APPLICATION FOR FEDERAL ASSISTANCE

SF 424 R&R

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION

❍Pre-application ●Application ❍Changed/Corrected Application

2. DATE SUBMITTED

Applicant Identifier

4. a. Federal Identifier

b. Agency Routing Identifier

c. Previous Grants.gov Tracking ID

5. APPLICANT INFORMATION **Organizational DUNS:** 092530369

Legal Name: Regents of the University of California, Los Angeles

Department: Division:

Street1: Office of Contract and Grant Administration Street2: 10889 Wilshire Boulevard, Suite 700

City: Los Angeles County/Parish: Los Angeles County State: CA: California

Province: Country: USA: UNITED STATES ZIP / Postal Code: 90095-1406

Person to be contacted on matters involving this application

Prefix:	First Name:	Middle Name:	Last Name:	Suffix:
Mr.	Frank		Falcon II	

Position/Title: Grant Analyst

Street1: 10889 Wilshire Blvd Street2: Suite 700

City: Los Angeles County/Parish: Los Angeles County State: CA: California

Province: Country: USA: UNITED STATES ZIP / Postal Code: 90095-1406

Phone Number: 310-206-9898 Fax Number: Email: frank.falcon@research.ucla.edu

6. EMPLOYER IDENTIFICATION NUMBER*(EIN) or (TIN)*: 1-956006143-A1

7. TYPE OF APPLICANT: H: Public/State Controlled Institution of Higher Education

Other (Specify):

Small Business Organization Type ❍Women Owned ❍Socially and Economically Disadvantaged

8. TYPE OF APPLICATION:

●New ❍Resubmission

❍Renewal ❍Continuation ❍Revision

If Revision, mark appropriate box(es).

❍A. Increase Award ❍B. Decrease Award ❍C. Increase Duration

❍D. Decrease Duration ❍E. Other*(specify)*:

Is this application being submitted to other agencies? ❍ Yes ● No What other Agencies?

9. NAME OF FEDERAL AGENCY:

National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER:

TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT:

The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

12. PROPOSED PROJECT:

Start Date	Ending Date
07/01/2018	06/30/2023

13. CONGRESSIONAL DISTRICT OF THE APPLICANT:

CA-033

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix:	First Name:	Middle Name:	Last Name:	Suffix:
Dr.	Jeffrey		Klausner	MD

Position/Title: Professor
Organization Name: UCLA David Geffen School of Medicine
Department: Medicine
Division: Infectious Diseases
Street1: 9911 West Pico Blvd
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Phone Number: 310-557-3044
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15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested	$3,017,639.00
b. Total Non-Federal Funds	$0.00
c. Total Federal & Non-Federal Funds	$3,017,639.00
d. Estimated Program Income	$0.00

16. IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:

DATE:

b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR

○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree

The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

18. SFLLL or other Explanatory Documentation. File Name: Mime Type:

19. Authorized Representative

Prefix:	First Name:	Middle Name:	Last Name:	Suffix:
Mr	Tac		Phung	

Position/Title: Grant Analyst
Organization Name: Regents of the University of California, Los Angeles
Department: Office of Contract & Grant Adm
Division:
Street1: 10889 Wilshire Blvd
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Signature of Authorized Representative **Date Signed**

20. Pre-application File Name: Mime Type:

21. Cover Letter Attachment File Name: cover_letter_rev1047970073.pdf Mime Type: application/pdf

UNIVERSITY OF CALIFORNIA, LOS ANGELES

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Jeffrey D. Klausner, MD, MPH
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December 13, 2017

Madelon Halula, PhD
Division of AIDS (DAIDS)
National Institute of Allergy and Infectious Diseases (NIAID)

RE: PA-16-160 (R01)

Dear Dr. Halula,

Dr. Medina-Marino and I are very pleased to submit this application for our study, entitled "***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy.***" In South Africa, "*Rea Phela*" means "We are Healthy." We submit this proposal for your consideration as an R01 in NIAID, building upon our current R21 award through NICHD. However, we also think NICHD could be an appropriate Institute for funding, and we spoke with Branch Chief Denise Russo, PhD at NICHD about this R01 application.

Bringing together a team of established investigators from both South Africa and the United States, our team has unique resources and solid expertise in HIV infection, microbiome analysis, molecular epidemiology, and sexually transmitted infection (STI) microbiology, care, and treatment.

This study will be led by two PIs, one from the University of California, Los Angeles (UCLA) and one from the Foundation for Professional Development (FPD) in Pretoria, South Africa. We think our proposed project is an outstanding fit for the R01 mechanism, and are enthusiastic about the potential for our findings to significantly impact STI screening and treatment guidelines for pregnant women living with HIV in low and middle-income countries.

In addition to faculty and staff at UCLA and FPD, this application involves Co-Investigators from the University of Cape Town, the University of Alabama at Birmingham, and Louisiana State University, as well as the expert consultation of an outstanding biostatistician from the University of Mississippi.

We appreciate your consideration of this application and look forward to hearing the results of the review.

Sincerely,

Jeffrey D. Klausner, MD, MPH
UCLA Professor of Medicine and Public Health

Andrew Medina-Marino, PhD
Head, FPD Research Unit

Project/Performance Site Location(s)

Project/Performance Site Primary Location

Organization Name: UCLA David Geffen School of Medicine/Infectious Diseases

* Street1: 10833 Le Conte Ave		Street2: 52-254 CHS
* City: Los Angeles	County: Los Angeles	* State: CA: California
Province:	* Country: USA: UNITED STATES	* Zip / Postal Code: 90095-1688
DUNS Number: 092530369	* Project/Performance Site Congressional District: CA-033	

Project/Performance Site Location 1

Organization Name: Lousiana State University Health Sciences Center - NO

* Street1: 533 Bolivar St		Street2: 6th Floor
* City: New Orleans	County: Orleans	* State: LA: Louisiana
Province:	* Country: USA: UNITED STATES	* Zip / Postal Code: 70112-1349
DUNS Number: 782627814	* Project/Performance Site Congressional District: LA-002	

Project/Performance Site Location 2

Organization Name: Foundation for Professional Development

* Street1: 173 Mary Road		Street2: The Willows
* City: Pretoria	County:	* State:
Province:	* Country: ZAF: SOUTH AFRICA	* Zip / Postal Code:
DUNS Number: 568904572	* Project/Performance Site Congressional District: 00-000	

Project/Performance Site Location 3

Organization Name: University of Alabama

* Street1: 1900 University Blvd		Street2: THT 229
* City: Birmingham	County: Jefferson	* State: AL: Alabama
Province:	* Country: USA: UNITED STATES	* Zip / Postal Code: 35293-2060
DUNS Number: 063690705	* Project/Performance Site Congressional District: AL-007	

Project/Performance Site Location 4

Organization Name: Annova Health Institute

* Street1: 12 Sherborne Road		Street2: 72193
* City: Parktown	County:	* State:
Province:	* Country: ZAF: SOUTH AFRICA	* Zip / Postal Code:
DUNS Number:	* Project/Performance Site Congressional District: 00-000	

Project/Performance Site Location 5

Organization Name: SA-MRC

* Street1: Francie Van Zijl Drive		Street2: Parow Valley
* City: Cape Town	County:	* State:
Province:	* Country: ZAF: SOUTH AFRICA	* Zip / Postal Code:
DUNS Number:	* Project/Performance Site Congressional District: 00-000	

Project/Performance Site Location 6

Organization Name: University of Cape Town

* Street1: Observatory Road, 7925		Street2:
* City: Cape Town	County:	* State:
Province:	* Country: ZAF: SOUTH AFRICA	* Zip / Postal Code:
DUNS Number:	* Project/Performance Site Congressional District: 00-000	

File Name	Mime Type

Additional Location(s)

RESEARCH & RELATED Other Project Information

1. * Are Human Subjects Involved? ● Yes ❍ No

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ❍ Yes ● No

If yes, check appropriate exemption number

Exemption Number: _ 1 _ 2 _ 3 _ 4 _ 5 _ 6

If no, is the IRB review Pending? ● Yes ❍ No

IRB Approval Date:

Human Subject Assurance Number 00004642

2. * Are Vertebrate Animals Used? ❍ Yes ● No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ❍ Yes ❍ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. * Is proprietary/privileged information included in the application? ❍ Yes ● No

4.a. * Does the Project have an Actual or Perceived Impact – positive or negative – on the environment? ❍ Yes ● No

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ❍ Yes ❍ No

4.d. If yes, please explain:

5.a. * Is the research performance site designated, or eligible to be designated, as a historic place? ❍ Yes ● No

5.b. If yes, please explain:

6.a. * Does this project involve activities outside the U.S. or partnership with International Collaborators? ● Yes ❍ No

6.b. If yes, identify countries: South Africa

6.c. Optional Explanation: Subaward with MPI

7. Project Summary/Abstract	project_abstract1047818676.pdf	Mime Type: application/pdf
8. Project Narrative	project_narrative1047818677.pdf	Mime Type: application/pdf
9. Bibliography & References Cited	References1047970066.pdf	Mime Type: application/pdf
10. Facilities & Other Resources	Facilities_and_Resources_rev1047970074.pdf	Mime Type: application/pdf
11. Equipment	EQUIPMENT1047970690.pdf	Mime Type: application/pdf
12. Other Attachments	Foreign_Justification1047970067.pdf	Mime Type: application/pdf

ABSTRACT

In 2012, WHO estimated that over 350 million cases of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV) occurred globally. Sexually transmitted infections (STIs) 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.

STIs 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 cost effective screening strategies that optimally decrease the burden of STIs during pregnancy, and reduce adverse pregnancy and infant outcomes, 2) elucidate the role of the vaginal microbiome in treatment outcomes, and 3) inform STI screening and treatment guidelines in other low-middle income countries, we propose a novel, highly innovative study with the following three Aims:

Aim 1: Evaluate different diagnostic screening interventions to decrease the burden of CT/NG/TV, and reduce adverse pregnancy and birth outcomes among pregnant women.

Aim 2: Evaluate the cost per pregnant woman diagnostically screened and treated, cost of adverse pregnancy and birth outcomes, and cost-effectiveness per STI and DALY averted.

Aim 3: Investigate the relationship between the vaginal microbiome and CT treatment failure 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. 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.

PROJECT NARRATIVE

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.

LITERATURE CITED

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FACILITIES AND OTHER RESOURCES

The proposed research will be conducted within the University of California, Los Angeles (UCLA) in Los Angeles and the Foundation for Professional Development (FPD) in Pretoria, South Africa, in collaboration with the University of Alabama at Birmingham (UAB), Louisiana State University (LSU), the University of Cape Town (UCT), The South African Medical Research Council and the Anova Health Institute / University of Pretoria. These organizations have years of experience with successful collaborations with each other, and look forward enthusiastically to combining their critical resources for the first time, for the implementation of this study.

University of California, Los Angeles (UCLA)

Division of Infectious Diseases
The Division of Infectious Diseases, Department of Medicine has a broad and growing portfolio of HIV/STD prevention and policy research, focused primarily on the US and developing country issues, with ongoing NIH-funded research projects in South Africa, Peru, China, Uganda, and Malawi.

Office Space:
Dr. Klausner's research unit occupies approximately 900 sq ft of office space at 10920 Wilshire Blvd, Suite 350, Los Angeles, CA 90024. In addition, he has a designated office space in the Community Health Sciences Building, located on the UCLA campus.

Computers, Telecommunications, IT:
The UCLA personnel named on this project all have computers, printers, telephones, fax, and copying capabilities. The informational technology infrastructure is maintained by the IT group in the UCLA Department of Medicine. UCLA routinely uses Skype and ReadyTalk for international telecommunications.

Administration:
Dr. Chrys Stafylis is the IRB Coordinator and Research Manager. He is supported by the administrative team, including Fund Manager Richard Tristan, within the Division of Infectious Diseases and the UCLA Department of Medicine on all fund, human resources, and grant-related issues.

