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

PRINCIPAL INVESTIGATOR: David Diemert

CONTRACTING ORGANIZATION: George Washington University, Washington, DC

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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. Participants 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 participants 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 completion of enrollment and vaccinations in Cohort 3 of Part A. All Cohort 3 participants will complete Part A by October 2021. An interim safety and immunogenicity analysis occurred in May 2021 after all Part A participants completed Day 140 of the study to determine which vaccine dose/formulation will be tested in Part B. The Safety Monitoring Committee recommended a dose of 100 mcg *Sm*-TSP-2/Alhydrogel vaccine with 5 mcg AP 10-701. Recruitment and screening for Part B began in July 2021. Screening and enrollment in Part B of the study will continue in Year 4.

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

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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 showed that the vaccine was well tolerated, safe, and resulted in dose-dependent antigen-specific IgG antibody responses that were enhanced by the addition of the AP 10-701 adjuvant. 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 participants
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

By the end of the project Year 3 annual reporting period, participants in Cohorts 1 and 2 of study Part A completed all study visits. As noted in previous reports, enrollment of Cohort 3 of study Part A began in March 2020 but was suspended until July 2020 due to restrictions imposed by the Ugandan government in response to the COVID-19 pandemic. Enrollment of Cohort 3 was completed in September 2020, with planned completion of all study visits for Part A on track for October 2021. Recruitment, pre-screening, and screening of Part B (Phase 2) study participants began in July 2021.

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

Major Task 1:

- Submission and approval of the annual continuing review by the local Ugandan IRB (Makerere University School of Public Health – MUSPH) (approved on 12FEB2021).
- Submission and approval of the continuing review by the George Washington University (GW) IRB (approved on 27JAN2021).
- Submission and approval of the continuing review to USAMRDC Human Research Protections Office (approved on 31MAR2021).
- Amendment of the modification of the clinical trial protocol (updated to version 5.0) to incorporate the addition of a pre-screening fecal examination for Part B of the clinical trial.
- Revision of the Part B informed consent form (updated to version 3.0) to incorporate the addition of a pre-screening fecal examination for Part B of the clinical trial.
- Creation of a new Part B Pre-Screening informed consent form (version 1.0) for the addition of the pre-screening fecal examination for Part B of the clinical trial.
- Submission and approval of version 5.0 of the clinical trial protocol, version 3.0 of the Part B main study informed consent form, and version 1.0 of the new Part B Pre-Screening informed consent form (including translations into Luganda) to the GW IRB (approved 08APR2021).
- Submission and approval of version 5.0 of the clinical trial protocol, version 3.0 of the Part B main study informed consent form, and version 1.0 of the new Part B Pre-Screening informed consent form (including translations) to the MUSPH IRB (approved 04JUN2021).
- Submission and approval of Part B pre-screening data collection form (version 2.0) and Part B screening data collection form (version 2.0) by the MUSPH IRB on 28JUL2021.
- Revision of the Part B informed consent form (updated to version 4.0, dated 03MAY2021) to incorporate the dose and formulation of *Sm*-TSP-2 to be tested in Part B.
- Submission and approval of version 4.0 of the Part B informed consent form (including translations into Luganda) by the GW IRB (approved on 04JUN2021).
- Submission and approval of version 4.0 of the Part B informed consent form (including translations into Luganda) by the MUSPH IRB (approved on 04JUN2021).
- Revision of Part B Assessment of Understanding (updated to version 3.0) to correct clerical error and ensure consistency between study documents.
- Submission and approval of version 3.0 of the Part B Assessment of Understanding by the GW IRB on 22AUG2021.
- Submission of version 3.0 of the Part B Assessment of Understanding to MUSPH on 11JUN2021.

