon initiation of recruitment and screening, Dr. Bakunda will implement the day to day clinical trials activities including eligibility checks, enrollment of the participants, collection of clinical data, specimens and follow-up of all participants enrolled.

Name:	Allan Tindikahwa, PharmD
Project Role:	Head, Quality Improvement & Compliance at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	No change.

Name:	Betty Mwesigwa, MD
Project Role:	Medical Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person month per year
Contribution to Project:	No change.

Name:	Amir Wamala, PharmD
Project Role:	Investigational Pharmacist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person month per year
Contribution to Project:	No change.

Name:	Immaculate Nakabuye
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	3 person month per year
Contribution to Project:	No change

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Jacqueline Sarah Namagabo
Project Role:	Quality Control/Quality Assurance Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person month per year
Contribution to Project:	No change.

Name:	Joseph Wandege
Project Role:	Laboratory Manager at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person month per year
Contribution to Project:	No change.

Name:	Christine Nanteza
Project Role:	Laboratory QA/QC Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person month per year
Contribution to Project:	No change.

Name:	Ezra Musingye
Project Role:	Data Manager at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person month per year
Contribution to Project:	No change.

Name:	Jauhara Nanyondo
Project Role:	Community Outreach Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person month per year
Contribution to Project:	No change.

Name:	Hilda Mutebe
Project Role:	Regulatory Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	3 person month per year
Contribution to Project:	No change.

Name:	Miriam Mutenyo Bwobi
Project Role:	Laboratory Administrator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Ms Mutenyo Bwobi serves as an administrator at MUWRP's principal laboratories and offices located the Makerere University Medical School in Kampala. Her primary responsibility is transferring lab data from paper formats into computer files or database systems and also preparing laboratory reports. She ensures continued information flow between the laboratory and the clinic with regards to study screening/safety results, laboratory data clarification forms and reconciliation reports coordination.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Harriet Nabirye
Project Role:	Lab QA/QC Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Ms. Nabirye serves as the QA/QC officer at the MUWRP's principal laboratories and offices located the Makerere University Medical School in Kampala. Her primary responsibility is performing QA/QC and ensuring that the study is conducted according to accreditation guidelines and standards.
Name:	Ronald Sanya
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Sanya serves as a biomedical scientist at the MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are to receive samples in the laboratory, perform safety laboratory tests (CBC, chemistries, hCG, urinalysis), screen fecal and urine samples for helminths and perform diagnostic viral serologic testing (HIV, Hepatitis B/C).
Name:	Andrew Disan Njawuzi
Project Role:	QA/QC Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	Mr. Njawuzi conducts QA/QC for all data entered into the electronic database for the study. His primary responsibility is to conduct and oversee data quality control checks, query resolution, and data cleaning up until database lock.
Name:	Herbert Kityo
Project Role:	Office Attendant at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Mr. Kityo maintains office operations by receiving and distributing communications; picking up and delivering items; serving customers, raising purchase requisitions and also providing general support on recruitment of eligible participants, regulatory oversight, and supply management. He ensures that all results received from the lab are documented and passed on to the responsible clinicians for action. He also supports clinic administrative functions as needed.
Name:	Roy Nassaka
Project Role:	Phlebotomist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Ms. Nassaka serves as a phlebotomist and her primary role is to obtain venipuncture blood samples as required by the study protocol. She is also required to complete study source documentation and data collection form completion, including when procedures have been performed.
Name:	Lucy Maria Nakayiza
Project Role:	Laboratory Administrator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Ms. Nakayiza serves as an administrator at MUWRP's principal laboratories and offices located the Makerere University Medical School in Kampala. Her primary responsibility is transferring lab data from paper formats into computer files or database systems and also preparing laboratory reports. She ensures continued information flow between the laboratory and the clinic with regards to study screening/safety results, laboratory data clarification forms and reconciliation reports coordination.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Maureen Mukyala
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Ms. Mukyala is an experienced clinical research nurse. She supervises the clinical research nursing activities on a day-to-day basis and is responsible for the implementation of processes and procedures for collection of clinical data, specimens and follow-up of all enrolled participants. She participates in recruitment and consenting of eligible participants, counselling, transcription of results and resolution of data queries.
Name:	Godfrey Zziwa
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	Mr. Zziwa serves as a biomedical scientist at MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are to receive samples in the laboratory, perform safety laboratory tests (CBC, chemistries, hCG, urinalysis), screen fecal and urine samples for helminths and perform diagnostic viral serologic testing (HIV, Hepatitis B/C). He is also IATA trained and responsible for shipment of samples to GW in the US following IATA guidelines.
Name:	Claire Beingana
Project Role:	QA/QC Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	Ms. Claire Beingana serves as a QA/QC officer, whose primary responsibility is ensuring the quality of study data collected. She performs real-time data quality checks and is also responsible for the periodic conduct of quality assurance procedures on the study. She also is the primary contact person for all reconciliation reports between the lab, the data management team and the clinic.
Name:	Richard Adegitho
Project Role:	Senior Sanitary Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Adegitho is responsible for the general cleanliness and maintenance of the laboratory. His primary responsibilities include inspection of facilities for cleanliness, cleaning and sanitizing the entire facility, identifying and reporting conditions or practices that may comprise overall sanitation effectiveness.
Name:	Rena Nakyeyune Patricia
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Ms. Nakyeyune Patricia serves as a biomedical scientist at the MUWRP's principle laboratories located at the Makerere University Medical School in Kampala. Her primary responsibility is to receive samples in the laboratory, perform safety laboratory tests (CBC, chemistries, hCG, urinalysis), screen fecal and urine samples for helminths, perform diagnostic serological testing (HIV, Hepatitis B/C), and handle shipments for the study.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Brenda Atwijuka
Project Role:	Data Management Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	7 person months per year
Contribution to Project:	Ms. Atwijuka, reporting to Senior Data Manager, is responsible for the day-to-day operations of the data management team including ensuring timely data entry and quality control and assurance with the research study.

