AWARD NUMBER: W81XWH-18-1-0672

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

PRINCIPAL INVESTIGATOR: David Diemert

CONTRACTING ORGANIZATION: George Washington University

REPORT DATE: October 2022

TYPE OF REPORT: Annual Technical 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 2022	Annual Technical Report	30 Sept 2021 – 29 Sept 2022

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

6. AUTHOR(S)
David Diemert, MD
Professor, Dept. of Medicine, School of Medicine and Health Sciences
George Washington University
E-Mail: ddiemert@gwu.edu

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. 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 Part A study visits on 29OCT2021 and completion of enrollment into Part B on 13JUL2022. All Part B vaccinations will be completed in NOV2022 and Part B participants are expected to complete follow-up visits in September 2024.

15. PARTICIPANT TERMS

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

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION**	**18. NUMBER**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRDC
U	U	U	UU	28	**19b. TELEPHONE NUMBER** *(include area code)*

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

Page

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 4 annual reporting period, follow-up visits for Part A were completed and enrollment into Part B was completed. In Part A of the study, 85 of the 90 enrolled participants completed the study whereas 5 participants were withdrawn early. Two hundred participants were successfully enrolled into Part B.

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

Major Task 1:
- Approval of Part B Assessment of Understanding V3.0 (AOU) by the Makerere University School of Public Health (MUSPH) IRB on 15NOV2021.
- Submission of Part B AOU V3.0 to the Uganda National Council of Science and Technology (UNCST) in November 2021.
- Submission and approval of Part B AOU V3.0 by the Ugandan National Drug Authority (NDA) on 23MAR2022.
- Submission and approval of Part B Informed Consent Form (ICF) V4.1, Pre-screening ICF V1.1, and Future Use ICF V2.1 by the George Washington University (GW) IRB on 28DEC2021.
- Submission and approval of Part B ICF V4.1, Pre-screening ICF V1.1, and Future Use ICF V2.1 by the Makerere University School of Public Health (MUSPH) IRB on 14JAN2022.
- Submission and acknowledgement of Part B ICF V4.1, Pre-screening ICF V1.1, and Future Use ICF V2.1 by the UNCST on 20JUN2022.
- Submission and acknowledgement of Part B Informed Consent Form (ICF) V4.1, Pre-screening ICF V1.1, Future Use ICF V2.1 by the NDA on 24JAN2022.
- Submission and approval of the annual continuing review by the GW IRB on 25JAN2022.
- Submission and approval of the annual continuing review by the MUSPH IRB on 04FEB2022.
- Submission and approval of the annual continuing review by the UNCST on 09MAY2022.
- Submission and approval of the annual continuing review by the NDA 04AUG2022.
- Shipment of investigational study product for Part B (65 vials of *Sm*-TSP-2/Alhydrogel® and 65 vials of AP 10-701) to Makerere University Walter Reed Project (MUWRP) (10MAR2022).

Major Task 2:
- Completion of Protocol V5.0 training for Part B and continued updating of training on GCP, HSP and SOPs.

Major Task 3:
- Follow-up visits for Part A were completed on 29OCT2021. 85 of the 90 enrolled participants completed study Part A and 5 participants were withdrawn from study Part A.

Major Task 4:
Completed tasks for Part B of the study during the reporting period:
- 551 participants were pre-screened.
- 330 participants completed study screening.

- *Milestone Achieved*: *First* participant enrolled into Part B on 11OCT2021.
- Enrollment target of 200 participants was reached on 13JUL2022.
- 189 participants completed second vaccinations.
- 159 participants completed third vaccinations.
- Completion of seventh interim monitoring visit in December 2021.
- Completion of eighth interim monitoring visit in March 2022.
- Completion of ninth interim monitoring visit in August 2022.