- Submission of annual report to US FDA for IND 017791 *Sm*-TSP-2/Alhydrogel® Schistosomiasis Vaccine ± GLA-AF on 22JAN2021 that included an update on TSP-18-03.
- Submission of the MUSPH IRB continuing review approval of the study to the national Ugandan IRB (Uganda National Council of Science & Technology - UNCST) in March 2021.
- Submission of the MUSPH IRB approval of version 5.0 of the clinical trial protocol, version 3.0 of the Part B informed consent form, and version 1.0 of the new Part B Pre-Screening informed consent form (including translations) to the UNCST on 08JUN2021.
- Acknowledgement of version 5.0 of the clinical trial protocol, version 3.0 of the Part B informed consent form, and version 1.0 of the new Part B Pre-Screening informed consent form by the UNCST on 13JUL2021.
- Submission of the MUSPH IRB approval of version 5.0 of the clinical trial protocol, version 3.0 of the Part B informed consent form, and version 1.0 of the new Part B Pre-Screening informed consent form (including translations) to the Uganda National Drug Authority (NDA) on 08JUN2021.
- Approval of version 5.0 of the clinical trial protocol, version 3.0 of the Part B informed consent form, and version 1.0 of the new Part B Pre-Screening informed consent form by the NDA on 15JUL2021.
- Submission and acknowledgement of the interim Safety Monitoring Committee (SMC) safety and immunogenicity report on study Part A (Phase I) and the SMC recommendation for the dose and formulation of *Sm*-TSP-2 to test in study Part B (Phase II) to the GW IRB (04JUN2021), MUSPH IRB (04JUN2021), NDA (13JUL2021), and UNCST (15JUL2021).
- Issuance of continuing review approval (Clinical Trial Certificate for clinical trial protocol TSP-18-03) by the NDA on 28AUG2021.
- Submission and approval of study product importation permits by the Ugandan NDA for all shipments of investigational study product from the USA into Uganda required for Part B of the study (June 2021).
- Submission and approval of recruitment materials (radio message, poster message, appointment outreach card) to GW IRB (approved 08APR2021).
- Importation of first shipment of investigational study product for Part B (49 vials of *Sm*-TSP-2/Alhydrogel® and 49 vials of AP 10-701) from the USA into Uganda (16JUL2021).
- Importation of second shipment of investigational study product for Part B (98 vials of *Sm*-TSP-2/Alhydrogel® and 98 vials of AP 10-701) from the USA into Uganda (13AUG2021).
- Importation of third shipment of investigational study product for Part B (98 vials of *Sm*-TSP-2/Alhydrogel® and 98 vials of AP 10-701) from the USA into Uganda (26AUG2021).
- Importation of fourth shipment of investigational study product for Part B (85 vials of *Sm*-TSP-2/Alhydrogel® and 85 vials of AP 10-701) from the USA into Uganda (17SEP2021). Temperature monitoring during transit indicated two major temperature excursions below 2°C (-31.6°C in Box 1 and -128.3°C in Box 2) due to improper handling by courier. This shipment was quarantined upon receipt and prepared for destruction as directed by the Sponsor.

Major Task 2:

- Site visit by GW laboratory team members (Dr. Bethony and Lara Hoeweler) to MUWRP 21-24JUN2021, in which GW laboratory personnel facilitated training of MUWRP laboratory staff for technology transfer of the anti-*Sm*-TSP-2 IgE assay required for Part B screening.
- Site visit by GW study team members (Drs. Diemert and Bethony, and Lara Hoeweler) to MUWRP 21-23JUN2021 in preparation for initiation Part B of the clinical trial. Training was conducted on the clinical protocol and associated study procedures for Part B.

Major Task 3:

- Completed Part A enrollment (08OCT2020); 90 participants enrolled out of 153 screened.
- Cohort 1:
    - 29 participants completed all Part A study visits as of 27JAN2021. One participant was withdrawn due to moving outside of the study area.

- Cohort 2:
    - 28 participants completed all Part A study visits as of April 2021. Two participants were withdrawn early: one participant was withdrawn due to moving outside of the study area; another participant was withdrawn due to incarceration.
- Cohort 3:
    - Cohort 3 enrollment completed (08OCT2020); 30 participants enrolled.
    - Initiated third vaccinations for second group of Cohort 3 (19NOV2020) that was enrolled after the COVID-19-required pause in enrollment.
    - 29 participants completed third vaccinations as of 28JUN2021. One participant was withdrawn before completing vaccinations due to moving outside of the study area.
    - 26 of the remaining 29 participants have completed Visit 19 (final study visit) as of 22Sep2021. The remaining 3 participants are scheduled to complete Visit 19 in October 2021.
- Fourth, fifth, and sixth interim monitoring visits were completed (OCT2020, FEB2021, AUG2021).
- Completion of interim safety and immunogenicity (*Sm*-TSP-2 IgG results to Day 140) study report.
- Completion of interim Safety Monitoring Committee (SMC) teleconference on 03MAY2021 to review the interim safety and immunogenicity report on Part A of the study.
    - SMC recommendation to proceed to Part B using the 100 µg *Sm*-TSP-2/Alhydrogel® plus AP 10-701 dose/formulation.