Name:	Festo Kyambadde Nelson
Project Role:	Data Entry at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	Mr. Nelson is responsible for transferring lab data from paper formats into computer files or database systems.

Name:	Mathias Ssekitoleko
Project Role:	Community Outreach Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	Mr. Ssekitoleko is responsible for ensuring that recruitment targets are met, designs recruitment strategy for the study and is responsible for community outreach, including ensuring adequate follow-up of participants to ensure adequate retention in the study.

Name:	Raymond Mayanja
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person month per year
Contribution to Project:	Mr. Mayanja serves as a biomedical scientist at the MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are to receive samples in the laboratory, perform safety laboratory tests (CBC, chemistries, hCG, urinalysis), screen fecal and urine samples for helminths, perform diagnostic serological testing (HIV, Hepatitis B/C), and handle shipments for the study.

Name:	Andrew Ssenyonga
Project Role:	Records Maintenance Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Mr. Ssenyonga serves as a Records Maintenance Officer. He is the custodian of trial documents such as participant charts, informed consent forms, and briefing and screening logs, which he maintains in a double-locked, access-restricted office and ensures that they are delivered to respective teams and secured at the end of each day as needed. He performs participants' clinical chart accountability on a daily basis.

Name:	Cynthia Mukisa Williams
Project Role:	Regulatory Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Ms. Mukisa Williams performs regulatory submissions including initial and continuing review reports, SAEs and deviations. She is responsible for communications to the local IRB and ensuring protocol adherence. She supports the Principal investigator with maintenance of the site Trial Master File.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Joanita Namuli
Project Role:	Clinic Administrative Assistant at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	3 person months per year
Contribution to Project:	Ms. Namuli oversees daily clinic operations, including ensuring that the clinic is in compliance with research rules and regulations and is in charge of participant/volunteer relations, personnel administration and the clinic's fiscal management and also provides support on recruitment and consenting of eligible participants. She is responsible for scheduling of participants, conducting pre-visit reminder calls and reimbursement.
Name:	Irene Rwomushana Tuhirirwe
Project Role:	Regulatory Affairs Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	7 person months per year
Contribution to Project:	Ms. Tuhirirwe, reporting to the CQI and Compliance Manager, assists in all regulatory submissions including initial, continuing review reports, SAEs and deviations and is also responsible for communications to the local IRB and ensuring protocol adherence. Responsible to support the Principal investigator with the maintenance of the site Trial Master File.
Name:	Joseph Okonye
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Okonye serves as a biomedical scientist at the MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are diagnostics testing, analysing specimens of blood, tissues, urine and feces for chemical constituents using sophisticated computer-aided and automated testing procedures, interpreting results and writing lab reports.
Name:	Morish Javuru
Project Role:	Sanitary Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Javuru is responsible for the general cleanliness and maintenance of MUWRP offices including the clinic. His primary responsibility is ensuring total cleanliness, sanitation, trimming of lawns and safety of all lab/office premises.
Name:	Jerry Nuwagaba
Project Role:	Laboratory Technologist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Nuwagaba serves as a biomedical scientist at the MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are to receive samples in the laboratory, perform safety laboratory tests (CBC, chemistries, hCG, urinalysis), screen fecal and urine samples for helminths, and perform diagnostics serological testing (HIV, Hepatitis B/C).
Name:	Gertrude Nassanga
Project Role:	Data Entry Specialist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	Ms. Nassanga conducts data entry, query resolution, data cleaning and final database lock.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Juliet Kizanye
Project Role:	Data Entry Specialist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	Ms. Kizanye conducts data entry, query resolution, data cleaning and final database lock.

