SUMMARY STATEMENT

PROGRAM CONTACT:
Delmyra Turpin
240-669-5597
turpindb@niaid.nih.gov

(Privileged Communication)

Release Date: **07/24/2019**
Revised Date:

Application Number: **1 R01 AI149339-01**

Principal Investigators (Listed Alphabetically):

KLAUSNER, JEFFREY DAVID (Contact)
MEDINA-MARINO, ANDREW

Applicant Organization: UNIVERSITY OF CALIFORNIA LOS ANGELES

Review Group: **IRAP**
Infectious Diseases, Reproductive Health, Asthma and Pulmonary Conditions Study Section

Meeting Date: **06/27/2019**
Council: **OCT 2019**
Requested Start: **09/01/2019**

RFA/PA: **PA19-055**
PCC: **M37C**

Project Title: **Clinical study of STI screening to prevent adverse birth and newborn outcomes**

SRG Action: **Impact Score:27 Percentile:10**
Next Steps: **Visit https://grants.nih.gov/grants/next_steps.htm**
Human Subjects: **30-Human subjects involved - Certified, no SRG concerns**
Animal Subjects: **10-No live vertebrate animals involved for competing appl.**
Gender: **2A-Only women, scientifically acceptable**
Minority: **5A-Only foreign subjects, scientifically acceptable**
Age: **1A-Children, Adults, Older Adults, scientifically acceptable**

Project Year	Direct Costs Requested	Estimated Total Cost
1	688,972	798,017
2	841,044	974,157
3	842,712	976,089
4	820,528	950,394
5	533,464	617,896
TOTAL	3,726,720	4,316,554

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

1R01AI149339-01 Klausner, Jeffrey

RESUME AND SUMMARY OF DISCUSSION: In this application, the investigators propose to conduct a 3-arm randomized control trial of antenatal care STI screening strategies to assess if decreasing STI burden reduces adverse birth outcomes and affects the vaginal microbiota. The reviewers recognized the significance of the innovative same day point of care screening as the optimal screening and treatment method and found the focus on cost-effectiveness and disability-adjusted life year to be interesting. The vaginal microbiome assessment is also poised to identify how the variation in the microbiome is related to persistent *Chlamydia trachomatis* infection. The rigorous prior research established STI prevalence in this population of HIV+ and HIV- women and the reviewers found the high proportion of HIV+ women to be a strength of the application. Aims 1 and 2 are well designed with solid recruitment and retention plans and appropriate methodology. However, aim 3 is underpowered and not well supported by the analysis plan. This aim raised concern that the study will not have the necessary taxonomic resolution leading to a call for more microbiome analysis expertise and an ecological approach. Following discussion, the reviewers considered this a minor addressable concern. Overall, the reviewers found this application an effective combination of implementation science with a well-grounded clinical trial that will provide high quality data for WHO and have a high impact on the STI field.

DESCRIPTION (provided by applicant): Infections with Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG) and Trichomonas vaginalis (TV) during pregnancy are associated with premature rupture of membranes, preterm labor and delivery, low birth weight, congenital infections, perinatal death and mother-to-child transmission of HIV infection. Sexually transmitted infections (STIs) like these are common in pregnant women globally, but often go undiagnosed; recent work by our group found a 41% STI prevalence amongst HIV-infected pregnant women, of which 64% of infections were asymptomatic. Recent research suggests the vaginal microbiome may play a critical role in STI acquisition, persistence and treatment outcomes. Our pilot work has shown that diagnostic testing for CT, NG, and TV in antenatal care services for HIV-infected pregnant women in South Africa is highly acceptable and feasible; however, our work has made clear that evaluating the impact and cost effectiveness of different diagnostic screening strategies that optimally decrease the burden of STIs during pregnancy and at time-of-delivery is urgently needed. Furthermore, our findings highlight that biological factors that increase the risk for STI persistence and/or treatment failures must be further investigated. In response to the need to 1) identify optimal, cost-effective screening strategies that decrease the burden of STIs during pregnancy and reduce adverse birth outcomes, 2) provide evidence to update WHO's syndromic management guidelines, and 3) elucidate the role of the vaginal microbiome in STI treatment outcomes, we propose a novel, highly innovative study with the following three Aims: Aim 1: Evaluate 3 different screening strategies to decrease the burden of CT/NG/TV among pregnant women, and reduce adverse birth outcomes. Aim 2: Evaluate cost per pregnant woman screened and treated, cost of adverse birth outcomes, and cost-effectiveness per STI and disability-adjusted life-year (DALY) averted. Aim 3: Investigate the relationship between the vaginal microbiome and persistent Chlamydial infections in pregnant women. Our proposed 5-year study will enroll 1250 HIV-infected and 1250 uninfected pregnant women from three large ANC clinics in Tshwane District, South Africa, as well as their ~2500 neonates and up to 834 male partners. Our research team, led by established researchers, has significant expertise and experience in all aspects of the proposed study. Our multi-institutional collaborations will allow us to leverage unique implementation platforms and resources, and allow for rapid dissemination of findings to South African and global stakeholders.