Foundation for Professional Development (FPD)

FPD was established in 1997 by the South African Medical Association (SAMA). In 2000, FPD became registered as a private institution of higher education. FPD prides itself on being one of a few private higher education institutions in South Africa that fully engages in the three scholarships of higher education- teaching and learning, research and community engagement/capacity development.

Office Space: The FPD office complex, made up of East and West block, is physically located at Struland Office Park, 173 Mary Road, The Willows, Pretoria. FPD's premises occupies approximately 1686m^2 of office space and has offices at the following locations around South Africa.

57 Western Avenue
Vincent
East London, 5247

206 Cape Road
Newton Park
Port Elizabeth, 6000

185 Duxbury Road
Hatfield
Pretoria, 0028

115 Marshal Street
Polokwane
0699

ERF 791
Thohoyandou
Polokwane East, 0699

2a Financial Square
Nelson Mandela Drive
Witbank, 1035

Computers, Telecommunications, IT: The FPD personnel named in the project have access to password-protected computers, printers, telephones, fax and photocopying machines and these are managed by the IT department of FPD. Tele-conference facilities are also available for communication. To address quality control of health information, FPD successfully developed and deployed a tier 3 electronic health information system in 52 facilities that covered 150 000 patient records and developed extensive experience in ensuring data quality in a public sector clinical environment. A data audit in 2011 by the USG reported very high data quality.

Administration: FPD's Finance Department is made up of 18 qualified accountants and bookkeepers and is overseen by the group Chief Financial Officer. Each year, the relevant financial staff undergo US Government Donor and International Financial Reporting Standards (IFRS) training to keep up-to-date with current developments and policies. The strength of FPD's Finance Team is proven by a history of unqualified statutory and donor audit reports. Due to the large number of donor and sponsor grants managed by FPD a state of the art financial management system – ACCPAC's Enterprise Resource Planning system (ERP) – was implemented in 2007 and customized to meet the requirements of reporting to multiple donors on multiple projects and to support decentralized office locations. Customized reporting modules were designed to process and match reporting requirements on large scale donor funded programs in multiple currencies, multiple locations and with multiple donors each requiring unique financial reporting at flexible intervals. This extensive customization includes an internal reporting and budgeting facility to effectively manage the different grants, donors and departments. To date this system has managed and met all reporting requirements for funders such as PEPFAR, the Bill and Melinda Gates Foundation, OFID,NHI, Atlantic Philanthropies, MRC, Department of Health (South African Government) etc. This system is also able to provide accurate and reliable financial statements, forecasting of cash flow and assessment of fund utilization rates and a purchasing system that is web based and controls all purchase orders against appropriate authorization and available funding. FPD is not only responsible for the financial control of its own funds, but performs treasury functions for all of its JV's and subsidiaries, and a number of international NGO's with whom FPD have MOU's to provide this particular function.

University of Alabama at Birmingham (UAB)

Division of Infectious Diseases

The UAB Division of Infectious Diseases (ID) and Department of Medicine provide a stimulating intellectual environment with regularly scheduled teaching conferences, journal clubs, research seminars, ID and Medicine Grand Rounds, and visiting speakers in a wide range of specialties. There is a long history of successful STI research studies conducted by investigators in the ID Division at UAB, including Dr. Muzny, particularly at the Jefferson County Health Department (JCDH) STD Clinic. Dr. Muzny has been conducting clinical research at the JCDH STD clinic and other locations on the UAB campus for the past 7 years. The Microbiome/ Bioinformatic/Gnotobiotic Animal Core of the UAB Comprehensive Cancer Center provides state of the art technology for the identification and functional analysis of complex microbial communities that have been shown to have a major impact on host metabolism and homeostasis. It provides services to support sample preparation, sequencing, bioinformatics analysis, and animal model hypothesis testing.

Office Space:

Dr. Muzny's office is located in the Zeigler Research Building on the UAB campus, directly down the hall from the UAB STD Research Laboratories, 1 block from the UAB Personal Health clinic, and 2 blocks from the Ryals Public Health Building. Administrative support is supplied by the ID Division. A 385 ft^2 room adjacent to these offices serves as the UAB STD Program Conference Room for scheduled meetings and presentations. The STD Research Program Data Manager's office is located directly across the hall from Dr. Muzny's office. All offices are fully furnished and equipped with phones, network-linked personal computers, fax machines, and copiers.

Computers, Telecommunications, IT:

Dr. Muzny has Windows Office and EndNote installed on her computer. Participant study questionnaires from UAB research studies are supported by the STD Research Program Data Manager using TeleForm, a powerful, high volume information capture solution. The TeleForm designer easily implements forms processing and document capture. In designing forms, a series of data checks is implemented to prevent entry of out-of-range and inconsistent values and to ensure entry of required fields. Utilization of the TeleForm designer facilitates

development of annotated case report forms for use in documentation of the database system. Forms designed using TeleForm designer will be exported to an Excel database. All data are stored on the ID Division's secure server at UAB. The UAB Bioinformatics Core owns and leases access to a large collection of servers, storage systems, workstations, laptops and peripherals. Separate servers are utilized for production web sites, production database systems, data entry databases, application development, database development, web site development, bioinformatics analysis, backup, and failover. High capacity data storage systems are available that are able to provide hundreds of terabytes of high performance network-attached and direct-attached storage. Over 25 different servers are currently utilized, comprising a mixture of dedicated hardware and Virtual Machines with a combination of Windows, Linux, Solaris, and Macintosh operating systems. In addition, the UAB Bioinformatics Core uses the High Performance Computing Facility of UAB Research Computing to run many of its analysis pipelines. This facility consists of a primary compute cluster with three generations of hardware totaling 896 cores connected with quad data rate Infiniband. This cluster is rated at over 6 Teraflops of computing capacity. Currently, a half of a petabyte of online storage is available directly connected to the cluster network.

Louisiana State University (LSU)

Health Sciences Center
The LSU Health Sciences Center-New Orleans is uniquely positioned to support an intellectually stimulating environment that will ensure the success of this proposed project. Promoting a highly interactive and intellectually stimulating environment was a central goal of the design of the computational laboratory. Weekly meetings are also held in the laboratory to discuss sequencing on the MiSeq and informatics approaches between the computational scientists, biologists, and clinicians involved in the sequencing lab. LSUHSC is committed to further developing strong computational analysis and bioinformatics capabilities, which will help to ensure the success of the Bioinformatics laboratory.

Office Space:
Dr. Taylor has a private office located on the 6th floor of the Clinical Sciences Research Building (CSRB) at LSUHSC equipped with phone, computer, printer, and high-speed Internet access. LSUHSC has an administrative staff and information technology staff available to all researchers.

Computational Laboratory:
Dr. Taylor's computational laboratory occupies 470 square feet of space on the 6th floor of LSUHSC's Clinical Sciences Research Building (CSRB) divided into the main laboratory and an attached private office (described above). The open floor plan of the renovated computational laboratory has seven workstations situated around the perimeter of the lab equipped with high-performance multi-processor computers. A meeting table in the center of the room provides space for up to six participants meeting face-to-face and a ceiling-mounted drop down projection screen allows for presentation of slides and remote meeting participation. This laboratory setup provides an ideal venue for collaborative meetings where data analysis results can be viewed and discussed with collaborators. The computer lab is equipped with high-performance computing workstations connected via a local Gbps network router. A Synology DiskStation 12-Bay Network Attached Storage (NAS) houses 48 TB (12 x 4TB Enterprise Class HDDs) of secondary storage configured in a Synology hybrid RAID with 2-Disk redundancy providing 36.2 TB usable storage. The NAS is connected to the same Gbps router using 4 ethernet cables with link aggregation providing sufficient throughput to serve all of the workstations. Current workstations installed in the lab include:

- 6 x dual processor 2.7 GHz Twelve-Core Intel Xeons with 24 physical cores each (48 logical cores each), each equipped with 512 GB 1333Mhz DDR3 ECC RAM, a 512 GB SSD for the operating system and 18 TB of additional secondary storage (3 x 6TB 7200 rpm HDDs), and NVIDIA Quadro NVS 510 2 GB DDR3 Graphics Cards
- 1 x dual processor 2.0 GHz Eight-Core Intel Xeon with 16 physical cores (32 logical cores)**,** equipped with 128 GB 1600MHz DDR3 ECC RAM, 4 TB (2 x 2TB 7200 rpm HDDs) secondary storage, and an NVIDIA Quadro 4000 2 GB GDDR5 Graphics Card
- 1 x quad processor 2.4 GHz Eight-Core Intel Xeon with 32 physical cores (64 logical cores), equipped with 512 GB 1600Mhz DDR3 ECC RAM, 4.25 TB (4TB 7200 rpm HDD, 256 Gb SSD) secondary storage, and an NVIDIA Kepler 4000 3 GB GDDR5 Graphics Card

In total these 8 multi-processor, high performance workstations provide 192 physical computing cores (384 logical computing cores) available for distributed analysis of sequencing data. These computers run Ubuntu

Linux 14.04.2 LTS (Trusty Tahr) and are equipped with all necessary analysis software and utilities. The machines are each protected by UPS for surge protection and battery backup. The Synology NAS is also protected by UPS and backed up to external storage.

Sequencing Laboratory: The sequencing laboratory occupies 1,210 square feet of space on the 7th floor of LSUHSC's Clinical Sciences Research Building (CSRB). Within the lab there are three rooms dedicated to DNA isolation, PCR preparation and sequencing. The lab is equipped with state-of-the-art instrumentation and provides a variety of genomic analyses including TaqMan real-time PCR, RNA/DNA extraction, purification and high-throughput Illumina MiSeq sequencing. A Clinical Specimen BSL-2 laboratory is available for processing human specimens. This facility is equipped with a laminar flow hood, refrigerated aerosol containment centrifuges, a cytospin, -80ºC freezer with liquid nitrogen back up, and a separate liquid nitrogen specimen storage dewer. Animal or environmental samples undergo initial processing and nucleic acid isolation in a laminar flow hood. Specimens are aliquotted and back-up samples stored in separate containers.

University of Cape Town (UCT) School of Public Health and Family Medicine

Division of Health Economics and Health Economics Unit

The Health Economics Unit was established in 1990 as a research unit within the then Department of Community Health at the University of Cape Town. The unit aims to build equitable health systems in South Africa and beyond through teaching, research and policy engagement. The unit has an impressive research and policy engagement track record particularly in the areas of cost-effectiveness analysis and health financing. Teaching in Health Economics is housed within the Division of Health Economics, including a postgraduate diploma, Masters in Public Health and PhD specializations in Health Economics.

Office Space:

The unit/division occupies its own building adjacent to the School of Public Health and Family Medicine, in the Faculty of Health Sciences at UCT. Space includes 14 private offices, a room for postgraduate students and a boardroom with full videoconferencing facilities.

Computers, Telecommunications, IT:

All staff and students dedicated computers and printers. Departmental and University-wide network and internet access is available to all users, with centralized printing services and library and electronic journal access.

Administration and Grants Management:

Research management at the Health Economics Unit is supported by numerous operational and support staff with the capacity to address pre- and post-award financial management, including review, approval and processing of all transactions associated with the sub-contract of this award. This includes financial projections and reports, grants compliance, and control and monitoring of subject payments in a way that maximizes confidentiality as well as security of funds.

South African Medical Research Council (SA-MRC)

Maternal and Infant Health Care Strategies Research Unit:

The unit is an extramural unit of the SA-MRC in partnership with the University of Pretoria. The Unit has been in existence since 1997. The Unit specializes in identifying the core problems, developing effective solutions and determining successful ways of implementing interventions to reduce deaths of pregnant women and their infants at primary and secondary levels of care. This research has been closely linked with helping to achieve the Millennium Development Goals (MDGs) 4 and 5, and now is concentrating on the Sustainable Development Goals. The research mandate of the Unit has been to develop health strategies at primary and secondary care levels for mothers and infants by seeking sellable and sustainable solutions; by seeking we mean performing research, by saleable we mean solutions that are acceptable to women, health care workers and health administrators, and by sustainable solutions we mean health strategies that have been developed to solve the problems identified and how they can be sustained.

