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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

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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 as 100-mcg with AP 10-701) 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. Part A study visits were completed on 29OCT2021 in Year 4. Progress to date in the current reporting period consists of completion of all Part B vaccinations in NOV2022. Part B participants are expected to complete follow-up visits in August 2024.

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

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

Major Task 1: Obtain IRB and Regulatory Approvals for Phase I/II Clinical Trial

- Submission and approval of 2022 Continuing Review by the George Washington University (GW) IRB on 10JAN2023.
- Submission and approval of 2022 Continuing Review by the Makerere University School of Public Health (MUSPH) IRB on 23FEB2023.
- Notification of MUSPH IRB 2022 Continuing Review Approval to the Uganda National Council of Science and Technology (UNCST) on 27FEB2023.
- Submission and approval of Protocol V6.0, Part B Informed Consent Form (ICF) V4.2, Future Use ICF V2.2, Withdrawal of Consent for Future Use V2.0, Withdrawal of Consent for Future Use V2.1 by the GW IRB on 21FEB2023.
- Submission and approval of Protocol V6.0, Part B ICF V4.2, Future Use ICF V2.2, Withdrawal of Consent for Future Use V2.1 by the MUSPH IRB on 12MAR2023.
- Approval of Protocol V6.0, Part B ICF V4.2, Future Use ICF V2.2, Withdrawal of Consent for Future Use V2.1 by the Ugandan National Drug Authority (NDA) on 19APR2023.
- Submission of Protocol V6.0, Part B ICF V4.2, Future Use ICF V2.2, Withdrawal of Consent for Future Use V2.1 by the UNCST on 15MAR2023.
- Submission and acknowledgement of Protocol V6.0, Part B ICF V4.2, Future Use ICF V2.2, Withdrawal of Consent for Future Use V2.1 to the Ugandan NDA on 15MAR2023.
- Submission and acknowledgement of Promptly Reportable Information Form (PRIF) for incarceration of TSP-UG-670 to GW IRB (26MAY2023) and MUSPH IRB (11MAY2023).

Major Task 2: Train MUWRP Study Staff for Clinical Trial

- Nothing to report.

Major Task 3: Study Part A (Phase I) Participant Recruitment, Vaccination, and Follow-up

- Nothing to report.

Major Task 4: Part B (Phase II) Participant Recruitment, Vaccination, and Follow-up

- All Part B vaccinations were completed in NOV2022 (184 participants completed third vaccinations).
- Of the 200 participants enrolled, 17 were withdrawn (mainly due to loss to follow-up or lack of availability) and 183 participants remain active.
- Completion of tenth interim monitoring visit in January 2023.
- Completion of eleventh interim monitoring visit in May 2023.

Major Task 5: Laboratory and Data Analyses (Product Stability Testing)

- Stability testing of *Sm*-TSP-2 Bulk Drug Substance Lot #11-69D-002 in April 2023 (M132).
- Stability testing of *Sm*-TSP-2 Drug Product Lot #11-69F-003 in July 2023 (M132).
- Stability testing of *Sm*-TSP-2 Drug Product Lot #1975 in March 2023 (M84).

- Stability testing of AP 10-701 Lot # 19E002 (M42) in December 2022 (lot rejected – no further testing).

Major Task 6: Laboratory and Data Analyses

- Completion of statistical analysis of IgG subclass ELISA assay results in November 2022.
- Shipment of biological specimens from Part B participants from MUWRP to GW for analysis.
- Ongoing of *Sm*-TSP-2 IgG and IgG subclassing assays on Part A participant serum samples collected on Visit 17 (day 200), Visit 18 (Day 290), and Visit 19 (day 380).
- Management of discrepancies and resolution of queries in study Part A clinical database throughout the reporting period to prepare for the Part A clinical database lock.
- Final data cleaning and approvals for Part A clinical database lock completed 06JUN2023.
- Part A immunology databases locked as of 12JUN2023.
- Completed cryopreservation of while blood derivatives (serum, plasma, and PBMCs) from Part B participants collected at protocol-designated time points throughout the reporting period.

Major Task 7: Report Findings

- Nothing to report.

Additional accomplishments:

- MUWRP site visit by members of the GW project team to share Part A immunogenicity results in OCT2022.
- Prepared Blinded Interim Safety Summary Report #3 with accumulated safety data for Part B through 02DEC2022 and presented to the Safety Monitoring Committee (SMC) on 04APR2023. The SMC recommended continuation of the trial without modification (i.e., “no issues”).
- Conference calls between the GW and MUWRP project teams continued throughout the reporting period to coordinate execution of the clinical trial.