PUBLIC HEALTH RELEVANCE: This effectiveness trial will increase understanding of the value and cost-effectiveness of diagnostic screening for sexually transmitted infections (STIs) among pregnant women in low and middle-income countries, to reduce adverse pregnancy and infant outcomes. Further, results from this study will provide important data on the role of the vaginal microbiome in

Chlamydia trachomatis (CT) testing outcomes and further rationale for studying the vaginal microbiome in pregnant women with CT treatment failure. Together, findings from this R01 are likely to inform changes to STI screening and treatment guidelines in low-middle income countries globally.

CRITIQUE 1

Significance: 1
Investigator(s): 2
Innovation: 3
Approach: 3
Environment: 1

Overall Impact: Pregnant women with genital *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV) have significant increases in risk to a number of obstetric outcomes including premature rupture of membranes, preterm labor and delivery, low birth weight, congenital infections, perinatal death and mother-to-child transmission of HIV infection. The investigators recently reported 41% STI prevalence among HIV-infected pregnant women in South Africa, of which 64% of the STIs were asymptomatic. In most maternal health clinics in Africa, diagnosis of maternal STIs relies on syndromic treatment and management. Further, vaginal discharge is not an adequate proxy for endocervical infection and more robust screening approaches are needed. The investigators noted a 9% cumulative incidence of STI between first ANC screening and delivery suggesting that a single screening was not optimal.

The issue under investigator in this proposal is the evaluation of 3 antenatal care (ANC) screening strategies based on frequency and timing in pregnancy (STI screening at baseline-only, baseline + test of cure, and baseline + 30-34 weeks of gestation). The investigators seek to assess (1) the relative influence of each screening approach on mother and child health outcomes, including fetal loss, preterm labor, birth weight, infant mortality, and change in STI prevalence and (2) the cost effectiveness and disability-adjusted life year (DALY) averted by the enhanced screening strategies. The investigators propose a three-arm randomized controlled hybrid-effectiveness trial of 2500 HIV+ and HIV- women to assess aim 1 and 2. A third aim seeks to evaluate if the vaginal microbiota are associated with CT persistence at the test of cure visit in a smaller secondary study (estimated at n=65 cases and 130 controls).

The investigators highlight that reducing STI persistence and treatment failures will not only decrease the burden of STIs during pregnancy and reduce adverse birth outcomes, but it will also provide cost effectiveness evidence that the World Health Organization (WHO) can use to modify current syndromic management guidelines. The PIs are well-regarded senior researchers in the field of sexually transmitted infections (STIs) and aims 1 and 2 which evaluate the ANC screening approaches are thoughtfully conceived, constructed and presented. The conceptual framework, study setting, research team, methodologies, data collection, specimen collection partner treatment are all well-described and thorough. Certainly this trial will generate the necessary data that WHO and government entities could use in their ANC program development.

The primary questions and concerns are (1) generalizability of this data to other middle and low income countries (other than South Africa), 2) providing additional clarity to the statistical analysis and study design in Aim 3 and 3) whether Aim 3 is sufficiently powered given the high prevalence of bacterial vaginosis (BV) type vaginal microbiota expected at baseline.

Overall, it is clear that affordable point of care STI tests are needed for ANC clinics in low and middle income countries and cost-effective approaches for STI screening and treatment for pregnant women will be critical to build infrastructure to address the burden of adverse infant outcomes attributed to maternal STIs.

1.Significance:

Strengths

- STIs remain a maternal and child health issue in resource-limited settings. Setting a priority for maternal STI diagnosis and treatment will lead to a reduction of adverse outcomes (including preterm birth and infant mortality).
- This trial will provide much needed data on the cost-effectiveness of diagnostic screening strategies for STIs among pregnant women in South Africa. Reducing STI burdens in pregnancy will reduce adverse obstetric and infant health outcomes and could result in recognizable cost savings in low and middle-income countries.
- Findings from this large trial will provide the impetus for governments to plan for and implement preventive STI screening and treatment guidelines in South Africa and possibly other low-middle income countries.
- The rigor of prior research is clear with a number of observational studies from various settings indicating both the association between STI and adverse pregnancy outcomes and also the cost effectiveness of STI screening. Screening appears to have greater cost effectiveness with increased STI prevalence (which is certainly present in this South African setting).
- Vaginal microbiota are associated with incidence of STIs, however there is less data available on the microbiota's role in persistence of STIs after antibiotic treatment.

Weaknesses

- It would be helpful for the investigators to summarize some of the observational findings (from large health system data or other studies) to further bolster why a large randomized trial is necessary and provide information on how actionable findings will be given low resource environments.
- Is the population of HIV+ and HIV- women in South Africa generalizable to other middle and low income countries? Some additional information on the use of this data to other countries would be helpful in review.

2.Investigator(s):

Strengths

- Dr. Klausner is a well-respected and highly regarded clinical researcher in STIs. He will provide the necessary expertise for oversight in study design, protocol development and implementation, data analysis and interpretation of results. He is an ideal contact PI to lead this trial.
- Andrew Medina-Marino, has expertise in the conduct of epidemiologic studies, including study design, protocol development and implementation, data analysis, interpretation and dissemination of results.
- Susan Cleary has the necessary expertise in the cost-effectiveness Aim 2.
- Robert Pattinson will devote attention to the collection of specimens from mother-infant pairs admitted to hospital during and after delivery, and the abstraction of medical records and discharge summaries for birth and pregnancy outcomes. He is clearly well suited for this position.