Office Space:
The Unit occupies a block an old nursing residence at Kalafong Provincial Tertiary Hospital. The agreement with the hospitals is that we will maintain the building and pay for its costs and the Hospital will not charge rent. There are at 20 workspaces along with all the other facilities. Furthermore the unit has space on the ground floor which can be used to see patients.

Computers, Telecommunications, IT:
The Unit has all the facilities necessary for modern communication, including high speed internet connect nodes. This infrastructure is maintained by the University of Pretoria.

Administration and Grants Management:
The University of Pretoria manages all the grants of the unit and we have an accountant who keeps our finances in order. The Unit has a fulltime programme manager who looks after the programmes on sites.

University of Cape Town (UCT) School of Medicine

Division of Medical Virology
UCT established the Institute of Infectious Disease and Molecular Medicine (IDM) in order to consolidate and expand major existing efforts to combat the most serious threats to health and overall prosperity in the region: infectious diseases including HIV/AIDS and TB and non-communicable diseases, and locally prevalent cancers and genetic disorders.

Laboratories & Equipment: The IDM has over 8000 square metres of laboratory space.In the areas that fall under the management of Prof Williamson that are available for this project: there is a 91m^2 dedicated Biosafety level-2 (BSL-2) molecular biology laboratory, a separate and dedicated PCR clean room, a separate and dedicated nucleic acid extraction room and a dedicated laboratory (BSL-2) to work with clinical material. The laboratories are located on the third floor of the Wernher Beit South Building at UCT. The molecular biology laboratory has standard equipment including micro-centrifuges, monitored fridges and freezers, BSL-2 safety cabinets, thermal cyclers, gel electrophoresis equipment, Dark Reader Illuminator. All freezers are connected to a 24-hour monitoring system. Access is available to Roche MagNA Pure Compact System, multiple conventional and gradient thermal cyclers, a FLUOstar OPTIMA (BMG Labtech) fluorescence microplate reader, NanoDrop and a Quantstudio 7 real-time PCR system and Roche LightCycler. A walk-in cold room (4°C) and freezer room (-20°C) are available for storage. Glassware washing and autoclave facilities are located on the same floor.

Office: Private Departmental offices for Dr Meiring and shared offices for senior scientists, postdocs, technologists and students are on the third floor of IDM, UCT. The building is secure with access control via individual identification cards. Every office is networked with one telephone connection and one or more desktop computer facilities.

Computers and Software: All staff, students and post-doctoral fellows have dedicated computers and printers. Departmental and University-wide network and internet access is available to all users, with centralized printing services and library and electronic journal access. High Performance Computing (HPC) laboratory: The University of Cape Town's Information and Communication Technology Services (ICTS) High Performance Computing (HPC) laboratory provides free computing resources and support to scientific computing users at UCT. The facilities and setup include 564 cores, large memory machines, Tesla M2090 GPUs, 25TB storage, Infiniband interconnect and OpenMPI Architecture. The ICTS HPC has also integrated their cluster resources into the South African National Computing Grid. Support is available for the installation and configuration of scientific applications (custom written, open source or commercial) on the HPC nodes, for modification of packages to grid format facilitating access to more computing resources and providing assistance for parallel coding requirements. H3 African bioinformatics network (H3ABioNet): The H3ABioNet was awarded to Prof Mulder of the Computational Biology Division and IDM. Our ties to this African bioinformatics network for H3Africa within the IDM will provide additional computing resources and access to cloud computing should this be required.

Administration and Grants Management: Research management at IDM is supported by numerous operational and support staff with the capacity to address pre- and post-award financial management, including review, approval and processing of all transactions associated with the sub-contract of this award. This includes financial projections and reports, grants compliance, and control and monitoring of subject payments in a way that maximizes confidentiality as well as security of funds.

Anova Health Institute / University of Pretoria Department of Medical Microbiology

Anova Health Institute is a South African-based non-governmental organization that receives its main funding from PEPFAR through USAID. The organization works as district support partner in various regions of South Africa and has a large portfolio of HIV, TB and STI implementation programs in the public healthcare sector. Anova's research portfolio is built around the same program areas. For microbiological research, Anova has a longstanding collaboration with the Department of Medical Microbiology at the University of Pretoria as evidenced by a large number of successful joint research projects. Prof Peters jointly works with Anova and the University of Pretoria Department of Medical Microbiology to ensure a strong collaborative relationship as well as access to and supervision of microbiological laboratory work.

Office Space:
Prof Peters occupies an office at the Anova Health Institute at 12 Sherborne Road, Parktown Johannesburg. In addition, he has a designated office space at the University of Pretoria, Department of Medical Microbiology in the Pathology Building (Room 3.11). There is ample space for storage of research documentation, consumables and resources.

Computers, Telecommunications, IT:
Prof Peters and laboratory staff all have computers, printers, telephone, email communication, and copying capabilities; both at Anova and at UP.

Administration:
Ms Linda McConnell is the Chief Executive Officer at Anova Health Institute and responsible for managing all donor organizations and all funds received by the organization. There is a specific compliance division at Anova who ensures that all criteria for good financial management are met.

Laboratory resources
The infrastructure to support this research project exists at the Department of Medical Microbiology, University of Pretoria/NHLS. This includes: SANAS accredited laboratories, specialized equipment for molecular analysis, skilled and trained technologists, clinicians and researchers, Internet access, E-mail and library facilities. The required allocated diagnostic and research laboratories as well as the necessary equipment which include: Biosafety cabinets, centrifuges, heating blocks, thermocyclers, Roche Version 2 LightCycler (Virtual Laboratory) and a Roche 480 LightCycler for Real-Time PCR platforms, Rotaphor PFGE system and the Bionumerics (GelCompar part) programme required for the genotypying analysis. Senior research team members will insure regular meetings and assessment of results to support and train junior researchers.

EQUIPMENT

None.

FOREIGN JUSTIFICATION

Our study team has outstanding, well-documented experience in the conduct and in-depth analysis of clinical cohort and laboratory studies for many years. Specifically, PIs Klausner and Medina-Marino have collaborated successfully on grants, publications, NIH-Fogarty training and infectious disease/ reproductive health projects since first meeting and working together at CDC-PEPFAR South Africa in 2010. Their current successful R21 (2015-2017) from NICHD directly informs this new proposal. That R21 is a pilot study that integrates molecular diagnostic testing for CT, NG and TV into antenatal care (ANC) services for HIV-infected pregnant women in South Africa. In that study, we found that diagnostic screening and targeted treatment (TT) during ANC was highly acceptable and feasible; 97.8% of all eligible women agreed to be tested, and >93% with an STI received same-day treatment. Importantly, we found a 41% STI prevalence in this patient population, of which 65% of infections were asymptomatic, demonstrating the importance of testing STI interventions among this patient population.

Overall, HIV and STIs among pregnant women in South Africa are a major problem. In 2013, the South African government estimated that 29.7% of women seeking antenatal care were HIV-infected, a prevalence that has remained relatively stable since 2007. That high HIV prevalence is compounded by high rates of STIs in women of reproductive age. Given that most STIs in women are asymptomatic and that the South African government currently only recommends symptomatic screening and syndromic management in line with WHOs global guidelines, the majority of STIs in HIV+ South African pregnant women go undiagnosed and untreated.

Our study will enhance knowledge of STIs during pregnancy, especially among high HIV prevalence populations, and the effectiveness of routinizing same-day PCR screening and treatment for these STIs in reducing adverse pregnancy and birth outcomes. Furthermore, until now there have been no studies in low and middle-income countries that have evaluated the costs and benefits of CT/NG/TV screening and treatment during pregnancy as it relates to pregnancy, neonatal and infant outcomes. Our cost/cost-effectiveness study has the potential to influence health policy in South Africa and globally, especially as it compares to syndromic management of STIs during pregnancy. If successful, this study would also provide reproducible cost-effectiveness analysis models for countries to better plan for and implement routine CT/NG screening and treatment in pregnancy.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Jeffrey Middle Name Last Name*: Klausner Suffix: MD

Position/Title*:	Professor
Organization Name*:	UCLA David Geffen School of Medicine
Department:	Medicine
Division:	Infectious Diseases
Street1*:	9911 West Pico Blvd
Street2:	Suite 955
City*:	Los Angeles
County:	Los Angeles County
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	90035-2738

Phone Number*: 310-557-3044 Fax Number: 310-557-3679 E-Mail*: JDKlausner@mednet.ucla.edu

Credential, e.g., agency login: jklausner

Project Role*: PD/PI Other Project Role Category:

Degree Type: MD Degree Year: 1991

	File Name
Attach Biographical Sketch*:	Biosketch_Klausner1047818701.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Warren Middle Name S Last Name*: Comulada Suffix: DrPH

Position/Title*:	Sr Statistician
Organization Name*:	UCLA David Geffen School of Medicine
Department:	NPI Semel Institue
Division:	NPI Semel Institute
Street1*:	10920 Wilshire Blvd
Street2:	Suite 350
City*:	Los Angeles
County:	Los Angeles
State*:	CA: California
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	90095-7051

Phone Number*: 310 794-0938 Fax Number: E-Mail*: scomulad@ucla.edu

Credential, e.g., agency login: comulada2

Project Role*: Other Professional Other Project Role Category: Biostatistician

Degree Type: DrPH Degree Year: 2006

	File Name
Attach Biographical Sketch*:	Biosketch_Comulada1047970139.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Andrew Middle Name Last Name*: Medina-Marino Suffix: PhD

Position/Title*: Head of Research Unit

Organization Name*:	Foundation for Professional Development
Department:	
Division:	
Street1*:	173 Mary Road
Street2:	
City*:	The Willows
County:	
State*:	
Province:	
Country*:	ZAF: SOUTH AFRICA
Zip / Postal Code*:	

Phone Number*: +27 (0) 12 816 9000 Fax Number: E-Mail*: andrewm@foundation.co.za

Credential, e.g., agency login: AMEDINA-MARINO

Project Role*: PD/PI Other Project Role Category:

Degree Type: PhD Degree Year: 2009

	File Name
Attach Biographical Sketch*:	Bios-ketch_Medina_Marino_rev1047970699.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Christopher Middle Name Last Name*: Taylor Suffix: PhD

Position/Title*:	Associate Professor
Organization Name*:	Lousiana State University
Department:	Microbiology & Immunology
Division:	Bioinformatics
Street1*:	533 Bolivar St
Street2:	Room 605
City*:	New Orleans
County:	Orleans
State*:	LA: Louisiana
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	70112-1349

Phone Number*: (504) 568-4065 Fax Number: E-Mail*: ctay15@lsuhsc.edu

Credential, e.g., agency login: CHRISTAYLOR

Project Role*: Other (Specify) Other Project Role Category: Site PI

Degree Type: PhD Degree Year: 2008

	File Name
Attach Biographical Sketch*:	Biosketch_Taylor1047818718.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Christina Middle Name Last Name*: Muzny Suffix:

Position/Title*:	Associate Professor
Organization Name*:	University of Alabama
Department:	Infectious Diseases
Division:	
Street1*:	1900 University Boulevard
Street2:	THT 229

City*:	Birmingham
County:	
State*:	AL: Alabama
Province:	
Country*:	USA: UNITED STATES
Zip / Postal Code*:	35293-2060

Phone Number*: 205-934-5191 Fax Number: E-Mail*: cmuzny@uabmc.edu

Credential, e.g., agency login: CMUZNY

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: MD Degree Year: 2003

	File Name
Attach Biographical Sketch*:	Biosketch_Muzny_rev21047970918.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Susan Middle Name M Last Name*: Cleary Suffix: PhD

Position/Title*:	Associate Professor
Organization Name*:	University of Cape Town
Department:	Health Economics
Division:	
Street1*:	Observatory, 7925
Street2:	
City*:	Cape Town
County:	
State*:	
Province:	
Country*:	ZAF: SOUTH AFRICA
Zip / Postal Code*:	

Phone Number*: +27 21 406 6755 Fax Number: E-Mail*: susan.cleary@uct.ac.za

Credential, e.g., agency login:

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: PhD Degree Year: 2007

	File Name
Attach Biographical Sketch*:	Biosketch_Cleary1047970089.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Tracy Middle Name L Last Name*: Meiring Suffix: PhD

Position/Title*:	NRF Career Award Fellow
Organization Name*:	University of Cape Town
Department:	Molecular Medicine
Division:	
Street1*:	Observatory, 7925
Street2:	
City*:	Cape Town
County:	
State*:	
Province:	
Country*:	ZAF: SOUTH AFRICA

Zip / Postal Code*:

Phone Number*: +27 21 406 6300 | Fax Number: | E-Mail*: tracy.meiring@uct.ac.za

Credential, e.g., agency login:

Project Role*: Co-Investigator | Other Project Role Category:

Degree Type: PhD | Degree Year: 2009

	File Name
Attach Biographical Sketch*:	Biosketch_Meiring1047970087.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Robert Middle Name Last Name*: Pattinson Suffix: MD

Position/Title*: Director
Organization Name*: University of Cape Town
Department: Obstetrics and Gynecology
Division:
Street1*: Atteridgeville, 0008
Street2:
City*: Pretoria
County:
State*:
Province:
Country*: ZAF: SOUTH AFRICA
Zip / Postal Code*:

Phone Number*: +27 12 318 6400 | Fax Number: | E-Mail*: robert.pattinson@up.ac.za

Credential, e.g., agency login:

Project Role*: Co-Investigator | Other Project Role Category:

Degree Type: MD | Degree Year: 1992

	File Name
Attach Biographical Sketch*:	biosketch_Pattinson1047970695.pdf
Attach Current & Pending Support:	

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Koleka Middle Name P Last Name*: Mlisana Suffix: PhD

Position/Title*: Associate Professor
Organization Name*: University of KwaZulu Natal
Department: Medicinal Microbiology
Division:
Street1*: 238 Mazisi Kunene Rd
Street2: Glenwood 4041
City*: Durban
County:
State*:
Province:
Country*: ZAF: SOUTH AFRICA
Zip / Postal Code*:

Phone Number*: +27 (0)31 260 2787 | Fax Number: | E-Mail*: mlisanak@ukzn.ac.za

Credential, e.g., agency login:

Project Role*: Co-Investigator	Other Project Role Category:
Degree Type: PhD	Degree Year: 2014
	File Name
Attach Biographical Sketch*:	Biosketch_Koleka_rev1047970697.pdf
Attach Current & Pending Support:	

BIOGRAPHICAL SKETCH

NAME: Jeffrey D. Klausner, MD, MPH

eRA COMMONS USER NAME (credential, e.g., agency login): jklausner

POSITION TITLE: Professor of Medicine and Public Health

EDUCATION/TRAINING*:*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, New York	A.B.	06/1986	Chemistry and Art
Cornell University Medical School, New York, NY	M.D.	06/1991	Medicine
Harvard School of Public Health, Boston, MA	M.P.H.	06/1995	International Health
Centers for Disease Control and Prevention, GA	EIS	06/1997	Epidemiology
University of Washington, Seattle, WA	Fellow	06/1998	Infectious Diseases

A. Personal Statement

Jeffrey D. Klausner, MD, MPH, is a board-certified internet, infectious disease specialist, and internationally recognized infectious disease researcher and expert in the prevention, control and epidemiology of HIV infection and other sexually transmitted diseases. Dr. Klausner is the Senior Editor of the McGraw-Hill Lange textbook *Current Diagnosis and Management of Sexually Transmitted Diseases*. Dr. Klausner is a member of the WHO STI Treatment Guidelines work group and plays a leadership advisory role in the WHO congenital syphilis elimination effort. He is a frequently invited speaker at national and international meetings on HIV and STDs. From 2009-2011 Dr. Klausner was the Branch Chief for the US CDC PEPFAR HIV and TB program in Pretoria, South Africa, the location of the proposed study. Upon his return to the US, he accepted a senior faculty position at UCLA in infectious disease research and global health with a particular focus on global women's health and infections in pregnancy. Dr. Klausner has served as Principal Investigator for numerous CDC, NIH and industry sponsored clinical trials and HIV/STD prevention studies and is Chair of the NIH/DMID STI Clinical Trials Group. This current proposal builds directly on his interest in furthering the understanding of the host and responses to STIs among HIV-infected pregnant women and his recent studies of infections in pregnant women in Botswana, Congo, South Africa, Vietnam, India, Haiti and Peru.

Dr. Klausner has known and collaborated with Dr. Medina-Marino since 2010, mentoring trainees, implementing USAID, CDC and NIH-funded research and co-authoring publications. As the Principal Investigator and STI clinical expert on this project, he will co-lead with Dr. Medina-Marino the oversight, design, implementation, and analysis of this study.

B. Positions and Honors

1991-1994	Intern and Resident, Medicine, NYU-Bellevue Hospital Center, NY
1995-1997	Officer, Epidemic Intelligence Service, Centers for Disease Control, Atlanta, GA
1997-1998	Senior Clinical Fellow, Infectious Diseases, University of Washington, Seattle, WA
1998-2004	Assistant Clinical Professor of Medicine, University of California, San Francisco
1998-2005	Medical Director, San Francisco City Clinic, San Francisco municipal STD Clinic
1998-2009	Director, San Francisco, Department of Public Health, STD Services
2004-2011	Associate Clinical Professor of Medicine, University of California, San Francisco
2009-2012	Member, WHO workgroup HIV and STD prevention for MSM/Transgender persons
2009-2011	Chief, HIV and TB Branch, Centers for Disease Control, South Africa
2012-Present	Professor of Medicine, University of California, Los Angeles
2013-Present	Professor of Public Health, University of California, Los Angeles
2013-Present	Member, WHO workgroup STI Treatment Guidelines

2002	San Francisco Suicide Prevention Community Award
2002	American STD Association, Young Investigator Award
2006	UCSF Association of Clinical Faculty Special Recognition Award

2009 Beyond AIDS Nettie Award
2010 Bay Area's Top Doctors and Dentists Award, Internal Medicine
2010 *Clinical Infectious Diseases* Award for Outstanding Review
2016 CDC Jack N. Spencer Career Achievement Award

C. Contributions to Science

1. Curable Infections in pregnant women: Since returning to the U.S. in 2012, I have launched a program to study the acceptability, feasibility, prevalence and outcomes of screening for curable STIs in pregnant women. I have completed studies in Peru, Haiti, India, Vietnam, Congo, Botswana and South Africa demonstrating the high acceptability of STI testing with self-collected vaginal swabs, the excellent performance of point-of-care PCR assays and the high frequency of treatment, partner treatment and clearance of infection. As a member of the WHO STI Guidelines Committee we are reviewing those and other data in anticipation of recommendations for universal STI screening in pregnancy.

a. Cabeza J, García PJ, Segura E, García P, Escudero F, La Rosa S, León S, **Klausner JD**. Feasibility of Chlamydia trachomatis screening and treatment in pregnant women in Lima, Peru: a prospective study in two large urban hospitals. Sex Transm Infect. 2015 Feb;91(1):7-10. doi: 10.1136/sextrans-2014-051531. PMID: 25107711; PMCID: PMC4417475.
b. Wynn A, Ramogola-Masire D, Gaolebale P, Moshashane N, Agatha Offorjebe O, Arena K, **Klausner JD**, Morroni C. Acceptability and Feasibility of Sexually Transmitted Infection Testing and Treatment among Pregnant Women in Gaborone, Botswana, 2015. Biomed Res Int. 2016;2016:1251238. doi: 10.1155/2016/1251238. PMID: 27119076; PMCID: PMC4826911.
c. Bristow CC, Mathelier P, Ocheretina O, Benoit D, Pape JW, Wynn A, **Klausner JD**. Chlamydia trachomatis, Neisseria gonorrhoeae, and Trichomonas vaginalis screening and treatment of pregnant women in Port-au-Prince, Haiti. Int J STD AIDS. 2017 Jan 1:956462416689755. doi: 10.1177/0956462416689755. PMID: 28134005.
d. Mudau M, Peters RP, De Vos L, Olivier DH, J Davey D, Mkwanazi ES, McIntyre JA, **Klausner JD**, Medina-Marino A. High prevalence of asymptomatic sexually transmitted infections among human immunodeficiency virus-infected pregnant women in a low-income South African community. Int J STD AIDS. 2017 Jan 1. doi: 10.1177/0956462417724908. PMID: 28799824.

2. Point-of-care and near care diagnostic testing for STIs: With over 500 million annual curable sexually transmitted infections (STIs) globally, STIs remain a common and preventable means of adverse pregnancy and birth outcomes. Prematurity is the leading cause of under age 5 years mortality and undiagnosed and untreated STIs are one of the most significant causes of prematurity. New diagnostics that are inexpensive, easy-to-use and accurate are urgently needed in low and middle income countries. Since the mid-2000s, I have been researching, developing and evaluation point-of-care diagnostics for HIV, syphilis, chlamydial and gonococcal infections (*CID*, 2008, *Trop Med Int Health* 2009, *PloS One* 2013, *Open Forum ID* 2014). Currently I have STI screening projects in Democratic Republic of Congo, Botswana, South Africa, Haiti and India building upon and extending earlier findings of high-rates of curable STIs in pregnancy associated with adverse pregnancy and birth outcomes including increased rates of mother-to-child transmission of HIV infection. Using those data, I aim to conduct clinical trials demonstrating the impact and cost-benefit of STI screening and treatment in pregnancy in low and middle income country settings.

a. Philip SS, Ahrens K, Shayevich C, de la Roca R, Williams M, Wilson D, Bernstein K, **Klausner JD**. Evaluation of a new point-of-care serologic assay for herpes simplex virus type 2 infection. Clin Infect Dis. 2008 Nov 15;47(10):e79-82. doi: 10.1086/592696. PMID: 18840082.
b. Madhivanan P, Krupp K, Hardin J, Karat C, **Klausner JD**, Reingold AL. Simple and inexpensive point-of-care tests improve diagnosis of vaginal infections in resource constrained settings. Trop Med Int Health. 2009 Jun;14(6):703-8. doi: 10.1111/j.1365-3156.2009.02274.x. Epub 2009 Apr 20. PMID: 19392745; PMCID: PMC3625926.
c. Pilcher CD, Louie B, Facente S, Keating S, Hackett J Jr, Vallari A, Hall C, Dowling T, Busch MP, **Klausner JD**, Hecht FM, Liska S, Pandori MW. Performance of rapid point-of-care and laboratory tests for acute and established HIV infection in San Francisco. PLoS One. 2013 Dec 12;8(12):e80629. doi: 10.1371/journal.pone.0080629. eCollection 2013. PMID: 24349007; PMCID: PMC3861178.

d. Bristow CC, Leon SR, Ramos LB, Vargas SK, Flores JA, Konda KA, Caceres CF, **Klausner JD**. Laboratory Evaluation of a Dual Rapid Immunodiagnostic Test for HIV and Syphilis Infection. Journal of clinical microbiology. 2014. Epub 2014/11/08. doi: 10.1128/jcm.02763-14. PMID: 25378568.