Major Task 5:
- Stability testing of *Sm*-TSP-2/Alhydrogel® Vaccine (Drug Product) Lot # 1975 (M72) in March 2022.
- Stability testing of AP 10-701 Lot # 19E002 (M33) in February 2022.
- Stability testing of AP 10-701 Lot # 19E002 (M36) in May 2022.
- Stability testing of AP 10-701 Lot # 19E002 (M39) executed in August 2022, results pending.

Major Task 6:
Completed laboratory and data analysis tasks during the reporting period:
- Managed discrepancies and resolved queries in study Part A clinical database to prepare for Part A clinical database lock.
- Configured and tested programmed edit checks for study Part B clinical database.
- Cryopreservation of whole blood derivatives (serum, plasma, and PBMCs) from Part A and Part B participants collected at protocol-designated time points.
- Completion of seven shipments of screening serum samples from MUWRP to GW for anti-*Sm*-TSP-2 IgE testing to determine eligibility of Part B volunteers.
- Completion of anti-*Sm*-TSP-2 IgE ELISA assays by GW on all screening serum samples by February 2022.
- Completion of anti-*Sm*-TSP-2 IgE ELISA assays by MUWRP and remote troubleshooting by GW as part of technology transfer of the anti-*Sm*-TSP-2 IgE screening assay from GW to MUWRP.
- Completion of fecal (Kato Katz) and urine microscopy testing for ova and parasites as part of pre-screening and screening for Part B volunteers.
- Initiation and completion of cell-mediated immunity assays on PBMC (peripheral blood mononuclear cell) aliquots from Part A volunteers (20SEP2022).
- Completion of anti-*Sm*-TSP-2 ELISA assays for all IgG subclasses on Part A study participant serum samples up to and including day 380 (31MAY2022).
- Statistical analysis of IgG subclass ELISA assay results.

Additional accomplishments:
- Weekly conference calls, conducted between the GW and MUWRP project teams to coordinate execution of the clinical trial, continued through June 2022, and were decreased to biweekly starting in July 2022 as enrollment was completed for 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 completed final study visits on 08OCT2021, concluding Part A of the study. We expect to lock the Part A clinical database in October-November 2022.

Enrollment of 200 participants into Part B was completed on 13JUL2022. In Year 5 of the project, we will continue follow-up and sample collection with Part B participants according to the 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

A protocol clarification memorandum was approved by the sponsor with respect to the current version of the protocol (Version 5.0), specifying that only 6 mL of venous blood should be collected for antibody assays, rather than the 10 mL of blood specified by the protocol. This change was made because the experience to date for this clinical trial is that the study's research laboratory can effectively and efficiently complete the per-protocol antibody assays per study visit using a volume of serum significantly less than what is obtained from 10 mL of whole blood. Given the volume of blood to be collected will be less than originally planned, this does not increase risk for study participants. This change will be incorporated into the next protocol amendment.

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 Oct. 8, 2020.
   Unfortunately, in June 2021, Uganda and especially Kampala began to experience a new wave of COVID-19 infections and the government imposed another stringent lockdown on June 18, 2021 lasting for 42 days that suspended public and private transportation, and restricted travel of study staff and participants to the study site(s). This resulted in another delay in the clinical trial and in particular, initial recruitment for Part B of the study. The Ugandan government partially lifted the lockdown on July 30, 2021, but maintained a nighttime curfew and restrictions on vehicle occupancy. Restrictions slowly eased in subsequent months and the curfew was fully lifted on January 24, 2022, allowing for an acceleration of the pace of screening and enrollment.
4. As previously reported, the team experienced multiple issues with shipping logistics that resulted in delayed initiation of Part B and loss of investigational product. 330 vials of *Sm*-TSP-2/Alhydrogel vaccines and 330 vials of AP-701, split among 4 shipments, were shipped from GW to Uganda by World Courier for Part B between July – September 2021. 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). Optimize Courier was used to ship vials of IP (65 vials of *Sm*-TSP-2/Alhydrogel® and 65 vials of AP 10-701) from GW to MUWRP in March 2022 to replace those that had been frozen during transit.
5. For various reasons, some participants deemed eligible during screening for Part B declined to enroll in the study. To encourage retention of eligible participants, MUWRP began to offer participants transportation services between the satellite clinic and the main clinic in Nakasero in November 2021.