- Koleka Mlisana will provide oversight for the implementation and operations of the GeneXpert diagnostic platform.
- Dr. Muzny is an expert in STIs who has had a research focus on BV, *Trichomonas vaginalis* and a number of important sexual health topics. With her K23 career development award, she has been building a research portfolio in epidemiologic and molecular aspects of the vaginal microbiota and BV.

Weaknesses

- It would be helpful to expand the expertise available on the microbiota statistical modeling in Aim 3. Dr. Redden has a long experience in general and clinical trials biostatistics but does not list on his biosketch any particular specialized or ecologic approaches to modeling microbiota (compositional) data.

3. Innovation:

Strengths

- Use of an innovative hybrid type 1 effectiveness-implementation study design that is grounded in the RE-AIM conceptual framework guiding for process evaluation (reach, effectiveness, adoption, implementation, maintenance).
- Utilizes same-day STI screening and treatment and assess if such screening program have a measurable influence on maternal and child health outcomes. Cost effectiveness models would be used by a number of low and middle income countries to plan for implement STI testing in pregnancy and particularly among HIV+ women.
- The design and research plan has strong potential to advance scientific knowledge, clinical practice and screening guidelines in low and middle-income countries.
- Primary, secondary and exploratory outcomes in Aim 1 are all meritorious (page 149) with a focus on adverse birth outcomes and change in STI prevalence. Development of a persistence STI risk score calculator is intriguing.
- Aim 2 is expertly designed to assess the cost per pregnant woman screened and treated, cost of adverse birth outcomes and cost effectiveness per STI and DALY averted. There is a focus on both the provider and patient perspectives.
- Currently, treatment guidelines are that asymptomatic BV is not treated, however, findings from the Aim 3 sub-study may suggest that pregnant women who are persistently positive for CT should be screened and treated for BV, even if they are asymptomatic.
- Utilizing a large longitudinal cohort to assess the role of the vaginal microbiota in CT persistence. The secondary aim of exploring indole-producing bacteria over time as well as the possible differential between symptomatic vs asymptomatic CT cases are both quite intriguing.

Weaknesses

- The vaginal microbiota studies are based on compositional surveys. Additional innovation could be found in more functional approaches, such as comparative genomics or host immune responses.

4. Approach:

Strengths

- Specific Aim 1 and 2 are well-designed and scientifically rigorous to test their respective hypotheses. The investigators propose a three-arm randomized controlled hybrid-effectiveness trial which was appropriately powered, and meticulously designed in all aspects from recruitment, follow-up, and data collection. It will clearly address the critical question of how increasing STI screening in pregnancy affects maternal and fetal outcomes in a HIV+ and HIV- cohort, as well as the cost effectiveness of enhanced screening.
- The parent study provides an interesting opportunity to assess the role of the vaginal microbiota in CT persistence following antibiotic treatment.

Weaknesses

- Aim 3 may be underpowered (n=65 cases). Given the preliminary data presented on vaginal microbiota and HPV, a large portion of the women included in Aim 3 will have BV (a diverse and low-*Lactobacillus* profile) at baseline and it is unclear that there will be enough sample size of the various bacterial community profiles to be able to detect a microbial signal associated with CT-persistence. The preliminary data presented on HIV-negative women suggests 21% *L. iners* dominated with the majority low-*Lactobacillus* (74%).
- The specific aims page lists Aim 3 as a nested case-control (1:2) study design and proposes using vaginal specimens collected from CT-infected women at first ANC, 1, 2 and 3 weeks post-treatment. The presentation of the longitudinal statistical modeling are somewhat unclear in how the approach matches to the descriptor of a nested case control design. The investigators list individual taxa, community state types and Nugent score will be evaluated at each study stage (at each longitudinally collected sample) as it pertains to the CT outcome but additional information on how the modeling of the longitudinal series and transitions will be integrated would be helpful.
- The text describing the bioinformatic pipeline cites a published paper from co-investigators (Van Der Pol *et al*, reference #105) in which they concluded that a shorter region of the 16S rRNA gene amplicon (V4) is superior to a longer region (V3-V4) for taxonomic assignment. The paper cites two sets of “V3-V4” primers (“commonly used universal”: 357-785R and the “vaginal microbiome study”: 319F 806R) but it appears they focus on the former (357-785R). These two primers capture a somewhat different region of the V4 (515-806). There are a number of studies which demonstrate the smaller V4 region is less informative than the larger V3-V4 region, however, the problem is that papers use different regions or combinations of regions, often also with different primers for the same regions, so comparisons with previous studies are not that straightforward. Concern is that the V4 region alone lacks the taxonomic resolution and will limit the impact of the research.
- Preliminary data cite indole-producing bacteria are associated with CT persistence but data or publications are not presented. (p. 145)

5. Environment:

Strengths

- The environments at each of the performance sites (University of California, Los Angeles (UCLA), University of Cape Town (UCT) School of Public Health and Family Medicine, South African Medical Research Council (SA-MRC), University of Cape Town (UCT) School of Medicine, University of Alabama Birmingham, Louisiana State University (LSU)) are all outstanding because they have the necessary computing power, space equipment, clinical infrastructure to implement the aims.