Major Task 4:
- Multiple meetings were held in APR-JUN2021 by the MUWRP community engagement team with community leaders in the areas bordering Lake Victoria that are being targeted for recruitment into Part B.
- Built electronic data capture (EDC) database for Part B using OpenClinica.
- Initiation of recruitment and pre-screening for Part B on 29JUL2021 (175 participants pre-screened as of 29SEP2021).
- Initiation of screening for Part B on 09AUG2021 (77 participants screened as of 29SEP2021).

Major Task 5:
- Stability testing of *Sm*-TSP-2/Alhydrogel® Vaccine (Drug Product) Lot # 1975 (M60) (March-May 2021).
- Stability testing of *Sm*-TSP-2/Alhydrogel® Vaccine (Drug Product) Lot #11-69F-003 (M108) (June 2021).
- Stability testing of *Sm*-TSP-2 Bulk Drug Substance Lot # 11-69D-002 (M108) (April 2021).

Major Task 6:
- Discrepancy management and query resolution for study Part A database (April-June 2021)
- Closing out of data management and medical monitor queries on safety data up to and including study Visits 16 (day 140) of all Part A study participants (JAN-MAR 2021).
- Clinical/safety interim database lock conducted in MAR2021 after closeout of all queries.
- Serum samples from Cohort 2 and 3 study participants shipped from MUWRP to GW for Part A interim analysis (received 23MAR2021).
- Optimization of anti-*Sm*-TSP-2 IgG ELISA at GW and completion of assays on Part A study participant serum samples up to and including study day 140 (JAN-APR 2021); this included cleaning, audit, and release of results in April 2021. Results of IgG levels to *Sm*-TSP-2 in serum samples collected from Part A study participants up to and including study day 140 were included in the interim study report that was evaluated by the SMC on 03MAY2021.
- Cryopreservation of whole blood derivatives (serum, plasma, and PBMCs) from Part A participants collected at protocol-designated time points throughout the reporting period.
- First shipment of screening serum samples (n = 30) for Part B volunteers for anti-*Sm*-TSP-2 IgE testing to determine eligibility from MUWRP to GW (received 22SEP2021).
    - Completion of anti-*Sm*-TSP-2 IgE ELISA assay on first shipment of screening serum samples for Part B volunteers and release of results (30SEP2021).

- Shipment of anti-*Sm*-TSP-2 IgE ELISA reagents from GW to MUWRP (SEP2021).
- Completion of fecal (Kato Katz) and urine microscopy testing for ova and parasites as part of pre-screening and screening for study Part B for volunteers recruited within the reporting period.

Additional accomplishments:

- Biweekly conference calls, conducted between the GW and MUWRP project teams to coordinate execution of the clinical trial, were increased to weekly starting in June 2021 to prepare for initiation of Part B.

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?

Cohort 3 of Part A is anticipated to complete final study visits in October 2021, concluding Part A of the study. Data analysis and reporting will begin.

In Year 4 of the project, we will continue recruitment and screening until enrollment into Part B is complete with 200 participants. We anticipate that all volunteers will receive all three vaccinations and follow up visits will be conducted according to study protocol.

Capacity to perform the anti-*Sm*-TSP-2 IgE assay is currently being transferred from GW to MUWRP in Uganda. As of September 2021, quality assurance and optimization activities were still underway prior to giving the green light to conduct this screening assay for Part B study participation.

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 or objectives were made during the reporting period. A minor change in study design was made, to perform a pre-screening step for Part B participation prior to full screening. During pre-screening, potentially eligible volunteers undergo fecal microscopy testing to determine if they are positive for *S. mansoni* eggs, since being positive is a requirement for eligibility in Part B. Only egg-positive participants are then invited to undergo full screening for this part of the study. This minor study design change was approved by all IRBs prior to implementation.

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 did not significantly impact 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 COVID-19 pandemic 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 participants' ability to come into the study site. Participants in Cohort 1 were in the process of receiving their third and final vaccinations just prior to the country lockdown and participants 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 participants. 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 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. Additionally, the Ugandan government announced another lockdown on 18JUN2021 lasting for 42 days that suspended public and private transportation, and restricted travel of study staff and participants to the study site(s).