It was furthermore decided that participants would only be invited to the main clinic for IP administration visits. All other follow-up visits, in addition to screening visits, would be conducted at Kasenyi or in the field. The study team issued a Recruitment Review Report (dated Jan. 25, 2022) wherein it was concluded that Kasenyi remained a viable recruitment site and would be used to complete the reminder of enrollment into the study, instead of opening recruitment at additional sites.

6. Despite conducting multiple investigational runs of the anti-*Sm*-TSP-2 IgE assay at MUWRP in Uganda under the remote oversight of GW, ongoing technical challenges prevented the successful transfer of capacity to perform the anti-*Sm*-TSP-2 IgE assay at MUWRP. All IgE screening assays for Part B were therefore conducted at GW.

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 were limitations in the number of passengers per public vehicle, which resulted in increased costs of public transportation. Additionally, there was an increased risk of exposure to COVID-19 as the majority of passengers were not following the recommended prevention guidelines and the vehicles were not sanitized. To that end, these issues impacted the number of participants that could be safely seen at the site particularly for screening activities. Therefore, MUWRP conducted field activities at a landing site on Lake Victoria (Kasenyi) and performed stool analysis as a pre-screening activity so that only eligible participants (stool positive for *Schistosoma* ova) were 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 continued into Year 4.

The study incurred 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 did 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

Nothing to report.

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:	0.5 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:	10 person months per year
Contribution to Project:	No change.

Name:	Laura Vasquez
Project Role:	Clinical Research Manager
Researcher Identifier:	n/a
Nearest person month worked:	0.5 person months per year
Contribution to Project:	No change.

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 left the study team on 08JUL2022

George Washington University (GW) Participants:

Name:	Hanna-Grace Rabanes
Project Role:	Clinical Research Coordinator
Research Identifier:	n/a
Nearest person month worked:	1 person month per year
Contribution to Project:	No change.

Name:	Lee, Han Na
Project Role:	Laboratory Technician, GW CIL
Research Identifier:	n/a
Nearest person month worked:	3 person months 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 <u>started</u> in reporting period:

a) **Title of the project:** Phase 2 Clinical Trial to Optimize Immune Coverage of SARS-CoV-2 Existing and Emerging Variants (COVID-19 Adaptive Variant Immunologic Landscape Trial) (COVAIL)
   1. Funding Agency: Leidos Biomedical Research, Inc. / NIH/NCI
   2. Goal: The goal of this phase 2 clinical trial is to evaluate the safety and immunogenicity of additional doses of prototype and variant (alone or in combination) vaccine candidates in previously vaccinated participants with or without prior SARS-CoV-2 infection and to evaluate innate, cellular, and humoral immune responses to inform on how to shift the immune response to cover new variants as they emerge.
   3. Specific Aims:
      i. Primary: To evaluate humoral immune responses of candidate SARS-CoV-2 variant vaccines, alone or in combination.
      ii. Secondary: To evaluate the safety of candidate SARS-CoV-2 variant vaccines, as assessed by:
         a. Local and systemic solicited Adverse Events for 7 days following each vaccine dose.
         b. Unsolicited Adverse Events from Dose 1 to 28 days following each vaccine dose.
         c. SAEs, MAAEs, AESIs, NOCMCs, and AEs leading to withdrawal from the study from Dose 1 to 12 months after last vaccine dose.
      iii. Exploratory:
         a. To assess, in at least a subset of samples, the B cell immune response of candidate SARS-CoV-2 variant vaccines.
         b. To assess, in at least a subset of samples, the SARS-CoV-2 spike protein-specific T cell responses of candidate SARS-CoV-2 variant vaccines.
         c. To assess, in at least a subset of samples, the magnitude, phenotype, and percentage of innate immune cells with candidate SARS-CoV-2 variant vaccines.
         d. To assess, in at least a subset of samples, the functional potential of SARS-CoV-2 specific antibodies to mediate Fc-effector functions across candidate SARS-CoV-2 variant vaccines.
         e. To evaluate breakthrough SARS-CoV-2 infection by sequencing strains for variant spike lineage and assessing anti- nucleocapsid serology.
   4. Start and end date (month/date/year – month/day/year): 2/19/2022 – 12/31/2023
   5. Level of Funding:
   6. Level (%) of effort in the project: 15%