- Participants will be recruited from three large ANC clinics located in the referral zone of two maternal obstetric units (MOUs).

Weaknesses

- N/A

Study Timeline:

Strengths

- Participants will be recruited from three large ANC clinics located in the referral zone of two maternal obstetric units (MOUs).
- Recruitment and retention plan are well detailed (p. 158) and include information/consenting sessions in which consent form are presented verbally in their preferred language, surveys are administered by ACASI, contact information is collected for the participant and her family, and follow-up contact is initiated soon after study start. The study will also utilize a UNICEF-funded MomConnect program which sends reminder messages to pregnant women's mobile phones via text messages to remind them about their upcoming ANC visits.
- The projected timeline (p. 159) is ambitious but it appears feasible and well justified.
- Data collection, specimen collection and storage, diagnostic testing and follow-up are all clearly presented

Weaknesses

- N/A

Protections for Human Subjects

Acceptable Risks and/or Adequate Protections

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Unacceptable

- Does not directly address the NIH Genomic Data Sharing policy

Inclusion Plans

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Not applicable
- Inclusion/Exclusion Based on Age: Distribution justified scientifically

Vertebrate Animals

Not Applicable (No Vertebrate Animals)

Biohazards

Not Applicable (No Biohazards)

Applications from Foreign Organizations

Justified

Select Agents

Not Applicable (No Select Agents)

Resource Sharing Plans

Unacceptable

- Data will be available on first publication. The genomic data sharing plan to release the vaginal microbiota sequencing files was not detailed.

Authentication of Key Biological and/or Chemical Resources

Not Applicable (No Relevant Resources)

Budget and Period of Support

Recommend as Requested

CRITIQUE 2

Significance: 1
Investigator(s): 1
Innovation: 1
Approach: 3
Environment: 1

Overall Impact*:* This is a highly significant study given the high prevalence of HIV and sexually transmitted infections (STIs) among pregnant women in low-middle income countries and the strong association between STIs and adverse birth outcomes (e.g., underweight birth, still birth, preterm birth). STIs are also associated with increased risk of vertical and horizontal HIV transmission. The current WHO guidelines recommending syndromic treatment during pregnancy has been shown to miss a larger proportion of asymptomatic infections. This application proposes a 3-arm randomized controlled trial among 2500 (50% HIV+) pregnant women presenting for antenatal care (ANC) in 3 clinics in Tshwane District, South Africa. The study will compare point of care (POC) screening for gonorrhea, chlamydia and trichomonas (GC/CT/TV) at first visit and 30-34 weeks of gestation (Arm 1), POC screening at first visit followed by test-of-cure (Arm 2), and the standard-of-care one-time screening with treatment at first visit with targeted treatment alone (Arm 3). The study includes a nested-case control study comparing the vaginal microbiota of women with CT infection who remained infected following treatment (cases) to women who were cured following treatment (controls). An innovative feature of the study is the efficiency gained by incorporating implementation science methods to collect and analyze cost and process measure data in conjunction with the trial rather than requiring subsequent studies to evaluate the intervention's effectiveness. The research team is excellent, and the environment is well-suited to successfully accomplish the study aims. The methods are strong, detailed and scientifically rigorous, with a few minor weaknesses. By design, the study includes only pregnant women, and age will be included in the analysis, but due to the location, all participants will be Black African limiting generalizability. The scientific premise for the study is strong and based on prior

literature and the investigators' preliminary studies. The proposal also discusses the limitations of the prior research and how the current study will overcome those limitations. Given the many strengths and minor weaknesses in this proposal, the overall impact is high.

1.Significance:

Strengths

- HIV and STIs are major health concerns among pregnant women in South Africa as well as other low-middle income countries. A very high proportion of HIV+ women in South Africa had an STI at their first ANC visit and nearly 2/3 were asymptomatic.
- Reduction in STIs among pregnant women will reduce the risk of adverse birth outcomes as well as sexual transmission of HIV.
- The proposal discussed limitations of prior research demonstrating scientific rigor. For example, while prior research showed that point-of-care screening for STIs can reduce their prevalence by >50% at the time of delivery compared to syndromic management, this approach missed incident infections leaving many women with untreated STIs at the time of delivery.
- The results will inform updates to WHO's syndromic management guidelines that currently only recommend STI testing for those with symptoms. This study will provide evidence to support routine STI screening, which will increase detection and treatment of STIs and reduce the amount of overtreatment for uninfected pregnant women.
- This study will provide cost and cost-effectiveness estimates necessary to drive policy in South Africa and elsewhere.
- This study will also identify risk factors associated with persistent STIs and will inform future interventions.
- This study will provide new data on the impact of the vaginal microbiome on persistence of STIs.
- Preliminary studies provide strong evidence to support the premise of this study.

Weaknesses

- None

2.Investigator(s):

Strengths

- Drs. Klausner and Madina-Marino (MPIs) Rhave had highly-productive collaborations over the last decade, which support the high probability of success of the proposed study.
- The research team has expertise and experience in all aspects of the proposed study including prior work at study sites.
- This will be the first RCT to evaluate the cost-effectiveness of STI testing and treatment during pregnancy in a low-middle income country.
- The prospective analysis of the vaginal microbiome to identify risk factors for STI persistence has not been done before.
- The Taylor lab has also developed methods to visualize changes in the vaginal microbiota over time, including graphic display of microbiome changes via longitudinal heat maps and analysis of CST changes.