Name:	Maimuna Nantabo
Project Role:	Data Entry Specialist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	8 person months per year
Contribution to Project:	Ms. Nantabo conducts data entry, query resolution, data cleaning and final database lock.

Name:	Justine Nalunga
Project Role:	Regulatory Affairs Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	Ms. Nalunga, reporting to the CQI and Compliance Manager, assists in all regulatory submissions including initial, continuing review reports, SAEs and deviations and is also responsible for communications to the local IRB and ensuring protocol adherence. Responsible to support the Principal investigator with the maintenance of the site Trial Master File.

Name:	Joan Nakazzi
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	9 person months per year
Contribution to Project:	Ms. Nakazzi is an experienced clinical research nurse. She supervises the clinical research nursing activities on a day-to-day basis and is responsible for the implementation of processes and procedures for collection of clinical data, specimens and follow-up of all enrolled participants. She participates in recruitment and consenting of eligible participants, counseling, transcription of results and resolution of data queries.

Name:	Stephen Mugamba
Project Role:	Community Documentation Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	Mr. Mugamba is responsible for ensuring that recruitment targets are met, designs recruitment strategy for the study and is responsible for community outreach, including ensuring adequate follow-up of participants to ensure adequate retention in the study.

Name:	Emmanuel Wasswa
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Wasswa serves as a biomedical scientist at the MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are diagnostics testing, analysing specimens of blood, tissues, urine and feces for chemical constituents using sophisticated computer-aided and automated testing procedures, interpreting results and writing lab reports.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Talbert Muhwezi
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	9 person months per year
Contribution to Project:	Ms. Muhwezi is an experienced clinical research nurse. She supervises the clinical research nursing activities on a day-to-day basis and is responsible for the implementation of processes and procedures for collection of clinical data, specimens and follow-up of all enrolled participants. She participates in recruitment and consenting of eligible participants, counseling, transcription of results and resolution of data queries.
Name:	Jowali Nangu
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Mr. Nangu serves as a biomedical scientist at the MUWRP's principal laboratories located at the Makerere University Medical School in Kampala. His primary responsibilities are to receive samples in the laboratory, perform safety laboratory tests (CBC, chemistries, hCG, urinalysis), screen fecal and urine samples for helminths and perform diagnostic viral serologic testing (HIV, Hepatitis B/C).

7.3.2 **Organization Name:** Baylor College of Medicine (BCM)

Location of Organization: *Houston, Texas*

Partner's contribution to the project:

- Regulatory support (US FDA IND holder of the *Sm*-TSP-2/Alhydrogel schistosomiasis vaccine)
- Collaboration

Baylor College of Medicine (BCM) Participants:

Name:	Peter Hotez, MD, PhD
Project Role:	Director, Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine; Subaward PI
Researcher Identifier:	0000-0001-8770-1042 (Orcid ID)
Nearest person month worked:	0.24 person months per year
Contribution to Project:	No change.

Name:	Maria Elena Bottazzi, PhD
Project Role:	Co-Director, Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine (TCH-CVD at BCM)
Researcher Identifier:	0000-0002-8429-0476 (Orcid ID)
Nearest person month worked:	0.24 person months per year
Contribution to Project:	No change.

Name:	Hilda Guerrero, BS
Project Role:	Director of Quality Assurance and Regulatory Affairs, TCH-CVD at BCM
Researcher Identifier:	n/a
Nearest person month worked:	0.60 person months per year
Contribution to Project:	No change.

Name:	Wen-Hsiang Chen, PhD
Project Role:	Director of Quality Control, TCH-CVD at BCM
Researcher Identifier:	n/a
Nearest person month worked:	2.16 person months per year
Contribution to Project:	No change.