4. The team experienced multiple issues with shipping logistics that resulted in delayed initiation of Part B and loss of investigational product. As previously reported in Section 3.2 under Major Task 1, 330 vials of *Sm*-TSP-2/Alhydrogel vaccines and 330 vials of AP-701 were shipped from GW to Uganda by World Courier for Part B, split among 4 shipments. One of these shipments had a major temperature excursion to significantly below 0˚C that resulted in the loss of 85 vials of *Sm*-TSP-2/Alhydrogel and 85 vials of the AP 10-701 adjuvant (neither *Sm*-TSP-2/Alhydrogel nor AP 10-701 can be frozen as both lose potency). Additionally, the team experienced prolonged shipping times of up to 10 days with World Courier. To mitigate potential future losses, a different company was selected (Optimize Courier). Reagents for the IgE testing were shipped and delivered by the new courier without issue. This shipping vendor will be used to ship vials of IP to replace those that were frozen during transit.

5.3 Changes that had a significant impact on expenditures

Given the COVID-19 pandemic, the site made changes to the recruitment strategy for Part B of the study 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 is conducting field activities at two landing sites (Ggaba and Kasenyi) and performing stool analysis as a pre-screening activity so that only eligible participants (stool positive for *Schistosoma* ova) are invited 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.) increased significantly in Year 3 of the project as recruitment, enrollment, vaccinations and study visits were initiated; these will continue into Year 4.

The study will incur significant expenditures to replace the ruined vials of vaccine and adjuvant that were frozen during shipment. Since these products do not have commercial value, it was not possible to insure them, and World Courier will not provide reimbursement even though they were directly responsible for the temperature excursion during transit.

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

Protocol version 5.0 was submitted and approved by both the GW and MUSPH IRBs. The changes from version 4.0 to 5.0 consisted primarily of the following:

- Increased screening window for Part B from 60 to 75 days due to the length of time required for shipment of samples to complete the anti-*Sm*-TSP-2 IgE antibody testing.
- Addition of pre-screening visit for Part B requiring provision of a stool sample. Volunteers must test positive for *Schistosoma mansoni* eggs in stool, as assessed by Kato Katz thick smear, to be eligible for Part B participation.
- Addition of a pre-screening informed consent form.
- Change in compensation due to addition of pre-screening visit.

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:	0.5 person months per year
Contribution to Project:	No longer on study team as of NOV2020. Replaced by Laura Vasquez 22DEC2020.
Name:	Samantha Daaka, MPH
Project Role:	Clinical Research Coordinator
Researcher Identifier:	n/a
Nearest person month worked:	1 person month per year
Contribution to Project:	No longer on the study team as of 25MAR2021.
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:	11 person months per year
Contribution to Project:	No change.

George Washington University (GW) Participants:

Name:	Laura Vasquez
Project Role:	Clinical Research Manager
Researcher Identifier:	n/a
Nearest person month worked:	1 person month per year
Contribution to Project:	Ms. Vasquez, an experienced project manager, joined the study team on 22DEC2020. She manages the implementation, data analysis, and reporting of the clinical trial by facilitating execution of clinical trial agreements; creating and managing internal budgets; managing database development; overseeing regulatory activities; and coordinating supply logistics.
Name:	Khadija Khan
Project Role:	Administrative Assistant
Research Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	Ms. Khan joined the study team on 08FEB2021. Ms. Khan performs work in coordinating communications with the trial site, and assisting in the preparation of correspondence, reports and other study documentation.
Name:	Hanna-Grace Rabanes
Project Role:	Clinical Research Coordinator
Research Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	Ms. Rabanes joined the study team on 07JUN2021. Ms. Rabanes coordinates submissions to the IRBs, maintains GCP essential documents related to the trial, assists in database development, and facilitates communications with the trial site.
Name:	Neha Rampally, MPH
Project Role:	Regulatory Compliance Associate
Research Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	Ms. Rampally joined the study team in OCT2020 and left in DEC2020. She performed work in coordinating submissions to the IRBs, coordinating maintenance of GCP essential documents related to the trial, and assisting in the preparation of clinical trial work plans, activity charts and correspondence.
Name:	Lee, Han Na
Project Role:	Laboratory Technician, GW CIL
Research Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Ms. Lee joined the study team in JUN2021. She receives, processes, and store samples received from study site.
Name:	Rafaela Saes
Project Role:	Laboratory Technician, GW CIL
Researcher Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	Ms. Saes joined the study team in NOV2020 and left the study team in MAY2021. She received, processed, and stored samples received from the study site.