- The Multi-PI Plan is appropriate for this study.

Weaknesses

- None

3. Innovation:

Strengths

- The trial design includes collection of process measures, which will allow for analysis of both effectiveness and implementation in the same study.
- This will be the first RCT to evaluate the cost-effectiveness of STI testing and treatment during pregnancy in a low-middle income country.
- The prospective analysis of the vaginal microbiome to identify risk factors for STI persistence has not been done before.
- Longitudinal changes in the vaginal microbiome is novel.

Weaknesses

- None

4. Approach:

Strengths

- Preliminary studies have demonstrated that rapid, point-of-care tests for STIs are feasible and acceptable in across multiple settings.
- Recruitment sites will capture all women seeking ANC in the referral zones of two maternal obstetric units, which will include those with low SES and living in informal settlements.
- This study utilizes methods that have been proven in the investigators' prior R21-funded study to successfully recruit and test women seeking ANC.
- The study leverages the National Health Laboratory Service and National HIV databases to ensure completeness of all study variables (e.g., HIV status, CD4 and viral load) to minimize missing data.
- Efforts will be made to provide partner treatment and determine whether treatment was taken are reasonable given the limitations. Potential inter-partner violence toward women who disclose STIs to their partners is addressed and appropriate protections will be employed.
- Methods proposed for participant retention will minimize loss-to-follow-up.
- Randomization strategy described is appropriate.
- Sample size calculations are detailed and appropriate.
- Data analyses are well described and appropriate. In addition, using data from a prior R21-funded study to assess the external validity of the models in Aim 1 is a strength.
- All participants will be women and age will be considered in the analyses.

Weaknesses

- No mention of how data will be reconciled if self-reports disagree with national databases.
- No methods are provided for testing urine specimens, nor does the proposal discuss the comparability of results based on vaginal swab vs. urine specimens.

- No mention of assessing parity.
- All participants will be Black African based on the location of the study.
- Description of costs and process measures is limited making it difficult to evaluate the rigor or reproducibility of this part of the study. Additionally, women might not be privy to their husband's income, thereby impacting the accuracy of household income measures.
- No mention of blinding during data collection or analyses.
- Sample size calculation for Aim 3 case-control study does not account for the number of participants ineligible due to multiple infections.

5. Environment:

Strengths

- The very high prevalence of HIV and STIs, as well as high incidence of adverse pregnancy outcomes, in this population make this an ideal setting for this study.
- The MIHCSRU and Kalafong Hospital are two of Africa's leadings centers for maternal-infant health research, with significant research funding and outputs.
- The computer and laboratory resources and expertise needed to complete the microbiome analyses are available in Dr. Taylor's lab at Louisiana State University.
- Dr. Mauzy's lab at University of Alabama Birmingham is appropriately equipped to perform STI testing needed by the study.

Weaknesses

- None

Study Timeline

Strengths

- The timeline is detailed and takes into account start-up activities, recruitment, retention and follow-up activities. Milestones are also provided.
- This study will use existing data sources (e.g., medical records, national laboratory databases) to maximize efficiencies.

Weaknesses

- The number of participants enrolled at each milestone increases over time; however, no rationale is provided support the feasibility of the increase.

Protections for Human Subjects

Acceptable Risks and/or Adequate Protections

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Acceptable

Inclusion Plans

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically

- For NIH-Defined Phase III trials, Plans for valid design and analysis:
- Inclusion/Exclusion Based on Age: Distribution justified scientifically

Vertebrate Animals

Not Applicable (No Vertebrate Animals)

Biohazards

Acceptable

Applications from Foreign Organizations

Not Applicable (No Foreign Organizations)

Select Agents

Not Applicable (No Select Agents)

Resource Sharing Plans

Acceptable

Authentication of Key Biological and/or Chemical Resources

Acceptable

Budget and Period of Support

Recommend as Requested

CRITIQUE 3

Significance: 1
Investigator(s): 1
Innovation: 5
Approach: 2
Environment: 1

Overall Impact: This is a new multi-PI R01 proposal to optimize the cost of screening strategies that decrease the burden of STIs during pregnancy and determine the role of the vaginal microbiome and persistent Chlamydial infections and treatment outcomes. The researchers propose to enroll 2500 pregnant women (50% HIV-infected/ 50% HIV-uninfected), in Pretoria. The proposed study could have a significant impact on preventing adverse birth outcomes in a region where HIV and STI in pregnant women represent an enormous public health problem. The strength of the application is that it will optimize testing costs and birth outcomes, with an expected high impact on the budget for developing countries for health services. It also may provide evidence for updated medical guidelines for optimal STD treatment in these high risk settings. The team is optimally suited to undergo this study, because of their relevant expertise, the scope of their experience in poor settings in different locations, and their current projects undergoing on HIV infected women in South Africa.

1. Significance:

Strengths

- The study will determine optimal cost-effective treatment to prevent STI in pregnant women in a region with high HIV prevalence, which is of high importance particularly for poor countries.
- The results can provide evidence to update WHO's guidelines to manage STI.