3. Pathophysiology and clinical aspects of syphilis: There are 6 million new cases of syphilis annually and a current exponentially growing epidemic of syphilis among men who have sex with men. Since first describing the elimination and re-introduction of syphilis in Seattle-King County in 1999 (*Am J Pub Health*, 1999), I have been one of the leading public health researchers describing clinical manifestations and pathogenesis of the disease and creating and evaluating new interventions to control syphilis and (*AIDS* 2004, *BMC ID* 2013; *STD* 2015). Based on my research and those replicated by others, the US DHHS recommendations for syphilis screening in HIV-infected patients include testing every 3-6 months. Furthermore, based on my prior clinical studies, the CDC STD Guidelines include recommendations for the use of both treponemal and non-treponemal testing in patient presenting symptomatically, in particular with primary stage manifestations. Currently I provide guidance in the frequency and type of STD screening in patients on Pre Exposure Prophylaxis or PrEP for HIV infection. My earlier work describing the frequency and clinical outcomes of patients with azithromycin-resistant syphilis infection resulted in the removal of azithromycin as recommended alternative therapy in patients with syphilis. My published work on the effectiveness of doxycycline treatment provided evidence to maintain doxycycline as a recommended alternative treatment.

a. Williams LA, **Klausner JD**, Whittington WL, Handsfield HH, Celum C, Holmes KK. Elimination and reintroduction of primary and secondary syphilis. Am J Public Health. 1999 Jul;89(7):1093-7. PMID: 10394323; PMCID: PMC1508824.
b. Buchacz K, Patel P, Taylor M, Kerndt PR, Byers RH, Holmberg SD, **Klausner JD**. Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. AIDS. 2004 Oct 21; 18(15): 2075-9. PMID: 15577629.
c. Jinno S, Anker B, Kaur P, Bristow CC, **Klausner JD**. Predictors of serological failure after treatment in HIV-infected patients with early syphilis in the emerging era of universal antiretroviral therapy use. BMC Infect Dis. 2013 Dec 26;13:605. doi: 10.1186/1471-2334-13-605. PMID: 24369955; PMCID: PMC3877955
d. Bolan RK, Beymer MR, Weiss RE, Flynn RP, Leibowitz AA, **Klausner JD**. Doxycycline prophylaxis to reduce incident syphilis among HIV-infected men who have sex with men who continue to engage in high-risk sex: a randomized, controlled pilot study. Sex Transm Dis. 2015 Feb;42(2):98-103. doi: 10.1097/OLQ.0000000000000216. PMID: 25585069; PMCID: PMC4295649.

4. Biomedical HIV Prevention: HIV infection continues to be hyper-epidemic in high-risk populations globally with annual incidence rates of 5-10%. Biomedical prevention and combinations thereof—testing, treatment and male circumcision—offer the best opportunity for reducing population-level incidence. From conducting early acceptability studies in various populations to describing the epidemiology of male circumcision in California (*PLoS One* 2007, *STD*, 2011), I have been a leading researcher and advocate informing the evidence base for newborn and adult male circumcision (*Science*, 2008).

a. Kojima N, Bristow C, Pollock N, Crouse P, Theodore H, Bonhomme J, Gaston C, Devieu J, J Pape, **Klausner, JD**. Rapid Training and Implementation of the Pollock Technique, a Safe, Effective Newborn Circumcision Procedure, in a Low-Resource Setting. Global Pediatric Health. Published June 11, 2015, January-December 2015 vol. 2 2333794X15589114. PMID: 27335959, PMCID: PMC4784613.
b. Madhivanan P, Krupp K, Kulkarni V, Kulkarni S, **Klausner JD**. Acceptability of male circumcision for HIV prevention among high-risk men in Pune, India. Sex Transm Dis. 2011 Jun;38(6):571. doi: 10.1097/OLQ.0b013e318219c930. PMID: 21836398.
c. Potts M, Halperin DT, Kirby D, Swidler A, Marseille E, **Klausner JD**, Hearst N, Wamai RG, Kahn JG, Walsh J. Public health. Reassessing HIV prevention. Science. 2008 May 9;320(5877):749-50. doi: 10.1126/science.1153843. PMID: 18467575; PMCID: PMC3501984.
d. **Klausner JD**. Newborn circumcision: ensuring universal access. Sex Transm Dis. 2013 Jul;40(7):526-7. doi: 10.1097/01.OLQ.0000431046.28649.23. PMID: 23965764.

5. Internet, social media and HIV/STD prevention: Networks of interconnected persons are critical to the introduction and spread of infectious diseases, in particular those transmitted through sexual activity. In 2000 I described the first outbreak of syphilis related to men meeting partners in an Internet chat room (JAMA, 2000)

and went on to develop and evaluate Internet-based interventions for disease control (AIDS Care, 2004; STD 2005; PloS Med 2008). In 2004, I started "AskDrK.org," at the time one of the most popular sites for up-to-date and clear sexual health information for adolescents and sexual minorities. The Internet and social media have since become the *sine qua non* opportunity for health education and interventions to reach high risk groups regarding sexual and reproductive health.

a. **Klausner JD**, Wolf W, Fischer-Ponce L, Zolt I, Katz MH. Tracing a syphilis outbreak through cyberspace. JAMA. 2000 Jul 26;284(4):447-9. PMID: 10904507.
b. **Klausner JD**, Levine DK, Kent CK. Internet-based site-specific interventions for syphilis prevention among gay and bisexual men. AIDS Care. 2004 Nov;16(8):964-70. PMID: 15511728.
c. McFarlane M, Kachur R, **Klausner JD**, Roland E, Cohen M. Internet-based health promotion and disease control in the 8 cities: successes, barriers, and future plans. Sex Transm Dis. 2005 Oct;32(10 Suppl):S60-4. Review. PMID: 16205295.
d. Levine D, Woodruff AJ, Mocello AR, Lebrija J, **Klausner JD**. inSPOT: the first online STD partner notification system using electronic postcards. PLoS Med. 2008 Oct 21;5(10):e213. doi: 10.1371/journal.pmed.0050213. PMID: 18942887; PMCID: PMC2570420.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/jeffrey.klausner.1/bibliography/47475064/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NIH-NIAID-SBSS-DMID-NIHAI201112 PI: Klausner 07/2013-06/2020
Title: Sexually Transmitted Infection Clinical Trials Group, 2013-2020
Role: Principal Investigator responsible for study network implementation
Goal: Implement clinical prevention and treatment trials in STIs

NIH-NIAID-1R21AI117256-01A1 PI: Klausner 04/2016-03/2018
Title: Reducing Excess Broad-Spectrum Antibiotic Use in Gonorrhea
Role: Principal Investigator responsible for overall study implementation
Goal: Evaluate a novel approach to controlling the spread of drug-resistant *N. gonorrhoeae*

NIH-NIAID-UM1AI104681 PIs: Chambers and Fowler 11/2014-10/2018
Title: Antibiotic Resistance Leadership Group
Role: Co-investigator/ Protocol Chair of Extra-genital CT/NG study
Goal: Evaluate various approaches to addressing antibiotic resistant infections

NIH-NICHD-R21HD084274-01 PI: Klausner 09/2015-08/2018
Title: Pilot Study of STI Screening and Treatment for PMTCT, South Africa
Role: Principal Investigator responsible for overall study implementation
Goal: Evaluate the impact of STI point-of-care screening and treatment on birth and newborn outcomes

Recently Completed Research Support

NIH-NIAID-R21AI120838 PI: Shin 08/2015-7/2017
Title: Utility of Deep Sequencing for Detecting Heteroresistant MTB Infections among HIV infected Persons
Role: Co-investigator assisting with study design and epidemiologic analysis
Goal: Determine the frequency and impact of multiple MTB infections

NIH/NIAID. 1R01AI099727 PI: Caceres 07/2012-06/2017
Title: Syphilis: Translating technology to understand a neglected epidemic
Role: Co-director of project responsible for overall implementation with specific emphasis on biologic measures, data quality and interpretation of findings.
Goal: Increase research capacity in Lima, Peru, through studying syphilis in high-risk men

C-200-2013-N15562 PI: Montoya 09/2013-06/2017
Title: A Waiting Room-Delivered Video to Enhance ART Care Continuum for HIV-Positive Minority Persons
Role: Co-investigator for video development and evaluation
Goal: Develop and evaluate a brief video to increase clinic retention in high-risk HIV-infected patients

NIH-NIAID-5R21AI109005-02 PI: Klausner 08/2014-03/2017
Title: Controlling Drug Resistant Gonorrhea with Real-Time PCR Susceptibility Testing
Role: Principal Investigator responsible for overall study implementation
Goal: Investigate use of real-time PCR to determine antimicrobial susceptibility of gonorrhea infections

NIH/NIAID. 1R01AI097045 PI: Zetola 09/2011-08/2016
Title: Molecular epidemiology of TB in low and high HIV prevalence settings, Botswana.
Role: Consultant responsible for assisting in intervention development, study design, outcome assessment, and interpretation of findings.
Goal: Understand the transmission of TB in different epidemiologic settings

CDC-200-2013-N15562 PI: Montoya 09/2013-06/2016
Title: A Video to Enhance ART Care Continuum for HIV-Positive Minority Persons
Role: Co-investigator for video development and evaluation
Goal: Develop and evaluate a video to increase clinic retention in HIV-infected patients

NIH-NIAID-1R21AI109005-01A PI: Klausner 08/2014-07/2016
Title: Controlling Drug Resistant Gonorrhea with Real-Time PCR Susceptibility Testing
Role: Principal Investigator responsible for overall study implementation
Goal: Develop and evaluate a new molecular assay for gonorrhea resistance on treatment

NSF-1549003 PI: Chiu 01/2016-06/2016
Title: Point-of-care enhanced lateral flow assay for *Chlamydia trachomatis*
Role: Co-investigator in *Chlamydia trachomatis* test development
Goal: Develop and evaluate a new point-of-care test for *Chlamydia trachomatis*

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Comulada, Warren Scott

eRA COMMONS USER NAME (credential, e.g., agency login): comulada2

POSITION TITLE: Associate Professor-in-Residence, Department of Psychiatry & Biobehavioral Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Pacific Union College	B.S.	06/1993	Biophysics
Loma Linda University	M.P.H.	06/1998	Biostatistics
University of California, Los Angeles	M.S.	06/2000	Biostatistics
University of California, Los Angeles	Dr.P.H.	01/2006	Biostatistics

A. Personal Statement

I am well-positioned to serve as a statistician in collaboration with Drs. Klausner and Medina-Marino (PIs) for this R01 application. I have served as a statistician on numerous NIH-funded behavioral intervention trials in the United States and other countries, including China and South Africa. International work is highlighted by publications immediately following this paragraph and in Section C. I am currently a Methods Core Co-Director for the Center for HIV Identification, Prevention and Treatment Services (CHIPTS; P30MH058107) and an Analytic Core Project Lead for an Adolescent Trials Network U19 (U19HD089886). I have collaborated as a statistician on prior HIV studies with Dr. Klausner (highlighted by two publications immediately following this paragraph). Prior collaboration on international projects will inform the develop of data management and sharing protocols that will be used in the current study where data collected in South Africa will be analyzed in the U.S.

1. Yan L, Liu E, McGoogan JM, Duan S, Wu LT, **Comulada S**, & Wu Z (2013). Referring heroin users from compulsory detoxification centers to community methadone maintenance treatment: a comparison of three models. BMC Public Health. 13(1): 747. PMCID: PMC3844356.
2. Bristow CC, Lee SJ, Severe L, Pape JW, Javanbakht M, **Comulada WS**, & Klausner JD (2016). Attributes of diagnostic tests to increase uptake of dual testing for syphilis and HIV in Port-au-Prince, Haiti. International Journal of STD & AIDs. 28(3): 259-264. PMCID in process.
3. Bristow CC, Severe L, Pape JW, Javanbakht M, Lee SJ, **Comulada WS**, & Klausner JD (2016). Dual rapid lateral flow immunoassay fingerstick wholeblood testing for syphilis and HIV infections is acceptable and accurate, Port-au-Prince, Haiti. BMC Infect Dis. 16(1): 302. PMCID: PMC4912739.
4. Li L, **Comulada WS**, Lin C, Hsieh J, Luo S, & Wu Z (2017). Factors related to client satisfaction with methadone maintenance treatment in China. Journal of Substance Abuse Treatment. 77: 201-206. PMCID: PMC5420338.