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:** Immunogenicity and Safety of SARS-CoV-2 Recombinant Protein Vaccines with AS03 Adjuvant in Adults 18 Years of Age and Older as a Primary Series and Immunogenicity and Safety of a Booster Dose SARS-CoV-2 Adjuvanted Recombinant Protein Vaccines (two Monovalent and one Bivalent)
   1. Funding Agency: Sanofi Pasteur
   2. Goal: The goal of this project is to conduct a Phase II/III clinical trial to test the immunogenicity and safety of the SARS-CoV-2 Recombinant Protein Vaccines with AS03 Adjuvant as well as the booster dose of SARS-CoV-2 Adjuvanted Recombinant Protein Vaccines, which are being developed to prevent COVID-19 disease.
   3. Specific Aims:
      i. Primary (Safety): To assess the safety profile of all participants in each age group and in each study intervention group.
      ii. Primary (Immunogenicity):
         a. Original Phase II Cohort: To assess the neutralizing antibody profile 14 days after the last vaccination in SARS-CoV-2-naïve adults in each study intervention group.
         b. Supplemental Cohort 1: To assess the immune response induced by a booster dose of Monovalent (D614)-AS03 vaccine in each study intervention group.
         c. Supplemental Cohort 2: To assess the immune response induced by a booster dose of Monovalent (B.1.351)-AS03 or Bivalent (D614 + B.1.351)-AS03 in each study intervention group.
         d. Supplemental Variant Prime Cohort 3: To assess the immune response induced by two doses of the Monovalent (B.1.351)-AS03 or the Bivalent (D614 + B.1.351)-AS03 vaccine in each study intervention group.
   4. Start and end date (month/date/year – month/day/year): 2/18/2021 – 10/31/2022
   5. Level of Funding:
   6. Level (%) of effort in the project: 10%

b) **Title of the project:** A Phase 1 Randomized, Double-blinded, Placebo-controlled, Dose-escalation Clinical Trial to Evaluate the Safety and Immunogenicity of rVSVΔG-LASV-GPC Vaccine in Adults in Good General Health
   1. Funding Agency: International AIDS Vaccine Initiative (CEPI is prime)
   2. Goal: The goal of this project is to conduct a Phase 1 clinical trial to test the safety and immunogenicity of the rVSVΔG-LASV-GPC Vaccine that is being developed to prevent Lassa fever.
   3. Specific Aims:
      i. Primary (Safety): To evaluate the safety and tolerability of rVSVΔG-LASV-GPC vaccine
      ii. Secondary:
         a. Immunogenicity: To determine LASV-GPC-specific antibody responses induced by rVSVΔG-LASV-GPC vaccine
         b. Viremia: To evaluate the distribution of the rVSVΔG-LASV-GPC vaccine in plasma in a subset of participants

c. Viral shedding in urine and saliva: To evaluate the viral shedding of the rVSVΔG-LASV-GPC vaccine in urine and saliva in a subset of participants

iii. Exploratory:

a. Immunogenicity: To explore the characteristics of the immune responses induced by rVSVΔG-LASV-GPC vaccine

b. Viral shedding in semen and vaginal fluid: To explore the viral shedding of the rVSVΔG-LASV-GPC vaccine in semen and vaginal fluid in a subset of participants

4. Start and end date (month/date/year – month/day/year): 05/03/2021 – 05/02/2023
5. Level of Funding: Per participant (estimated total =
6. Level (%) of effort in the project: 5%

c) **Title of the project:** A Phase 1, Randomized, First-in-human, Open-label Study to Evaluate the Safety and Immunogenicity of eOD-GT8 60mer mRNA Vaccine (mRNA-1644) and Core-g28v2 60mer mRNA Vaccine (mRNA-1644v2-Core) in HIV-1 Uninfected Adults in Good General Health