b) **Title of the project:** A Phase 2 Randomized, Open-Label, Multisite Trial to Evaluate the Immunogenicity of Dose Reduction Strategies of the MVA-BN Vaccine (DoSES)
   1. Funding Agency: Leidos Biomedical Research, Inc. / NIH/NIAID
   2. Goal: The goal of this study is to evaluate dose sparing strategies to extend the vaccine supply during this global public health crisis.
   3. Specific Aims:
      i. Primary:

a. To determine if peak humoral immune responses following an ID regimen of 2 x 10^7 $TCID_{50}$ MVA-BN are non-inferior to the licensed regimen of 1 x 10^8 MVA-BN administered SC
b. To determine if peak humoral immune responses following an ID regimen of 1 x 10^7 $TCID_{50}$ MVA-BN are non-inferior to the licensed regimen of 1 x 10^8 MVA-BN administered SC

ii. Secondary:
a. To determine if individual peak humoral immune responses following each ID regimen are non-inferior to the licensed regimen administered SC
b. To evaluate humoral immune responses of each ID regimen (separately) compared to licensed SC regimen each study day.
c. To evaluate the kinetics of the humoral immune responses of each ID regimen (separately) compared to licensed SC regimen through Day 365
d. To compare relative safety among study arms as assessed by systemic and local reactogenicity for 14 days after each vaccination, unsolicited adverse events for 28 days after each vaccination, and serious adverse events (SAE) and medically attended events (MAAE) from Day 1 through Day 57, and related SAE/MAAEs through Day 181

iii. Exploratory:
a. To evaluate other measures of the humoral immune responses for each regimen
b. To evaluate humoral immune responses of each ID regimen (separately) compared to licensed dose administered SC to monkeypox virus.

4. Start and end date (month/date/year – month/day/year): 9/1/2022 – 8/31/2024
5. Level of Funding:
6. Level (%) of effort in the project: 2%

c) **Title of the project:** Controlled Infection Trial to Test Efficacy of Hookworm Vaccine with Different TLR Agonists
1. Funding Agency: NIH/NIAID
2. Goal: The overall goal is to conduct a Phase 2a clinical trial of the efficacy of different formulations of the *Na*-GST-1 hookworm vaccine assessed using the Controlled Human Hookworm Infection model in unexposed adults. Note that this is the T4 extension mechanism of the original award.
3. Specific Aims:
i. Primary:
a. To compare the impact of vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on controlled human hookworm infection (CHHI) with *N. americanus* larvae in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
b. To evaluate the safety and reactogenicity of *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on Days 0, 56 and 112, in healthy, hookworm-naïve adults.

ii. Secondary:
a. To compare the impact of vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on fecal egg counts, as determined by the McMaster method, after controlled human hookworm infection (CHHI) with *N. americanus* larvae in healthy, hookworm-naïve adults.

b. To assess the relationship between antibody responses to *Na*-GST-1 induced by vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701or CpG 10104 and responses to CHHI in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
c. To assess the duration of antibody responses to *Na*-GST-1 induced by vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104.
d. To assess the impact of vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on the affinity of antibody-antigen interactions, and how affinity relates to responses to CHHI in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
e. To assess the relationship between *Na*-GST-1 specific memory B cells induced by vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 and responses to CHHI in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
f. To assess the relationship between innate immune responses to *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 and responses to CHHI in healthy, hookworm-naïve adults.

iii. Exploratory:
a. To assess the relationship between the functional capacity of vaccine-induced antibodies that neutralize the *in vitro* activity of native *Na*-GST-1 enzyme and responses to CHHI in healthy, hookworm-naïve adults.
b. To compare the impact of vaccination with Na-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on levels of hookworm DNA as detected by real-time PCR in healthy, hookworm-naïve adults challenged with CHHI, as determined by the presence of eggs using a qualified flotation technique.