B. Positions and Honors

Positions and Employment

1997-1998 Graduate assistant, School of Dentistry, Loma Linda University, Loma Linda, CA (LLU)
1997 Lab assistant, School of Public Health, LLU
1997-1998 Research assistant, Teaching Learning Center, LLU

1999-2005	Statistician, Center for Community Health, Univ of Calif, Los Angeles, CA (UCLA)
2006-2007	Senior Statistician, Center for Community Health, UCLA
2007-2010	Assistant Research Statistician, Center for Community Health, UCLA
2009-2010	Associate Director, Methods Core, Center for HIV Identification, Prevention, and Treatment Services (CHIPTS), UCLA
2010-2017	Scientist, Methods Core, CHIPTS, UCLA
2010-2015	Assistant Professor-in-Residence, Department of Psychiatry and Biobehavioral Sciences, UCLA
2015-2017	Scientist, Policy Core, CHIPTS, UCLA
2015-	Associate Professor-in-Residence, Department of Psychiatry and Biobehavioral Sciences, UCLA
2016-	Project Lead, Adolescent Trials Network (ATN) Analytic Core
2017-	Co-Director, Methods Core, CHIPTS, UCLA

Other Experience and Professional Memberships

2006-	Member, American Statistical Association
2007-	Statistical reviewer, Data and Safety Monitoring Board, UCLA Addiction Medicine, Department of Family Medicine
2010-	Chair, Data and Safety Monitoring Board, Lumbee Rite of Passage Study, Maya
2010-	Member, International Network for Social Network Analysts

Honors

2000-2001	Graduate fellowship, Department of Biostatistics, UCLA

C. Contribution to Science

1. **Analysis of multivariate longitudinal data.** Standard regression models a single outcome and one or more predictors. Specification of outcomes and predictors is often difficult for the analysis of multiple measures that are collected over time as causal relationships may not be established a priori. Longitudinal models that allow for multivariate outcomes provide a more flexible modeling framework but have yet gain widescale popularity in the literature. As a statistician, one of my goals has been to demonstrate the utility of multivariate-outcome longitudinal models and develop statistical methods and software to make these types of models more accessible to researchers. Disentangling longitudinal relationships is especially important in the field of behavioral research that I work in. For example, it is well understood that illicit substance use and mental health symptoms often co-occur, but it is not clear whether mental health symptoms precede substance use, or vice versa. I applied bivariate-outcome models to examine longitudinal relationships between illicit substance use and mental health symptoms in a cohort of HIV-positive individuals (Publication a. immediately following this paragraph). As part of my work in the development of statistical methods for multivariate outcomes, I developed a computer program that is implemented in R to allow researchers to conduct power and sample size calculations for bivariate-outcome study designs. Calculations are discussed in Publication b. immediately following this paragraph.
    a. **Comulada WS**, Rotheram-Borus MJ, Pequegnat W, Weiss RE, Desmond K, Arnold E, Remien RH, Morin SF, Weinhardt L, Johnson MO, & Chesney MA. Relationships over time between mental health symptoms and transmission risk among persons living with HIV. (2010). Psychology of Addictive Behaviors. 24(1): 109-118. PMCID: PMC2845324.
    b. **Comulada WS** & Weiss RE. (2010). Power calculations for correlations between bivariate longitudinal data. Statistics in Medicine. 29(27): 2811-2824. PMCID: PMC2845324.
    c. **Comulada WS**, Muth SQ, & Latkin CA. (2012). The analysis of multiple ties in longitudinal egocentric network data: A case study on bidirectional relationships between trust and drug use. Social Networks. 34(4): 691-700. PMCID: PMC3519439.

2. **Additional statistical methods.** In addition to the application and development of multivariate outcome models, I have applied and developed other innovative statistical methods for the analysis of longitudinal and clustered data in the behavioral sciences. This includes the development of methods to analyze

clustered data with proportions that contain zeros in the denominator, such as the proportion of protected sex acts when a study participant is abstinent during the reporting period (Publication a. immediately following this paragraph). Publication c. was motivated by a common problem in behavioral intervention trials where it is impractical to specify a single primary outcome. In this instance, an intervention trial was conducted in South Africa to positively influence nutrition, mental health, and HIV-related outcomes in mothers and their infants. There were over 20 outcomes of interest, too many for multivariate-outcome methods described above. Instead we used an innovative simulation-based method to simultaneously test the effect of the intervention across all outcomes.

a. **Comulada WS** & Weiss RE. (2007). On models for binomial data with random numbers of trials. Biometrics. 63(2): 610-617. PMCID: PMC2843591.
b. **Comulada WS** (2015). Model specification and bootstrapping for multiply imputed data: an application to count models for the frequency of alcohol use. The Stata Journal. 15(3): 833-44. PMCID: PMC4782976.
c. Harwood JM, Weiss RE, & **Comulada WS** (2017). Beyond the primary endpoint paradigm: A test of intervention effect in HIV behavioral intervention trials with numerous correlated outcomes. Prevention Science. Epub ahead of print. PMCID in process.

3. **Statistical support for behavioral intervention trials in Africa**. I have provided statistical and technology support for numerous behavioral intervention trials in Africa with a focus on South Africa. Statistical support has included the setup and implementation of study design components, such as the randomization of neighborhoods across study arms and implementation of mHealth systems for data collection, and the analysis of data collected over several time points to evaluate interventions.
    a. Lightfoot MA, Kasirye R, **Comulada WS**, & Rotheram-Borus MJ (2007). Efficacy of a culturally adapted intervention for youth living with HIV in Uganda. Prevention Science. 8(4): 271-73. PMCID: PMC2819813.
    b. Richter L, Rotheram-Borus MJ, Van Heerden A, Stein A, Tomlinson M, Harwood JM, Rochat T, Van Rooyen H, **Comulada WS**, & Tang Z. Pregnant women living with HIV (WLH) supported at clinics by peer WLH: a cluster randomized controlled trial (2014). AIDS Behav. 18(4): 706-15. PMCID in process. PMCID: PMC4109271.
    c. Rotheram-Borus MJ, Tomlinson M, le Roux IM, Harwood JM, **Comulada S**, O'Connor MJ, Weiss RE, & Worthman CM (2014). A cluster randomized controlled effectiveness trial evaluating perinatal home visiting among South African mothers / infants. PLoS One. 9(10): e105934. doi: 10.1371/journal.pone.0105934. PMCID: PMC4207699.
    d. Tsai AC, Tomlinson M, **Comulada WS**, & Rotheram-Borus MJ (2016). Food insufficiency, depression, and the modifying role of social support: Evidence from a population-based, prospective cohort of pregnant women in peri-urban South Africa. Social Science and Medicine. 151: 69-77. PMCID: PMC4766046.

4. **Development of mobile phone-based assessment tools for behavioral interventions.** In my role as an mHealth expert and statistician, I have collaborated with teams of scientists, including psychologists, computer scientists, and other mHealth experts to develop mobile phone-based assessment tools to both better understand health-related behaviors and help individuals to better self-monitor health-related behaviors, including dietary intake, exercise, stress, substance use, and sexual behavior. Better understanding and self-monitoring results from the ability of individuals to use their mobile phones to report on behaviors in the moment and in situ, often referred to as ecological momentary assessment (EMA). As an example, I examined the context of substance use by Latino youth in outpatient treatment. Through mobile phone-based EMA, participants reported on substance use episodes, as well as the physical and social context, time of day, and day of the week when substance use occurred. By capturing context and substance use on a daily basis, we were able to examine substance use context with much greater granularity than past studies that relied on retrospective self-report. Study findings are discussed in the third publication in Section A. EMA also introduces methodological challenges that have yet to be tackled on a broad scale in the EMA literature. One key issue is that participants may not report on days when certain behaviors occur, such as substance use. Inferences that are drawn from EMA may be biased. Publication d., immediately following this paragraph, explores factors that relate to EMA compliance and missing data.
    a. **Comulada WS** (2014). Mobile phone assessment in egocentric networks: a pilot study on gay men and their peers. Connections. 34(1&2): 43-51. PMCID: PMC4380161.

b. Swendeman D, **Comulada WS**, Ramanathan N, Lazar M, & Estrin D (2015). Reliability and validity of daily self-monitoring by smartphone application for health-related quality of life, antiretroviral adherence, substance use, and sexual behaviors among people living with HIV. AIDS and Behavior. 19(2): 330-40. PMCID: PMC4344409.
c. **Comulada WS**, Swendeman D, & Wu N (2016). Cell phone-based ecological momentary assessment of substance use context for Latino youth in outpatient treatment: Who, what, when and where. Drug and Alcohol Dependence. 167: 207-13. PMCID: PMC5037042.
d. van Heerden A, Harris DM, van Rooyen H, Barnabas R, Ramanathan N, Ngcobo N, Mpiyakhe Z, & **Comulada WS** (2017). Perceived mHealth barriers and benefits for home-based HIV testing and counseling and other care: Qualitative findings from health officials, community health workers, and persons living with HIV in South Africa. Social Science & Medicine. 183: 97-105. PMCID in process.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/warren.comulada.1/bibliography/42284147/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

R21MH106351 Comulada (PI) 9/1/2015 – 6/30/2018
An mHealth platform for health care workers to link South Africans to HIV care
This grant will develop and test an mHealth platform that community health workers can use to enroll South African household members in HIV care and track their movement between health facilities within the current infrastructure.
Role: Principal Investigator

U90HA28859-01-00 Brooks (PI) 9/1/2015-8/31/2019
HRSA-SPNS Social Media Evaluation and Technical Assistance Center (ETAC)
This grant provides funding for an ETAC to evaluate and provide technical assistance for 10 demonstration projects to improve linkage and retention in HIV care for HIV-positive youth and young adults.
Role: Co-investigator / Statistician

U19HD089886 Rotheram-Borus (PI) 9/1/2016 – 8/31/2021
A comprehensive community-based strategy to optimize the HIV prevention and treatment continuum for youth at HIV risk, acutely infected and with established HIV infection
This randomized trial will evaluate interventions for three groups of adolescents in Los Angeles and New Orleans: adolescents acutely infected with HIV, adolescents with established HIV infection, and adolescents at risk for acquiring HIV.
Role: Project Lead, Analytic Core

P30MH058107 Shoptaw (PI) 3/1/2017 - 1/31/2022
Center for HIV Identification, Prevention, and Treatment Services (CHIPTS)
This grant provides infrastructure funding to promote collaborative research and education on effective HIV detection, prevention, and treatment programs for HIV at the societal, community, provider, and individual levels.
Role: Co-Director, Methods Core

Completed Research Support

K01MH089270 Comulada (PI) 10/1/2010 – 8/31/2015
Predicting HIV-related Behaviors of Social Networks in a MPS Environment
This is a career development grant for the principal investigator to transition from a statistician to an independent investigator who is a methodologist in mobile-phone based HIV interventions. The study will culminate in a pilot study to assess the feasibility of collecting social network data on HIV-transmission risk behaviors via mobile phone.

Role: Principal Investigator

P30MH058107 Rotheram-Borus (PI) 9/30/1997 - 1/31/2017
Center for HIV Identification, Prevention, and Treatment Services (CHIPTS)
This grant provides infrastructure funding to promote collaborative research and education on effective HIV detection, prevention, and treatment programs for HIV at the societal, community, provider, and individual levels.
Role: Associate Director of Methods Core (10/2009 – 9/2010), Methods Core Scientist (10/2010 – 1/31/2017)

P20MD000182 Milburn(PI) 9/1/2012 – 5/31/2017
Support to reunite, involve, and value each other (STRIVE)
This project will intervene with juvenile delinquents who are reentering the community and will attempt to improve behavioral and health outcomes. This is a problem of enormous importance in minority populations. An intervention of a scale that could be widely applied has the potential to have an important impact on health.
Role: Co-investigator / Statistician

R01DA033609 Li (PI) 6/1/2012 – 5/31/2017
Enhancing the Role of Commune Health Workers in HIV and Drug Control in Vietnam
This is an implementation science project that aims to enhance the role of commune health workers (CHWs) in HIV and drug use prevention and treatment in Vietnam. We will demonstrate the process of development, implementation, and evaluation of an integrated intervention for CHWs, injecting drug users, and their family members.
Role: Co-investigator / Statistician

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Andrew G.A. Medina-Marino, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): AMEDINA-MARINO

POSITION TITLE: Head, Research Unit, Foundation for Professional Development (FPD)

EDUCATION/TRAINING*:*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Swarthmore College	B.A.	06/2000	Biology/Race Relations
California Institute of Technology	M.S.	06/2003	Molecular Biology
Johns Hopkins University, School of Public Health	Certificate	06/2006	Infectious Diseases
California Institute of Technology	PhD	06/2009	Molecular Biology
U.S. Centers for Disease Control and Prevention	EIS	06/2011	Epidemiology

A. Personal Statement

I am a molecular biologist and epidemiologist. As Head of FPD's Research Unit, I am the PI or co-investigator for a number of large NIH and USIAD funded research studies (see Ongoing Research Support section below). As Senior Technical Advisor for Disease Surveillance and Laboratory Systems, I work directly with a number of South Africa's 52 health districts to support systems strengthening activities focused on 1) assessing and enhancing pre- and post-analytical laboratory service at the clinic-lab interface, 2) capacity development to detect and respond to disease outbreaks, 3) supporting the use of surveillance and district health information systems data for decision making, and 4) rapid field investigations in support of district health department priorities.