Weaknesses

-

2. Investigator(s):

Strengths

- Dr Klausner has published extensively in the field, and has assembled a strong research team from 6 Institutions.

Weaknesses

-

3. Innovation:

Strengths

- There isn't much novelty in the methods, analyses or idea, but this is an optimization that is needed, and will benefit of millions of women and their babies.

Weaknesses

-

4. Approach:

Strengths

- The study design is robust and adequate for each aim.

Weaknesses

- Given the effort to recruit and access these women, the researchers should take samples from multiple body sites, for microbiome characterization in mothers and infants.

5. Environment:

Strengths

- Available resources in the US and in Pretoria seem appropriate for the needs of the project.

Weaknesses

-

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: ACCEPTABLE

INCLUSION OF WOMEN PLAN: ACCEPTABLE

INCLUSION OF MINORITIES PLAN: ACCEPTABLE

INCLUSION ACROSS THE LIFESPAN PLAN: ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Footnotes for 1 R01 AI149339-01; PI Name: Klausner, Jeffrey David

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-14-074 at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-074.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

Infectious Diseases, Reproductive Health, Asthma and Pulmonary Conditions Study Section
Population Sciences and Epidemiology Integrated Review Group
CENTER FOR SCIENTIFIC REVIEW
IRAP
06/27/2019 - 06/28/2019

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-14-073 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-073.html and NOT-OD-15-106 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-106.html, including removal of the application from immediate review.

CHAIRPERSON(S)

COULL, BRENT ANDREW, PHD
PROFESSOR AND ASSOCIATE CHAIR
DEPARTMENT OF BIOSTATISTICS
HARVARD UNIVERSITY
BOSTON, MA 02115

MEMBERS

ARGOS, MARIA, BS, MPH, PHD *
ASSISTANT PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY
SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, IL 60612

BAO, WEI, MD, PHD *
ASSISTANT PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY
COLLEGE OF PUBLIC HEALTH
UNIVERSITY OF IOWA
IOWA CITY, IA 52242

BELONGIA, EDWARD, MD *
DIRECTOR
CENTER FOR CLINCAL EPIDEMIOLOGY
AND POPULATION HEALTH
MARSHFIELD CLINIC RESEARCH INSTITUTE
MARSHFIELD, WI 54449

BROTMAN, REBECCA M, MPH, BA, PHD *
ASSOCIATE PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY AND PUBLIC HEALTH
INSTITUTE FOR GENOME SCIENCES
UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE
BALTIMORE, MD 21201

DEAN, CHARMAINE B, PHD
PROFESSOR
UNIVERSITY OF WATERLOO
WATERLOO, ON N6L 3G1
CANADA

DEVOTO, MARCELLA, PHD
PROFESSOR
DEPARTMENT OF PEDIATRICS
PERELMAN SCHOOL OF MEDICINE
UNIVERSITY OF PENNSYLVANIA
THE CHILDREN'S HOSPITAL OF PHILADELPHIA
PHILADELPHIA, PA 19104

DEWAN, ANDREW, PHD, MPH, BS *
ASSOCIATE PROFESSOR
DEPARTMENT OF CHRONIC DISEASE EPIDEMIOLOGY
YALE SCHOOL OF PUBLIC HEALTH
NEW HAVEN, CT 06510

DOMINGUEZ-BELLO, MARIA GLORIA, PHD *
PROFESSOR
INTERIM DIRECTOR, NJ INSTITUTE FOR FOOD, NUTRITION
DEPARTMENT OF BIOCHEMISTRY AND MICROBIOLOGY AND OF
ANTHROPOLOGY
RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY
NEW BRUNSWICK, NJ 08901

DONG, QUNFENG, PHD *
ASSOCIATE PROFESSOR AND DIRECTOR
DEPARTMENT OF PUBLIC HEALTH SCIENCES
BIOMEDICAL INFORMATICS CENTER
STRITCH SCHOOL OF MEDICINE
LOYOLA UNIVERSITY CHICAGO
MAYWOOD, IL 60153

DUCONGE, JORGE, BS, MS, PHD *
PROFESSOR
UNIVERSITY OF PUERTO RICO
MEDICAL SCIENCES CAMPUS
BOX 36-5067
SAN JUAN, PR 00936

ENDY, TIMOTHY PAUL, MD, MPH *
PROFESSOR AND CHIEF OF INFECTIOUS DISEASE
DEPARTMENT OF MEDICINE
SUNY UPSTATE MEDICAL UNIVERSITY
STATE UNIVERSITY OF NEW YORK
SYRACUSE, NY 13210

FAIRFAX, KEKE CELESTE, PHD *
ASSISTANT PROFESSOR
DIVISION OF MICROBIOLOGY AND IMMUNOLOGY
DEPARTMENT OF PATHOLOGY
UNIVERSITY OF UTAH
SALT LAKE CITY, UT 84112

FEINGOLD, BETH, PHD *
ASSISTANT PROFESSOR
DEPARTMENT OF ENVIRONMENTAL HEALTH SCIENCES
UNIVERSITY AT ALBANY, SCHOOL OF PUBLIC HEALTH
RENSSELAER, NY 12144