4. Start and end date (month/day/year – month/day/year): 5/1/2022 – 4/30/2023
5. Level of Funding:
6. Level (%) of effort in the project: 10%

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

a) **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 master protocol to further evaluate the efficacy and safety of co-administered REGN10933+REGN10987 in ambulatory patients (i.e., outpatients) with COVID-19.
3. Specific Aim:
i. Phase 1: The primary objectives of phase 1 are:
a. To evaluate the safety and tolerability of REGN10933+REGN10987 compared to placebo
b. To evaluate the virologic efficacy of REGN10933+REGN10987 compared to placebo in reducing viral load of SARS-CoV-2
ii. Phase 2: The primary objective of phase 2 is to evaluate the virologic efficacy of REGN10933+REGN10987 compared to placebo in reducing viral load of SARS-CoV-2.
iii. Phase 3:

a. Cohort 1 (≥18 Years Old, Not Pregnant at Randomization): The primary objective is to evaluate the clinical efficacy of REGN10933+REGN10987 compared to placebo as measured by COVID-19-related hospitalizations or all-cause death.
b. Cohort 2 (<18 Years Old, Not Pregnant at Randomization): The primary objectives are to evaluate the safety and tolerability of REGN10933+REGN10987 compared to placebo and to further characterize the concentrations of REGN10933 and REGN10987 in serum over time.
c. Cohort 3 (Pregnant at Randomization): The primary objective is to evaluate the safety and tolerability of REGN10933+REGN10987

4. Start and end date (month/day/year – month/day/year): 6/19/2020 – 6/30/2022
5. Level of Funding:
6. Level (%) of effort in the project: 5%

b) **Title of the project:** Controlled Infection Trial to Test Efficacy of Hookworm Vaccine with Different TLR Agonists
1. Funding Agency: NIH/NIAID
2. Goal: The overall goal is to conduct a Phase 2a clinical trial of the efficacy of different formulations of the *Na*-GST-1 hookworm vaccine assessed using the Controlled Human Hookworm Infection model in unexposed adults. Note that this is the original award.
3. Specific Aims:
   i. Primary:
      a. To compare the impact of vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on controlled human hookworm infection (CHHI) with *N. americanus* larvae in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
      b. To evaluate the safety and reactogenicity of *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on Days 0, 56 and 112, in healthy, hookworm-naïve adults.
   ii. Secondary:
      a. To compare the impact of vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on fecal egg counts, as determined by the McMaster method, after controlled human hookworm infection (CHHI) with *N. americanus* larvae in healthy, hookworm-naïve adults.
      b. To assess the relationship between antibody responses to *Na*-GST-1 induced by vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701or CpG 10104 and responses to CHHI in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
      c. To assess the duration of antibody responses to *Na*-GST-1 induced by vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104.
      d. To assess the impact of vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on the affinity of antibody-antigen interactions, and how affinity relates to responses to CHHI in healthy, hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.
      e. To assess the relationship between *Na*-GST-1 specific memory B cells induced by vaccination with *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 and responses to CHHI in healthy,

hookworm-naïve adults, as determined by the presence of eggs using a qualified flotation technique.

f. To assess the relationship between innate immune responses to *Na*-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 and responses to CHHI in healthy, hookworm-naïve adults.

iii. Exploratory:

a. To assess the relationship between the functional capacity of vaccine-induced antibodies that neutralize the *in vitro* activity of native *Na*-GST-1 enzyme and responses to CHHI in healthy, hookworm-naïve adults.

b. To compare the impact of vaccination with Na-GST-1/Alhydrogel® delivered with or without AP 10-701 or CpG 10104 on levels of hookworm DNA as detected by real-time PCR in healthy, hookworm-naïve adults challenged with CHHI, as determined by the presence of eggs using a qualified flotation technique.