Prior to FPD, I was Laboratory Branch Chief for CDC-South Africa. In this capacity, I supported and advised the South African National Health Laboratory Service and the National Department of Health on national point-of-care diagnostics policy and guidelines. As an outbreak investigation specialist, I was twice deployed to West Africa in 2015 to work with *Médecins Sans Frontières* (*MSF*; a.k.a., Doctors without Borders) to contain the on-going Ebola outbreak. While there, I specifically led disease surveillance, case investigation and contact tracing activities in affected communities. I also supported and optimized epidemiologic data flow from Ebola Treatment Units to the Ministry of Health.

As a Molecular Biologist, I have conducted research into the molecular mechanisms of *Neisseria gonorrhea* adherence and invasion at Rockefeller University, and helped identify a key cell receptor that facilitates NG adherence and invasion. In 2010, I was awarded the Donald C. Mackel Memorial Award by the Centers for Disease Control and Prevention for my investigation into a fatal laboratory-acquired infection with an attenuated *Yersinia pestis* strain; the Mackel Award is given annually to the CDC Epidemic Intelligence Service Officer that best exemplifies the effective application of a combined epidemiologic and laboratory approach to an investigation.

Dr. Klausner and I have known and collaborated with each other since 2010, mentoring trainees, implementing USAID, CDC and NIH-funded research, and co-authoring publications. Our long-running collaborations will allow us to successfully co-lead our study team, and the implementation of this project. As the Principal Investigator and implementation expert on this project, I will co-lead with Dr. Klausner the oversight, design, implementation, and analysis of this study. I will specifically be responsible for the coordination of all in-country study implementation efforts and quality assurance, and will provide direct oversight for the South African-based study team, including clinic-based research staff who will have direct contact with patient-participants and data managers. My strong knowledge of and relationship with the Tshwane District Department of Health, in my capacities as a Systems Strengthening Technical Advisor and on Dr. Klausner's and my current R21 study, has provided me with key insights and experiences that will allow me to successfully risk manage and implement all aspects of this proposed study.

B. Positions and Honors

Positions and Employment

1995 – 1996	Undergraduate Researcher, Rockefeller University
1999 – 2000	Undergraduate Researcher, Laboratory of Molecular Systematics, Smithsonian Institution
2000 – 2001	Postbaccalaureate Researcher, National Institute of Allergy and Infectious Diseases, U.S. NIH
2002 – 2008	Howard Hughes Medical Institute Fellow, California Institute of Technology
2009 – 2011	Epidemic Intelligence Service (EIS) Officer, Centers for Disease Control and Prevention
2012	Objective Review Panel Member, U.S. President's Emergency Plan for AIDS Relief
2011 – 2012	Chief, Laboratory Branch, U.S. Centers for Disease Control, South Africa
2014 – 2015	Epidemiologist, *Médecins Sans Frontières*, West Africa Ebola Response
2012 – Present	Senior Technical Advisor, Disease Surveillance and Laboratory Systems Strengthening, Foundation for Professional Development
2014 – Present	Head, Research Unit, Foundation for Professional Development
2016 – Present	Member, South African National TB Think Tank
2016 – Present	Member, South African National HIV Think Tank

Awards and Honors

1996	Undergraduate Research Fellow, U.S. Department of Energy
1998	Best Undergraduate Thesis, American Society for Cell Biology
1999	Research Training Award, Smithsonian Institution
2001	McCallum Research Award, California Institute of Technology
2001	Benjamin Rosen Graduate Fellowship, California Institute of Technology
2002	Ford Foundation Fellowship
2002	Howard Hughes Medical Institute Fellow
2010	Donald C. Mackel Award, Centers for Disease Control and Prevention
2011	Remsen Bird Lecture, Occidental College
2017	Global Health Grand Rounds Lecture, Vanderbilt University

C. Contribution to Science

1. Optimizing STI Screening and Testing Programs in South Africa: The burden of bacterial and viral STIs, and their subsequent sequelae, is unacceptably high in South Africa and other low-middle income countries. Moreover, the sub-optimal sensitivity and specificity of current screening protocols (i.e., syndromic management of CT, NG and TV), and poor screening coverage (i.e., HPV/ cervical cancer screening), leave a large number of women undiagnosed and untreated. The impact of this is on-going transmission to sexual partners, increased risk of mother-to-child transmission of HIV, and increased morbidity and mortality, especially among reproductive age women. With the advent of new molecular diagnostic tests and point-of-care test platforms, I have been working to improve access to and implementation of bacterial and viral STIs screening and treatment programs. This work is particularly highlighted by two recent research projects where I serve as PI: 1) Evaluating the acceptability and accuracy of cervical cancer screening using a self-collected tampon for HPV messenger-RNA testing among HIV-infected women in South Africa; and 2) Pilot Study of STI Screening and Treatment for PMTCT (R21HD084274). Both of these studies have been conducted in Tshwane District (the proposed study district for the current proposal), allowing me to develop excellent relationships with the local health department, and have key insights into the barriers and facilitators for new test implementation in Tshwane District health clinics.

1. Price CM, Peters RPH, Mudau M, Olivier D, De Vos L, Morikawa E, Kock MM, **Medina-Marino A**, Klausner JD. Prevalence and Detection of *Trichomonas Vaginalis* in Human Immunodeficiency Virus-Infected Pregnant Women. Sex Transm Dis (In Press)
2. Peters RPH, Mudau M, Liteboho M, de Vos L, Klausner JD, Kock MM, **Medina-Marino A*** Laboratory reproducibility of Xpert® CT/NG and TV testing as performed by nurses at three primary healthcare facilities in South Africa. J Clin Microbiol. 2017 Oct 11. pii: JCM.01430-17. doi: 10.1128/JCM.01430-17 (**Senior/Corresponding Author*)

3. Mudau M, Remco Peters P, De Vos L, Olivier D, Joseph Davey D, Mkhwanazi E, McIntyre JA, Klausner JD, **Medina-Marino A***. High prevalence of asymptomatic sexually transmitted infections among Human Immunodeficiency Virus (HIV)-Infected pregnant women in a low-income South African community. Int J STD *AIDS* 2017 Aug 11 DOI: 10.1177/0956462417724908 (**Senior/Corresponding Author*)

4. Adamson PC, Huchko MJ, Moss AM, Kinkel HF, **Medina-Marino A*** Acceptability and Accuracy of Cervical Cancer Screening Using a Self-Collected Tampon for HPV messenger-RNA Testing Among HIV-Infected Women in South Africa. PLoS One 2015 Sep 2;10(9):e0137299. doi: 10.1371/journal.pone.0137299. eCollection 2015. (**Senior/Corresponding Author*)

2. TB Epidemiology, Program Evaluation and Case Finding: Despite health systems strengthening activities aimed at improving the national TB control program, South Africa still bears one of the highest TB burdens in the world. Improving TB surveillance, case finding and retention in care are paramount to improving national TB programmatic indicators, and decreasing the burden of TB throughout the country. Towards this, I have worked closely with a number of health districts around South Africa to evaluate their TB surveillance systems, and to identify the magnitude of cases being missed by the health system. This work is highlighted by the below references. In addition, I was recently awarded an NIH R21 grant (R21EB023679; NIBIB) to investigating the acceptability and feasibility of true home-based TB testing of household contacts using the new, portable point-of-care GeneXpert Omni platform. My team and I will be 1 of only 10 teams, globally, given early access to this new portable TB testing platform to pilot its use in a host of settings. This work may open up an entirely new way of conducting TB case finding, with potential global implications.

1. Kweza PF, van Schalkwyk C, Abraham N, Claassens MM, **Medina-Marino A*** Estimating the magnitude of missed pulmonary tuberculosis patients by primary health facilities, South Africa. Int J Tuberc Lung Dis (In Press; **Senior/Corresponding Author*)

2. Mlotshwa M, Smit S, Williams S, Reddy S, **Medina-Marino A*** Evaluating the Electronic Tuberculosis Register Surveillance System in Eden District, Western Cape, South Africa, 2015 Glob Health Action. 2017;10(1):1360560. doi: 10.1080/16549716.2017.1360560. (**Senior/Corresponding Author*)

3. Mlotshwa M, Abraham N, Beery M, Williams S, Smit S, Uys M, Reddy C, **Medina-Marino A***. Risk factors for tuberculosis smear non-conversion in Eden district, Western Cape, South Africa, 2007-2013: a retrospective cohort study. BMC Infect Dis. 2016 Aug 2;16:365. doi: 10.1186/s12879-016-1712-y. PMID: 27484399 (**Senior/Corresponding Author*)

3. Field Epidemiology, Disease Surveillance and Outbreak Investigations: Identification and rapid response to adverse health events in a population is of particular importance to the prevention and control of infectious diseases. As a trained field epidemiologist, I have honed my skills to perform rapid field investigations and utilize surveillance and routine collected data to inform outbreak containment, program implementation and evaluation. Though my work with *Médecins Sans Frontières* during the 2014-2016 Ebola outbreak in West Africa did not result in any publications, my skills and leadership were recognized by the request for a second deployment with MSF to Liberia in 2015. While there, I specifically led disease surveillance, case investigation and contact tracing activities in affected communities. I also supported and optimized epidemiologic data flow from Ebola Treatment Units to the Ministry of Health.

1. Soyemi K, **Medina-Marino A**, Sinkowitz-Cochran R, Schneider A, Njai R, McDonald M, Glover M, Garcia J, Aiello AE. Disparities among 2009 pandemic influenza A (H1N1) hospital admissions: a mixed methods analysis--Illinois, April-December 2009. PLoS One. 2014;9(4):e84380. Epub 2014/04/30. doi: 10.1371/journal.pone.0084380. PMID: 24776852; PMCID: PMC4002432.

2. **Medina-Marino A**, Reynolds D, Finley C, Hays S, Jones J, Soyemi K. Communication and mass vaccination strategies after pertussis outbreak in rural Amish communities-Illinois, 2009-2010. J Rural Health. 2013;29(4):413-9. Epub 2013/10/04. doi: 10.1111/jrh.12019. PMID: 24088215.