1. Funding Agency: International AIDS Vaccine Initiative (Bill & Melinda Gates Foundation is prime)
2. Goal: The goal of this project is to conduct a Phase 1 clinical trial test the safety and immunogenicity of the eOD-GT8 60mer mRNA Vaccine (mRNA-1644) and Core-g28v2 60mer mRNA Vaccine (mRNA-1644v2-Core) that are being developed to prevent infection with HIV
3. Specific Aims:
    i. Primary (Safety and Tolerability): To evaluate the safety and tolerability of the study regimen.
    ii. Secondary (Immunogenicity):
        a. To evaluate the induction of VRC01-class IgG B-cell responses by the study regimen
        b. To evaluate the induction of vaccine-specific and epitope-specific binding antibody responses by the study regimen.
    iii. Exploratory (Immunogenicity):
        a. To assess the degree of maturation of VRC01-class IgG B-cells pre- and post-IP administration within each participant
        b. To evaluate the induction of serum antibody binding responses to the Lumazine synthase component of the study products
        c. To evaluate the induction of CD4 T-cell responses to the study regimen
        d. To evaluate serum neutralization post-IP administration
        e. To evaluate the influence of human antibody gene alleles on the vaccine induction of VRC01-class responses
4. Start and end date (month/date/year – month/day/year): 07/16/2021 – 06/30/2023
5. Level of Funding: Per participant (estimated total =)
6. Level (%) of effort in the project: 7%

ci) **Title of the project:** A Phase 2 Study to Assess the Virologic Efficacy of Regn10933+Regn10987 Across Different Dose Regimens in Outpatients with SARS-CoV-2 Infection

1. Funding Agency: Regeneron Pharmaceuticals, Inc.
2. Goal: This is a Phase 2 randomized, double-blind, placebo-controlled, parallel group study to assess the dose response profile of single intravenous (IV) or single subcutaneous (SC) doses ofREGN10933+REGN10987 in outpatients with SARS-CoV-2 infection.
3. Specific Aims:
    i. Primary: To assess the virologic efficacy of REGN10933+REG10987 across different intravenous and subcutaneous doses compared to placebo.

ii. Secondary:
    a. To evaluate additional indicators of virologic efficacy of REGN10933+REGN10987 compared to placebo.
    b. To evaluate the safety and tolerability of REGN10933+REGN10987 compared to placebo
    c. To assess the concentrations of REGN10933+REGN10987 in serum over time.
    d. To assess the immunogenicity of REGN10933+REGN10987.
4. Start and end date (month/date/year – month/day/year): 01/07/2021 – 08/31/2021
5. Level of Funding:
6. Level (%) of effort in the project: 2%

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

a) **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%.

b) **Title of the project:** A Phase 2 Study to Assess the Virologic Efficacy of Regn10933+Regn10987 Across Different Dose Regimens in Outpatients with SARS-CoV-2 Infection
   1. Funding Agency: Regeneron Pharmaceuticals, Inc.
   2. Goal: This is a Phase 2 randomized, double-blind, placebo-controlled, parallel group study to assess the dose response profile of single intravenous (IV) or single subcutaneous (SC) doses of REGN10933+REGN10987 in outpatients with SARS-CoV-2 infection.
   3. Specific Aims:
      i. Primary: To assess the virologic efficacy of REGN10933+REG10987 across different intravenous and subcutaneous doses compared to placebo.
      ii. Secondary:
          a. To evaluate additional indicators of virologic efficacy of REGN10933+REGN10987 compared to placebo.
          b. To evaluate the safety and tolerability of REGN10933+REGN10987 compared to placebo
          c. To assess the concentrations of REGN10933+REGN10987 in serum over time.
          d. To assess the immunogenicity of REGN10933+REGN10987.
   4. Start and end date (month/date/year – month/day/year): 01/07/2021 – 08/31/2021
   5. Level of Funding:
   6. Level (%) of effort in the project: 2%

7.2.2 Jeffrey Bethony (GW Clinical Immunology Laboratory Director)

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

a) **Title of the project:** Immunogenicity and Safety of SARS-CoV-2 Recombinant Protein Vaccines with AS03 Adjuvant in Adults 18 Years of Age and Older as a Primary Series and

Immunogenicity and Safety of a Booster Dose SARS-CoV-2 Adjuvanted Recombinant Protein Vaccines (two Monovalent and one Bivalent)