Name:	Rakhi Tyagi Kundu, PhD
Project Role:	Senior Research Assistant
Researcher Identifier:	n/a
Nearest person month worked:	2.40 person months per year
Contribution to Project:	Ms. Kundu works under the supervision of Dr. Chen to execute stability testing and quality control of the vaccine.

Name:	Amy Gonzalez, BS, RN
Project Role:	QA/Regulatory Affairs Manager, TCH-CVD at BCM
Researcher Identifier:	n/a
Nearest person month worked:	0.60 person month per year
Contribution to Project:	Supports QC activities including quality management support for the ongoing stability testing of the vaccine. Also supports the preparation of all regulatory documentation in support of this project, in particular for the investigational product and regulatory submissions for this clinical trial to the FDA.

Name:	Ghada Launey, BS
Project Role:	QA/Regulatory Affairs Program Associate, TCH-CVD at BCM
Researcher Identifier:	n/a
Nearest person month worked:	0.60 person month per year
Contribution to Project:	Supports QC activities including quality management support for the ongoing stability testing of the vaccine. Also supports the preparation of all regulatory documentation in support of this project, in particular for the investigational product and regulatory submissions for this clinical trial to the FDA.

8 SPECIAL REPORTING REQUIREMENTS

- QuadChart for Year 2 of the project (see Appendix A)

9 APPENDICES

Appendix A: QuadChart for Year 2 of the project.

Phase 1/2b Testing of the *Sm*-TSP-2 Schistosomiasis Vaccine in Uganda

Proposal #: PR172460
Award #: W81XWH1810672

PI: David Diemert **Org:** George Washington University **Award Amount:** $4,758,022

Study Aims

•Assess the safety and immunogenicity of the *Sm*-TSP-2/Alhydrogel® vaccine with or without AP 10-701 (a synthetic Toll-like Receptor-4 agonist) in individuals living in areas of Uganda endemic for *S. mansoni* and *S. haematobium*
•Compare the incidence and intensity of reinfection with *S. mansoni* at 12 and 18 months following vaccination with *Sm*-TSP-2/Alhydrogel® vs. the licensed Hepatitis B Virus (HBV) vaccine as a comparator
•Assess the cellular immune response to vaccination with *Sm*-TSP-2/Alhydrogel

Approach

Conduct a Phase 1/2 proof-of-concept trial of the *Sm*-TSP-2/Alhydrogel schistosomiasis vaccine in healthy, schistosomiasis-exposed adults living in endemic areas of Uganda. Objectives are to tests the safety, immunogenicity and efficacy of the vaccine in this population.

Figure: Dr. Betty Mwesigwa consenting a volunteer for particiaptiion in Study TSP-18-03, at the Makerere University Walter Reed Project (MUWRP) research clinic in Kampala, Uganda.

Accomplishment: Completion of screening for study Part A.

Timeline and Cost

Activities / CY	18	19	20	21	22
Obtain IRB and Regulatory Approvals for Phase I/II Clinical Trial					
Train MUWRP Study Staff for Clinical Trial					
Study Part A (Phase I) Participant Recruitment, Vaccination, and Follow-up					
Study Part B (Phase II) Participant Recruitment, Vaccination, and Follow-up					
Product Stability Testing					
Laboratory and Data Analyses					
Report Findings					
Estimated Budget ($K)	**$291**	**$1,218**	**$1,373**	**$1,234**	**$642**

Updated: 31OCT2020

Goals/Milestones

CY18 Goal – Ethical & Regulatory Submissions
☑ Submission to GW and MUWRP IRBs
CY19 Goals – Ethical & Regulatory Approvals
☑ Approval by all Ugandan and US IRBs and regulators
☑ Initiation of recruitment and vaccinations in Part A of study
CY20 Goal – Completion of Study Part A & Initiation of Part B
☐Complete study visits in Part A
☐Initiation of recruitment and vaccinations in Part B of study
CY21 Goal – Completion of Vaccinations in Study Part B
☐Completion of vaccinations in Study Part B
CY22 Goal – Research laboratory analyses & reporting results
☐Completion of research laboratory analyses
☐Completion of Clinical Study Report

Comments/Challenges/Issues/Concerns

- Full IRB approval took longer than anticipated due to new requirement for local MUWRP IRB approval prior to national Ugandan IRB review. Budget expenditures have been delayed accordingly.
- The COVID-19 pandemic resulted in a 5-month delay in completion of enrollment into Cohort 3 of Part A.

Budget Expenditure to Date
Projected Expenditure: $2,542,731 Actual Expenditure: $1,269,407.19