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?

In Year 6 of the project, we will continue follow-up and sample collection with Part B participants according to the study protocol. All visits are expected to be completed in SEP2024. Database queries will remain ongoing until Part B database lock.

We will complete Part A serum analyses (for visits 17-19) and Part B serum analyses (for visits 2-15). We will complete Part A immunological analyses and begin Part B immunological analyses. We will conduct parasitological analyses on biological specimens collected from study participants from visit 17.

The GW team will conduct two additional oversight visits at MUWRP in the next period.

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 modification from Version 5.0 to Version 6.0 was approved to incorporate provisions from protocol clarification memos, as previously reported.

A protocol clarification memorandum was approved by the sponsor 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.

Additional protocol changes included the removal of blood collection for cellular immunology assays on days 290 and 800. Preliminary review of Part A immunogenicity results suggests that sufficient cellular immunology data can be obtained with sampling at fewer time points, thus reducing the amount of blood required per study participant and thereby reducing risk. Furthermore, the inclusion of a blood collection for cellular immunology assays at the final study visit was an error given that the reason for performing these assays is to correlate with risk of subsequent infection with *Schistosoma mansoni.*

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.

The contracted vendor for local site monitoring has not satisfactorily fulfilled the duties of the agreement, despite repeated attempts to resolve the issue over the course of the year. This challenge necessitates additional site visits by the GW team to conduct source document verification and will result in increased travel expenses compared to local site monitoring.

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:	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:	8 person months per year
Contribution to Project:	No change.

Name:	Hanna-Grace Rabanes
Project Role:	Clinical Research Coordinator
Research Identifier:	n/a
Nearest person month worked:	0.5 person month per year
Contribution to Project:	Left study on 30 June 2023.

Name:	Norma Nardi
Project Role:	Clinical Research Coordinator
Research Identifier:	n/a
Nearest person month worked:	2 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 started in reporting period:

a) **Title of the project:** Phase 1/2 study to assess the safety and immunogenicity of a broadly protective mRNA vaccine JCXH-221 against SARS-CoV-2 infection and diseases (Protocol #JCXH-221-001)
   1. Funding Agency: Immorna Biotherapeutics
   2. Goal: The overall goal is to conduct a Phase 1/2 clinical trial to evaluate the safety and immunogenicity of the JCXH-221 against SARS-CoV-2 vaccine in adults.
   3. Start and end date: 04/2023 – 03/2025
   4. Level of Funding: $600,000
   5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2023	0.48 calendar
2. 2024	0.48 calendar

b) **Title of the project:** A Master Protocol to Evaluate the Safety, Tolerability, and Immunogenicity of Respiratory Syncytial Virus (RSV) Prefusion F Subunit Vaccine in Adults at High-risk of Severe RSV Disease.
   1. Funding Agency: Pfizer, Inc
   2. Goal: The overall goal is to conduct a Phase 3 clinical trial to evaluate the safety and immunogenicity of an investigational RSV vaccine in adults at high risk of severe RSV disease.
   3. Start and end date: 10/2022 – 10/2024
   4. Level of Funding:
   5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2023	0.24 calendar
2. 2024	0.08 calendar

c) **Title of the project:** Next Generation Covid-19: Vaccine Development Program
   1. Funding Agency: HHS/NIH/NATIONAL INSTITUTES OF HEALTH
   2. Goal: Planning and protocol development for NextGen clinical trials of novel COVID-19 vaccines.
   3. Start and end date: 08/2023 – 12/2025
   4. Level of Funding:
   5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2024	0.38 calendar
2. 2025	1.15 calendar

Other Support that ended in reporting period:

a) Nothing to report.

7.2.2 Jeffrey Bethony (GW Clinical Immunology Laboratory Director)

Other Support that started in reporting period:

a) **Title of the project:** Ultrasensitive Env Detection Assay for Broadly Neutralizing Antibody Screening
   1. Funding Agency: NIH/NIAID
   2. Goal: To develop an ultra-sensitive Env binding assay whose results will correlate to neutralization assay results but will take hours, and that can directly measure translationally competent virus directly in cells lysates, increasing the sampling depth.
   3. Start and end date: 04/2023 – 03/2026
   4. Level of Funding
   5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2024	0.36 calendar
2. 2025	0.36 calendar
3. 2026	0.36 calendar
4. 2027	0.36 calendar
5. 2028	0.36 calendar