1. Funding Agency: Sanofi Pasteur
2. Goal: The goal of this project is to conduct a Phase II/III clinical trial to test the immunogenicity and safety of the SARS-CoV-2 Recombinant Protein Vaccines with AS03 Adjuvant as well as the booster dose of SARS-CoV-2 Adjuvanted Recombinant Protein Vaccines, which are being developed to prevent COVID-19 disease.
3. Specific Aims:
    i. Primary (Safety): To assess the safety profile of all participants in each age group and in each study intervention group.
    ii. Primary (Immunogenicity):
        a. Original Phase II Cohort: To assess the neutralizing antibody profile 14 days after the last vaccination in SARS-CoV-2-naïve adults in each study intervention group.
        b. Supplemental Cohort 1: To assess the immune response induced by a booster dose of Monovalent (D614)-AS03 vaccine in each study intervention group.
        c. Supplemental Cohort 2: To assess the immune response induced by a booster dose of Monovalent (B.1.351)-AS03 or Bivalent (D614 + B.1.351)-AS03 in each study intervention group.
        d. Supplemental Variant Prime Cohort 3: To assess the immune response induced by two doses of the Monovalent (B.1.351)-AS03 or the Bivalent (D614 + B.1.351)-AS03 vaccine in each study intervention group.
4. Start and end date (month/date/year – month/day/year): 2/18/2021 – 10/31/2022
5. Level of Funding:
6. Level (%) of effort in the project: 3%

b) **Title of the project:** A Phase 1 Randomized, Double-blinded, Placebo-controlled, Dose-escalation Clinical Trial to Evaluate the Safety and Immunogenicity of rVSVΔG-LASV-GPC Vaccine in Adults in Good General Health

1. Funding Agency: International AIDS Vaccine Initiative (CEPI is prime)
2. Goal: The goal of this project is to conduct a Phase 1 clinical trial to test the safety and immunogenicity of the rVSVΔG-LASV-GPC Vaccine that is being developed to prevent Lassa fever.
3. Specific Aims:
    i. Primary (Safety): To evaluate the safety and tolerability of rVSVΔG-LASV-GPC vaccine
    ii. Secondary:
        a. Immunogenicity: To determine LASV-GPC-specific antibody responses induced by rVSVΔG-LASV-GPC vaccine
        b. Viremia: To evaluate the distribution of the rVSVΔG-LASV-GPC vaccine in plasma in a subset of participants
        c. Viral shedding in urine and saliva: To evaluate the viral shedding of the rVSVΔG-LASV-GPC vaccine in urine and saliva in a subset of participants
    iii. Exploratory:
        a. Immunogenicity: To explore the characteristics of the immune responses induced by rVSVΔG-LASV-GPC vaccine
        b. Viral shedding in semen and vaginal fluid: To explore the viral shedding of the rVSVΔG-LASV-GPC vaccine in semen and vaginal fluid in a subset of participants
4. Start and end date (month/date/year – month/day/year): 05/03/2021 – 05/02/2023
5. Level of Funding: Per participant (estimated total =)
6. Level (%) of effort in the project: 8%

c) **Title of the project:** A Phase 1, Randomized, First-in-human, Open-label Study to Evaluate the Safety and Immunogenicity of eOD-GT8 60mer mRNA Vaccine (mRNA-1644) and Core-g28v2 60mer mRNA Vaccine (mRNA-1644v2-Core) in HIV-1 Uninfected Adults in Good General Health
   1. Funding Agency: International AIDS Vaccine Initiative (Bill & Melinda Gates Foundation is prime)
   2. Goal: The goal of this project is to conduct a Phase 1 clinical trial test the safety and immunogenicity of the eOD-GT8 60mer mRNA Vaccine (mRNA-1644) and Core-g28v2 60mer mRNA Vaccine (mRNA-1644v2-Core) that are being developed to prevent infection with HIV
   3. Specific Aims:
      i. Primary (Safety and Tolerability): To evaluate the safety and tolerability of the study regimen.
      ii. Secondary (Immunogenicity):
         a. To evaluate the induction of VRC01-class IgG B-cell responses by the study regimen
         b. To evaluate the induction of vaccine-specific and epitope-specific binding antibody responses by the study regimen.
      iii. Exploratory (Immunogenicity):
         a. To assess the degree of maturation of VRC01-class IgG B-cells pre- and post-IP administration within each participant
         b. To evaluate the induction of serum antibody binding responses to the Lumazine synthase component of the study products
         c. To evaluate the induction of CD4 T-cell responses to the study regimen
         d. To evaluate serum neutralization post-IP administration
         e. To evaluate the influence of human antibody gene alleles on the vaccine induction of VRC01-class responses
   4. Start and end date (month/date/year – month/day/year): 07/16/2021 – 06/30/2023
   5. Level of Funding: Per participant (estimated total =)
   6. Level (%) of effort in the project: 7%

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

a) **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%

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:	Musabe Chrispus Bakunda MD
Project Role:	Medical Officer and Study Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	No change.