GARFEIN, RICHARD S, PHD, MPH
PROFESSOR
DIVISION OF EPIDEMIOLOGY
DEPARTMENT OF FAMILY MEDICINE AND PUBLIC HEALTH
SCHOOL OF MEDICINE
UNIVERSITY OF CALIFORNIA, SAN DIEGO
LA JOLLA, CA 92093

GROBMAN, WILLIAM ADAM, MD
PROFESSOR
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY
NORTHWESTERN UNIVERSITY
CHICAGO, IL 60611

HARLOW, SIOBAN D, PHD
PROFESSOR
DIRECTOR, CENTER FOR MIDLIFE SCIENCE
DEPARTMENT OF EPIDEMIOLOGY
SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MICHIGAN
ANN ARBOR, MI 48109

HARRISON, LEE H, MD
PROFESSOR
DEPARTMENTS OF MEDICINE
AND EPIDEMIOLOGY
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PA 15261

HARTERT, TINA V, MD, MPH
PROFESSOR AND LULU H OWEN CHAIR
DEPARTMENT OF MEDICINE
DIRECTOR, CENTER FOR ASTHMA RESEARCH
ASSISTANT VICE PRESIDENT FOR TRANSLATIONAL
SCIENCE
VANDERBILT UNIVERSITY SCHOOL OF MEDICINE
NASHVILLE, TN 37232

HOLLAND, NINA T, PHD
PROFESSOR
ENVIRONMENTAL HEALTH SCIENCES DIVISION
SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF CALIFORNIA, BERKELEY
BERKELEY, CA 94720

HOUGH, CATHERINE LEE, MD
PROFESSOR
DEPARTMENT OF MEDICINE
UNIVERSITY OF WASHINGTON
SEATTLE, WA 98104

JAIN, SONIA, PHD *
PROFESSOR
DIVISION OF BIOSTATISTICS AND BIOINFORMATICS
DEPARTMENT OF FAMILY MEDICINE AND PUBLIC HEALTH
UNIVERSITY OF CALIFORNIA AT SAN DIEGO
LA JOLLA, CA 92093

KENAH, EBEN, MS, BA, SCD *
ASSISTANT PROFESSOR
DEPARTMENT OF BIOSTATISTICS
UNIVERSITY OF FLORIDA
GAINESVILLE, FL 32611

KISSINGER, PATRICIA J, PHD, MPH, BSN
PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY
SCHOOL OF PUBLIC HEALTH AND TROPICAL MEDICINE
TULANE UNIVERSITY
NEW ORLEANS, LA 70112

LAI, HUICHUAN J, PHD *
PROFESSOR
DEPARTMENT OF NUTRITIONAL SCIENCES
UNIVERSITY OF WISCONSIN - MADISON
MADISON, WI 53706

LEDERER, DAVID J, MD, MS
ASSOCIATE PROFESSOR
DEPARTMENTS OF MEDICINE AND EPIDEMIOLOGY
COLUMBIA UNIVERSITY MEDICAL CENTER
NEW YORK, NY 10032

LEVIN, ALBERT M, PHD, MPH
SENIOR SCIENTIST
DEPARTMENT OF PUBLIC HEALTH SCIENCES
HENRY FORD HEALTH SYSTEM
DETROIT, MI 48202

MARSIT, CARMEN JOSEPH, PHD
PROFESSOR
DEPARTMENT OF ENVIRONMENTAL HEALTH
ROLLINS SCHOOL OF PUBLIC HEALTH
EMORY UNIVERSITY
ATLANTA, GA 30322

MCDERMOTT, SUZANNE W, PHD, BS, MS *
PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS
SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF SOUTH CAROLINA
COLUMBIA, SC 29208

MELIKER, JAYMIE R, PHD
PROFESSOR
DEPARTMENT OF FAMILY POPULATION
AND PREVENTIVE MEDICINE
STONY BROOK UNIVERSITY
STONY BROOK, NY 11794

MEYERS, LAUREN ANCEL, PHD *
PROFESSOR OF INTEGRATIVE BIOLOGY
DEPARTNMENTS OF INTEGRATED BIOLOGY
AND STATISTICS AND DATA SCIENCE
THE UNIVERSITY OF TEXAS AT AUSTIN
AUSTIN, TX 78712

MURPHY, SUSAN KAY, BA, PHD *
ASSOCIATE PROFESSOR
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY
DIVISION OF GYNECOLOGIC ONCOLOGY
DUKE UNIVERSITY MEDICAL CENTER
DURHAM, NC 27710

NEMBHARD, WENDY N, MPH, PHD *
ASSOCIATE PROFESSOR AND CHAIR
DEPARTMENT OF EPIDEMIOLOGY
COLLEGE OF PUBLIC HEALTH
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
LITTLE ROCK, AR 72205

NOONAN, CURTIS WILLIAM, PHD
PROFESSOR
DIRECTOR
CENTER FOR POPULATION HEALTH
SCHOOL OF PUBLIC HEALTH AND COMMUNITY HEALTH
UNIVERSITY OF MONTANA, MISSOULA
MISSOULA, MT 59812

PEEL, JENNIFER L, PHD
PROFESSOR
DEPARTMENT OF ENVIRONMENTAL AND
RADIOLOGICAL HEALTH SCIENCES
COLORADO SCHOOL OF PUBLIC HEALTH
COLORADO STATE UNIVERSITY
FORT COLLINS, CO 80523