4. Start and end date (month/day/year – month/day/year): 5/01/2017 – 4/30/2022
5. Level of Funding:
6. Level (%) of effort in the project: 7%

c) **Title of the project:** Current Good Manufacturing Practice Production of *Trichuris trichiura* for Controlled Human Infection

1. Funding Agency: Medical Science & Computing LLC / NIH/NIAID
2. Goal: The major goals of this contract are for cGMP production of eggs from the human parasite *Trichuris trichiura*, which will be isolated from a healthy human donor for use in a Controlled Human Trichuris Infection model as well as the preparation of an Investigational New Drug Application (IND) to the US-FDA for Controlled Human Trichuris Infection model.
3. Specific Aims:
    i. cGMP production of eggs from the human parasite Trichuris trichiura.
    ii. Preparation of an Investigational New Drug Application (IND) to the US-FDA for Controlled Human Trichuris Infection model.
4. Start and end date (month/day/year – month/day/year): 9/8/2021 – 9/9/2022
5. Level of Funding:
6. Level (%) of effort in the project: 3%

7.2.2 Jeffrey Bethony (GW Clinical Immunology Laboratory Director)

Other Support that started in reporting period:

a) **Title of the project:** Phase 2 Clinical Trial to Optimize Immune Coverage of SARS-CoV-2 Existing and Emerging Variants (COVID-19 Adaptive Variant Immunologic Landscape Trial) (COVAIL)

1. Funding Agency: Leidos
2. Goal: The goal of this phase 2 clinical trial is to evaluate the safety and immunogenicity of additional doses of prototype and variant (alone or in combination) vaccine candidates in previously vaccinated participants with or without prior SARS-CoV-2 infection and to evaluate innate, cellular, and humoral immune responses to inform on how to shift the immune response to cover new variants as they emerge.
3. Specific Aims:
    i. Primary: To evaluate humoral immune responses of candidate SARS-CoV-2 variant vaccines, alone or in combination.
    ii. Secondary: To evaluate the safety of candidate SARS-CoV-2 variant vaccines, as assessed by:
        a. Local and systemic solicited Adverse Events for 7 days following each vaccine dose.

b. Unsolicited Adverse Events from Dose 1 to 28 days following each vaccine dose.
c. SAEs, MAAEs, AESIs, NOCMCs, and AEs leading to withdrawal from the study from Dose 1 to 12 months after last vaccine dose.

iii. Exploratory:

a. To assess, in at least a subset of samples, the B cell immune response of candidate SARS-CoV-2 variant vaccines.
b. To assess, in at least a subset of samples, the SARS-CoV-2 spike protein-specific T cell responses of candidate SARS-CoV-2 variant vaccines.
c. To assess, in at least a subset of samples, the magnitude, phenotype, and percentage of innate immune cells with candidate SARS-CoV-2 variant vaccines.
d. To assess, in at least a subset of samples, the functional potential of SARS-CoV-2 specific antibodies to mediate Fc-effector functions across candidate SARS-CoV-2 variant vaccines.
e. To evaluate breakthrough SARS-CoV-2 infection by sequencing strains for variant spike lineage and assessing anti- nucleocapsid serology.

4. Start and end date (date (month/date/year – month/day/year): 2/18/2022 – 12/31/2023
5. Level of Funding:
6. Level (%) of effort in the project: 2%

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

a) 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:	0000-0001-6911-2199 (ORCID ID)
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:	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:	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:	Allan Tindikahwa left the study team on 31MAY2022.