Other Support that ended in reporting period:

a) **Title of the project:** Controlled Infection Trial to Test Efficacy of Hookworm Vaccine with Different TLR Agonists
   1. Funding Agency: NIAID (NIH)
   2. Goal: The goal of this project is to utilize a novel paradigm for the early assessment of vaccine efficacy and the selection of optimal vaccine formulation.
   3. Start and end date: 05/01/2017 – 04/30/2023
   4. Level of Funding:
   5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2022	0.12
2. 2023	0.12
3. 2024	0.12

b) **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 *Primary Place of Performance: University of California, Los Angeles
   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. Start and end date: 09//2021 – 09/2022
   4. Level of Funding:
   5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2022	0.36 calendar
2. 2023	0.36 calendar

c) **Title of the project:** A Phase 1 Randomized, Double-blinded, Placebo-controlled, Dose-escalation Clinical Trial to Evaluate the Safety and Immunogenicity of rVSV∆G-LASV-GPC Vaccine in Healthy Adults (C102)

1. Funding Agency: International AIDS Vaccine Initiative (IAVI); Coalition for Epidemic Preparedness Innovations (CEPI is Prime)
*Primary Place of Performance: University of California, Los Angeles
2. Goal: The major goals of this project is to test the safety and immunogenicity of the G-LASV-GPC Vaccine (Lassa Fever vaccine) in healthy adults in the USA.
3. Start and end date: 05/03/2021 – 04/30/2023
4. Level of Funding:
5. Person Months (Calendar/Academic/Summer) per budget period:

Year (YYYY)	Person Months
1. 2021	0.96 calendar
2. 2022	0.96 calendar
3. 2023	0.96 calendar

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:	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:	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:	CQI and Compliance 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:	Left study on 31 December 2022.

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: Job Kasule, MD
Project Role: Medical Officer
Research Identifier: n/a
Nearest person month worked: 12 person months per year
Contribution to Project: No change.

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.

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.

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Joanita Namuli
Project Role:	Clinic Administrative Assistant at MUWRP
Researcher Identifier:	n/a
Nearest person month worked:	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:	Left study on 30 November 2022.

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:	Justine Nalunga
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:	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:	Left study on 13 December 2022.

Makerere University Walter Reed Project (MUWRP) Participants:

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:	Left the study on 13 July 2023.

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:	No change.

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:	No change.

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

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 left the study on 31 July 2023.

Name:	Zulaika Namusisi
Project Role:	Research Nurse
Researcher Identifier:	n/a
Nearest person month worked:	12 person months per year
Contribution to Project:	No change.

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

Makerere University Walter Reed Project (MUWRP) Participants:

Name:	Agatha Mukanza
Project Role:	Regulatory Officer
Researcher Identifier:	n/a
Nearest person month worked:	3 person months per year
Contribution to Project:	Agatha is an experienced research personnel who joined the study on 13 February 2023. She provides assistance to the CQI and Compliance coordinator and liaises with investigators and other research staff to ensure compliance with local and international regulatory and ethical guidelines/regulations.

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

<u>Baylor College of Medicine (BCM) Participants</u>:

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 month 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 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 month per year
Contribution to Project:	No change.

8 SPECIAL REPORTING REQUIREMENTS

- Quad Chart for Year 5 of the project (see Appendix A)

9 APPENDICES

Appendix A: Quad Chart for Year 5 of the project.

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

Proposal #: PR172460
Award #: W81XWH1810672

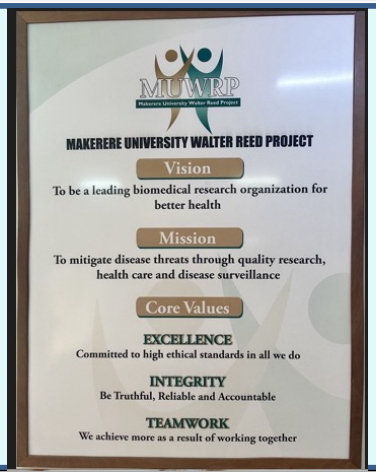
PI: David Diemert **Org:** George Washington University **Award Amount:** $4,857,840

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.



MUWRP Vision and Mission Statement displayed at MUWRP clinic in Kampala, Uganda

Accomplishment: Completion of study vaccines for Part B.

Timeline and Cost

Activities CY	18	19	20	21	22	23	24
Obtain IRB and Regulatory Approvals for Phase I/II Clinical Trial							
Train MUWRP Study Staff for Clinical Tria							
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	$282	

Updated: 30OCT2023

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 enrollment.

Budget Expenditure to Date

Projected Expenditure: $4,857,840 Actual Expenditure: $4,271,708