Name:	Allan Tindikahwa, PharmD
Project Role:	Head, Quality Improvement & Compliance at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	1 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 months 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 months per year
Contribution to Project:	No change.

Name:	Immaculate Nakabuye
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	11 person months per year
Contribution to Project:	No change.

Name:	Jacqueline Sarah Namugabo
Project Role:	Quality Control/Quality Assurance Coordinator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	No change.

Name:	Joseph Wandege
Project Role:	Laboratory Manager at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	No change.

Makerere University Walter Reed Project (MUWRP) Participants:

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

Name:	Ezra Musingye
Project Role:	Data Manager at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	No change.

Name:	Hilda Mutebe
Project Role:	Regulatory Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	No change.

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:	No change.

Name:	Herbert Kityo
Project Role:	Office Attendant at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	3 person months per year
Contribution to Project:	No change.

Name:	Roy Nassaka
Project Role:	Phlebotomist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	No change.

Name:	Lucy Maria Nakayiza
Project Role:	Laboratory Administrator at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	No change.

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:	No change.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Godfrey Zziwa
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	7 person months per year
Contribution to Project:	No change.

Name:	Daniel Kibirige, MD
Project Role:	Medical Officer
Research Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	Dr. Kibirige, an experienced medial officer, joined the study on 11DEC2020. He implements 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:	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:	No change.

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:	No change.

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:	No change.

Name:	Festo Kyambadde Nelson
Project Role:	Data Entry at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	3 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:	6 person months per year
Contribution to Project:	No change.

Name:	Raymond Mayanja
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person month per year
Contribution to Project:	No change.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Andrew Ssenyonga
Project Role:	Records Maintenance Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	No change.

Name:	Joanita Namuli
Project Role:	Clinic Administrative Assistant at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	No change.

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:	No change.

Name:	Jerry Nuwagaba
Project Role:	Laboratory Technologist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	No change.

Name:	Gertrude Nassanga
Project Role:	Data Entry Specialist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	7 person months per year
Contribution to Project:	No change.

Name:	Juliet Kizanye
Project Role:	Data Entry Specialist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	8 person months per year
Contribution to Project:	No change.

Name:	Maimuna Nantabo
Project Role:	Data Entry Specialist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 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:	6 person months per year
Contribution to Project:	No change.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Stephen Mugamba
Project Role:	Community Documentation Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	No change.

Name:	Emmanuel Wasswa
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	No change.

Name:	Talbert Muhwezi
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	Mr. Muhwezi is an experienced clinical research nurse. He 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. He participates in recruitment and consenting of eligible participants, counseling, transcription of results and resolution of data queries. (Misgendered in Y2 annual report. Corrected in Y3Q1 report.)

Name:	Jowali Nangu
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	No change.

Name:	Josephine Nakakeeto
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 person months worked
Contribution to Project:	Ms. Nakakeeto is an experienced clinical research nurse who joined the study on 15DEC2020. 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 participants enrolled. She participates in recruitment and consenting of eligible participants, counseling, transcription of results and resolution of data queries.

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:	0.5 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:	0.5 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:	1 person month 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 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 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:	1 person month per year
Contribution to Project:	No change.

Name:	Ghada Launey, BS
Project Role:	QA/Regulatory Affairs Program Associate, TCH-CVD at BCM
Researcher Identifier:	n/a
Nearest person month worked:	1 person month per year
Contribution to Project:	No change.

8 SPECIAL REPORTING REQUIREMENTS

- Quad Chart for Year 3 of the project (see Appendix A)

9 APPENDICES

Appendix A: Quad Chart for Year 3 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: From left to right, Dr. Chrispus Bakunda, Dr. David Diemert, Lara Hoeweler, Dr. Jeffrey Bethony, and Dr. Betty Mwesigwa at the study site in the fishing village of Kisenyi, Uganda, in preparation for the Phase 2 portion of the trial.

Accomplishment: Completion of Cohorts 1 and 2 study visits for study Part A. Initiation of study Part B recruitment.

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: 25OCT2021

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.
- COVID-19 restrictions in Uganda led to delays initiating Part B recruitment.

Budget Expenditure to Date

Projected Expenditure: $3,902,321 Actual Expenditure: $2,446,470