Name:	Grace Mirembe, MD
Project Role:	Medical Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	4 person months per year
Contribution to Project:	Dr. Mirembe is an experienced medical officer who joined the study on 16NOV2021. She implements the day-to-day clinical trial activities including eligibility checks, enrollment of participants, collection of clinical data, specimens and follow-up of all participants enrolled.

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.

Makerere University Walter Reed Project (MUWRP) Participants:

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.

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 left the study team on 15DEC2021.

Name:	Job Kasule, MD
Project Role:	Medical Officer
Research Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	Dr. Kasule is an experienced medical officer who joined the study on 21DEC2021. He implements the day-to-day clinical trial activities including eligibility checks, enrollment of 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:	No change.

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.

Makerere University Walter Reed Project (MUWRP) Participants:

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.

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:	Maimuna Nantabo left the study team on 19OCT2021.

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:	No change.

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:	No change.

Name:	Winfred Nansalire
Project Role:	Research Nurse at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	Ms. Nansalire is an experienced clinical research nurse who joined the study team on 16NOV2021. 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.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Annet Namusisi
Project Role:	QA/QC Officer at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	Ms. Namusisi is an experienced QA/QC officer who joined the study team on 20OCT2021. She works with the PI, study coordinator, CQI and Compliance coordinator to ensure that study activities and processes are conducted as per protocol and related SOPs as well as keeping up to date with all related quality and research ethics legislation and compliance issues.
Name:	Sharon Namubiru
Project Role:	Clinic Administrative Assistant at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	5 person months per year
Contribution to Project:	Ms. Namubiru is an experienced Clinical Administrative Assistant who joined the study team on 16NOV2021. She is responsible for directing volunteers to the required offices, ensuring that they are kept posted of the clinic procedures/processes and works with the research team to increase efficiency of their flow in the clinic as well as filing of documents as directed.
Name:	Habert Mabonga
Project Role:	Phlebotomist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	2 person months per year
Contribution to Project:	Mr. Mabonga is an experienced phlebotomist who joined the study team on 16NOV2021. He supports the research team to draw blood from participants as per protocol, prepares samples collected for shipment to the appropriate Labs and received and files laboratory results per site SOPs.
Name:	Alex Ogwal
Project Role:	Biomedical Scientist at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	6 person months per year
Contribution to Project:	Mr. Ogwal was responsible for (among other duties) Specimen processing, molecular and immunological diagnostics and results reporting. Alex Ogwal left the study team on 12APR2022.
Name:	Irene Karungi
Project Role:	Medical Officer
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	Dr Karungi is an experienced medical officer who joined the study on 17FEB2022. She implements the day-to-day clinical trial activities including eligibility checks, enrollment of participants, collection of clinical data, specimens and follow-up of all

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Zulaika Namusisi
Project Role:	Research Nurse
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	Ms. Namusisi is an experienced clinical research nurse who joined the study team on 17FEB2022. She 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.

Name:	Lilian Kalenda
Project Role:	Data Entry Specialist
Researcher Identifier:	n/a
Nearest person month worked:	7 person months per year
Contribution to Project:	Ms. Kalenda is an experienced data entry specialist who joined the study team on 17FEB2022. She is responsible for capturing and cleaning data as well as filing CRFs and other data documentation. She also carries out manual and electronic data capture and query resolution.

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:	1 person month 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:	1 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:	0.5 person month per year
Contribution to Project:	Amy Gonzalez left the study team on 17JUN2022

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 4 of the project (see Appendix A)

9 APPENDICES

Appendix A: Quad Chart for Year 4 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:** $4,857,840

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: Members of the Makerere University Walter Reed Project (MUWRP) team with visitors Dr. Jeffrey Bethony, Lara Hoeweler and Dr. David Diemert at the primary research clinic in Kampala.

Accomplishment: Completion of Part A study visits and enrollment of 200 volunteers into study Part B.

Timeline and Cost

Activities / CY	18	19	20	21	22	23
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: OCT2022

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 in Part B recruitment.

Budget Expenditure to Date

Projected Expenditure: $4,758,022 Actual Expenditure: $3,518,460