POLGREEN, PHILIP M., MD *
ASSOCIATE PROFESSOR
DEPARTMENT OF INTERNAL MEDICINE
DIVISION OF INFECTIOUS DISEASES
UNIVERSITY OF IOWA
CARVER COLLEGE OF MEDICINE
IOWA CITY, IA 52242

SANCHEZ, PABLO J, MD
PROFESSOR
DEPARTMENT OF PEDIATRICS
CENTER FOR PERINATAL RESEARCH
NATIONWIDE CHILDRENS HOSPITAL
THE OHIO STATE UNIVERSITY
COLUMBUS, OH 43205

SHRESTHA, SADEEP, PHD *
ASSOCIATE PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY
SCHOOL OF PUBLIC HEALTH
THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
BIRMINGHAM, AL 35294

SILVEYRA, PATRICIA, BS, MS, PHD *
ASSISTANT PROFESSOR
DEPARTMENT OF PEDIATRICS
COLLEGE OF MEDICINE
PENNSYLVANIA STATE UNIVERSITY
HERSHEY, PA 17033

STARR, JACQUELINE R, PHD, MS, MPH, BS *
ASSOCIATE MEMBER
DIRECTOR OF EPIDEMIOLOGY AND BIOSTATISTICS CORE
THE FORSYTH INSTITUTE
CAMBRIDGE, MA 98145

STEIN, CATHERINE MARIE, PHD *
ASSOCIATE PROFESSOR
POPULATION AND QUANTITATIVE HEALTH
CENTER FOR PROTEOMICS & BIOINFORMATICS, AND
TUBERCULOSIS RESEARCH UNIT
CASE WESTERN RESERVE UNIVERSITY
CLEVELAND, OH 44106

STROUD, LAURA R, PHD *
PROFESSOR
DEPARTMENT OF PSYCHIATRY AND HUMAN BEHAVIOR
THE MIRIAM HOSPITAL
ALBERT MEDICAL SCHOOL
BROWN UNIVERSITY
PROVIDENCE, RI 02903

TALGE, NICOLE, PHD *
ASSISTANT PROFESSOR
DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS
MICHIGAN STATE UNIVERSITY
EAST LANSING, MI 48824

WENDELBOE, AARON M, PHD, MS, BS *
ASSOCIATE PROFESSOR
DEPARTMENT OF BIOSTATISTICS AND EPIDEMIOLOGY
WILLIAMS PRESIDENTIAL PROFESSOR
DEPARTMENT OF BIOSTATISTICS AND EPIDEMIOLOGY
OKLAHOMA CITY, OK 73126

ZHU, YIFANG, PHD *
PROFESSOR
CENTER FOR CLEAN AIR
DEPARTMENT OF ENVIRONMENTAL HEALTH SCIENCES
UNIVERSITY OF CALIFORNIA, LOS ANGELES
LOS ANGELES, CA 90095-1772

MAIL REVIEWER(S)

BLOW, FREDERIC C, PHD
PROFESSOR AND DIRECTOR
DEPARTMENT OF PSYCHIATRY
UNIVERSITY OF MICHIGAN AT ANN ARBOR
SENIOR RESEARCH SCIENTIST
ANN ARBOR VETERAN AFFAIRS MEDICAL CENTER
ANN ARBOR, MI 48109

KERSHAW, KIARRI N, BS, MS, MPH, PHD
ASSOCIATE PROFESSOR
DEPARTMENT OF PREVENTIVE MEDICINE
FEINBERG SCHOOL OF MEDICINE
NORTHWESTERN UNIVERSITY
CHICAGO, IL 60611

LEE, MIRYOUNG, BS, MPH, MS, PHD
ASSOCIATE PROFESSOR
LIFESPAN HEALTH RESEACH CENTER
WRIGHT STATE UNIVERSITY BOONSHOFT SCHOOL OF MED.
DEPARTMENT OF COMMUNITY HEALTH AND PEDIATRICS
KETTERING, OH 45420-4006

LEMAS, DOMINICK JOSEPH, PHD
RESEARCH ASSISTANT PROFESSOR
INSTITUTE OF CHILD HEALTH POLICY
UNIVERSITY OF FLORIDA
GAINESVILLE, FL 32608

MOLDAWER, LYLE L, PHD
PROFESSOR
DEPARTMENT OF SURGERY
UNIVERSITY OF FLORIDA COLLEGE OF MEDICINE
GAINESVILLE, FL 32610

WILLIAMS, SCOTT MATTHEW, PHD
PROFESSOR
DEPARTMENT OF POPULATION AND QUANTITATIVE HEALTH
INSTITUTE FOR COMPUTATIONAL BIOLOGY
CASE WESTERN RESERVE UNIVERSITY
CLEVELAND, OH 44106

SCIENTIFIC REVIEW OFFICER

STEELE, LISA, PHD
SCIENTIFIC REVIEW OFFICER
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MD 20892

EXTRAMURAL SUPPORT ASSISTANT

YOBOUET, REBECCA SAVITRI
EXTRAMURAL SUPPORT ASSISTANT (INTERN)
CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITTUES OF HEALTH
BETHESDA, MD 20892

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