3. Dalhatu IT, **Medina-Marino A***, Olsen SJ, Hwang I, Gubio AB, Ekanem EE, Coker EB, Akpan H, Adedeji AA. Influenza viruses in Nigeria, 2009-2010: results from the first 17 months of a national influenza sentinel surveillance system. J Infect Dis. 2012;206 Suppl 1:S121-8. Epub 2012/11/28. doi: 10.1093/infdis/jis584. PMID: 23169957. *(*Note: This was a co-first authored paper).*

4. Cardemil CV, Cortese MM, **Medina-Marino A**, Jasuja S, Desai R, Leung J, Rodriguez-Hart C, Villarruel G, Howland J, Quaye O, Tam KI, Bowen MD, Parashar UD, Gerber SI, Rotavirus Investigation Team. Two rotavirus outbreaks caused by genotype G2P[4] at large retirement communities: cohort studies. Ann Intern Med. 2012;157(9):621-31. Epub 2012/11/07. doi: 10.7326/0003-4819-157-9-201211060-00006. PMID: 23128862

4. Molecular Mechanisms of Infectious Disease Pathogenesis: Insights into the pathogenic mechanisms of infectious diseases can be informed by both basic cell biology research and outbreak investigations. Colleagues and I identified the 180-kD carcinoembryonic antigen (CEA) cell surface protein as a receptor and mediator of *Neisseria gonorrhoeae* adherence and invasion into epithelial cells. As an Epidemic Intelligence Service Officer, I led a field investigation into a fatal laboratory-acquired infection with an attenuated strain of *Yersinia pestis*, the causative agent of plague. Our work uncovered the previously unknown risk associated with hereditary hemochromatosis and susceptibility and enhanced virulence of the pgm- KIM D27 strains of *Yersinia pestis.*

1. **Medina-Marino A**, Sheih W-J, Zaki S, Schriefer M, Molins C, Mead P, King B, Metzger K, Soyemi K, Conover C, Gerber S, Jones J, Weaver K, Black S, Ritger K, Centers for Disease Control and Prevention. Fatal laboratory-acquired infection with an attenuated Yersinia pestis Strain--Chicago, Illinois, 2009. MMWR Morb Mortal Wkly Rep. 2011;60(7):201-5. PMID: 21346706.
2. Chen T, Grunert F, **Medina-Marino A**, Gotschlich EC. Several carcinoembryonic antigens (CD66) serve as receptors for gonococcal opacity proteins. J Exp Med. 1997;185(9):1557-64. Epub 1997/05/05. PMID: 9151893; PMCID: PMC2196295.

5. Molecular Phylogenetics: As a Research Fellow in molecular evolution at the Smithsonian Institution, I used molecular sequence data to reconstruct the phylogenetic history of organismal adaptive radiations. Though the work was focused on plants, the techniques and applications behind my work in molecular phylogenetics will allow me to contribute to data analysis and interpretations relating to the molecular epidemiology of *Chlamydia trichomonas* and *Trichomonas vaginalis* that will be a self-funded sub-study emanating from our currently proposed study.

1. Whittall JB, **Medina-Marino A**, Zimmer EA, Hodges SA. Generating single-copy nuclear gene data for a recent adaptive radiation. Mol Phylogenet Evol. 2006;39(1):124-34. Epub 2005/11/30. doi: 10.1016/j.ympev.2005.10.010. PMID: 16314114.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1pEG7AXedlkQM/bibliograpahy/43304628/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1R01MH114648 (NIMH/NIH) PIs: Medina-Marino, Bekker 09/01/2017 – 08/31/2022

Title: *Leveraging Community-based Platforms to Improve Access and Adherence to PrEP*

Goals: 1) Assess YW's uptake of PrEP when delivered through large-scale community-based HIV counseling and testing (CBCT) platforms in urban and rural settings in South Africa
2) Evaluate community-based scalable interventions to achieve prevention-effective adherence to PrEP among YW
3) Evaluate the cost per YW initiated on PrEP and provided adherence support through community-based platforms, and the cost-effectiveness per incident HIV infection averted

1U19MH113203 (NIMH/NIH) PIs: Wainberg, Oquendo 05/01/2017 – 04/30/2022

Title: PRIDE SSA- Partnership in Research to Implement and Disseminate Sustainable and Scalable Evidence Based Practices in Sub-Saharan Africa

Goals: 1) In partnership with policy makers, conduct rigorous scale-up research to identify and implement the best task-sharing delivery pathway for community-based mental health care and treatment

2) Train, develop and support a research network in sub-Saharan Africa
3) Develop sub-Saharan Africa in-country formal capacity-building programs in mental health implementation science
4) Establish an administrative structure to robustly support and oversee the scale-up research and capacity building components

Role: Lead data collection implementation and quality assurance processes and procedures, and oversee academic capacity-building component

5R21EB023679 (NIBIB/NIH) PI: Medina-Marino 08/15/2016 – 05/31/2018

Title: Investigating the acceptability and feasibility of home-based TB testing of household contacts using a new, mobile point-of-care technology

Goals: 1) Determine the acceptability and feasibility of using point-of-care technology to perform home-based TB testing of household contacts of TB patients
2) Describe the outcomes of household contacts screened and tested for TB in their home compared to those screened and referred for testing in a health facility

5R21HD084274 (NICHHD/NIH) PIs: Medina-Marino, Klausner 09/23/2015 – 7/31/2018

Title: Pilot Study of STI Screening and Treatment for PMTCT

Goals: 1) Determine the acceptability and feasibility of screening and treating HIV-infected pregnant women for NG and CT at first antenatal care visit.
2) Describe longitudinal birth and infant outcomes for HIV-infected pregnant women screened for CT and NG in their first antenatal care visit.

AID-3569023-102-2015-02/03 (USAID) PI: Burke/ Site PI: Medina-Marino 08/01/2015 – 05/31/2018

Title: A randomized study evaluating an intervention integrating economic strengthening and HIV prevention programs for vulnerable youth in South Africa

Goals: 1) Assess whether the integration of an economic strengthening (ES) intervention with an HIV-prevention education intervention improves economic and health outcomes beyond singular interventions;
2) Estimate the resources required at the program level to support the ES and HIV-prevention education interventions; and
3) Describe whether the interventions were perceived as effective in addressing economic and health outcomes and to describe how and why the interventions were perceived as effective or not.

AID-674-A-14-0006 (USAID) PI: Wolvaardt 09/13/2013 – 01/01/2019

Title: Communities Forward- A Comprehensive Community–Based HIV Prevention, Counselling and Testing Program for Reduced HIV Incidence

Goals: To conduct evaluations and implementation science activities in conjunction with implement of community-based HIV counselling and testing activities in 13 high burden districts throughout South Africa.

Role: Head of all research activities associated with CoAg

Recently Completed Research Support

AID-674-A-12-00017 (USAID) PI: Wolvaardt 10/31/2012 – 12/31/2018

Title: Strengthening systems for better HIV/TB patient outcomes

Goals: To conduct pragmatic evaluations and implementation science activities in conjunction with the implementation of health systems strengthening strategies to improve the quality of service delivery.

Role: Head of all research activities associated with CoAg

Projects: 1) Estimating the magnitude of TB cases missed by the health system
2) Factors affecting presentation for first antenatal care visit in Tlokwe sub-district, Northwest Province and Capricorn District, Limpopo Province, South Africa
3) Evaluating the acceptability and accuracy of cervical cancer screening using a self-collected tampon for HPV messenger-RNA testing among HIV-infected women in South Africa
4) In-clinic laboratory services assessment in PHCs and CHCs in Tshwane, Nkangela, Vhembe and Capricorn Districts

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: Taylor, Christopher Michael

eRA COMMONS USER NAME: CHRISTAYLOR

POSITION TITLE: Associate Professor of Microbiology, Immunology, and Parasitology
Director of Bioinformatics, Biostatistics & Computational Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Mary Washington College, Fredericksburg, VA	B.S.	05/2000	Computer Science, Math
University of Virginia, Charlottesville, VA	M.S.	08/2002	Computer Science
University of Virginia, Charlottesville, VA	Ph.D.	05/2008	Computer Science

A. Personal Statement

Christopher Michael Taylor, PhD, is a computer scientist and mathematician by training. He began studying computational biology in graduate school where he developed algorithms for analysis and visualization of human genome tiling array data [1,2]. Dr. Taylor has been working with high-throughput DNA sequencing data for over a decade now and his lab has a primary focus on the development of analysis and visualization methods for high-throughput sequencing data of microbial communities. His lab developed a novel method called oligotyping for looking in great detail at 16S rRNA sequences for subtle nucleotide variations that can reveal community composition down to a strain level [3]. This was one of the first methods for analysis of 16S rRNA data that did not rely on clustering of sequences into Operational Taxonomic Units. They applied this method in a paired sexual partner study of vaginal swabs from women and urethral swabs from their male sexual partners and their oligotyping method showed a strong correlation between *Gardnerella vaginalis* sequences shared across sexual partners [3]. In a recent follow-up study, They extended this analysis to the entire vaginal microbiome and showed that the vaginal microbiota of women with bacterial vaginosis is more similar to her male sexual partner's penile skin and urethral microbiota supporting the hypothesis of sexual transmission of bacterial vaginosis associated bacteria [4]. Dr. Taylor's lab has recently been awarded a multi-PI R01 to study the relationship between the vaginal microbiota and natural clearance of Chlamydia infection. Dr. Taylor's lab has also developed software systems for analysis of high throughput sequencing data including RNA CoMPASS, PARSES, and Viamics.

As an expert in the analysis and visualization of microbial communities with a particular focus on the human vaginal microbiome, Dr. Taylor is ideally positioned to act as Co-Investigator of this project, leading sequencing, analysis, and data visualization aspects.

1. Karnani N, **Taylor CM**, Dutta A. Microarray analysis of DNA replication timing. Methods Mol Biol. 2009;556:191-203. doi: 10.1007/978-1-60327-192-9_14. PMID: 15499007. PMCID: PMC4201590.
2. Karnani N, **Taylor C**, Malhotra A, Dutta A. Pan-S replication patterns and chromosomal domains defined by genome-tiling arrays of ENCODE genomic areas. Genome Research. 2007 Jun;17(6), 865-876. PMCID: PMC1891345.
3. Eren AM, Zozaya M, **Taylor CM**, Dowd SE, Martin DH, Ferris MJ. Exploring the diversity of Gardnerella vaginalis in the genitourinary tract microbiota of monogamous couples through subtle nucleotide variation. 2011;6(10):e26732. doi: 10.1371/journal.pone.0026732. PMID: 22046340; PMCID: PMC3201972.
4. Zozaya M, Ferris MJ, Siren JD, Lillis R, Myers L, Nsuami MJ, Eren AM, Brown J, **Taylor CM**, Martin DH. Bacterial communities in penile skin, male urethra, and vaginas of heterosexual couples with and without bacterial vaginosis. Microbiome. 2016 Apr 19:4:16. doi: 10.1186/s40168-016-0161-6. PMID: 27090518; PMCID: PMC4835890.

B. Positions and Honors

Positions and Employment

2008-2012 Assistant Professor of Computer Science, University of New Orleans, New Orleans, LA
2012-Present Associate Professor of Microbiology, Immunology & Parasitology, Louisiana State University Health Sciences Center, New Orleans, LA
2016-Present Director of Bioinformatics, Biostatistics & Computational Biology Core for the Louisiana Biomedical Research Network, Baton Rouge, LA

Other Experience and Professional Memberships

2008 Session Chair of Pattern Recognition in Bioinformatics (PRIB 2008), Melbourne, AUS
2009 Local Arrangements Chair of High Performance Graphics (HPG 2009), New Orleans, LA
2010-2011 Coach of ACM South Central USA Regional Programming Contest Team
2013 Panelist for LBRN Computational Biology Workshop, New Orleans, LA
2013 Session Chair for ASM TX/SC Branch Meeting, New Orleans, LA
2015 Session Chair for 3rd Microbiome R&D and Business Collaboration Forum, San Diego, CA
2015 Scientific Committee for the 3rd Annual LA Conference on Bioinformatics, Baton Rouge, LA
2017 Organizational co-Chair for the 5th Annual LA Conference on Bioinformatics, New Orleans, LA

Honors

2009 Best Presentation Award for Invited Talk at Louisiana State University Pediatrics Day
2015 Winner of Illumina's MiSeq My Focus Contest and Recipient of $5,000 in Sequencing Reagents

C. Contribution to Science

1. My early work in the field of computational biology involved the analysis of data from Genome Tiling Microarrays. After the full human genome sequence was released, the NIH initiated the ENCODE project with the purpose of studying and annotating all of the functional elements in the human genome. I joined Dr. Anindya Dutta's lab in 2003 which was funded on an ENCODE pilot project to study the timing of DNA replication in the human genome. I used my skills in computer science and mathematics to develop a method for generating a continuous profile of DNA replication timing from discrete pools of replicated DNA that were hybridized to genome tiling microarrays. I also proposed a method for finding origins of replication and discovering regions of the genome where alleles replicated asynchronously. This approach was presented at Pattern Recognition in Bioinformatics 2008 in Melbourne, Australia and later published as part of an invited chapter for Methods in Molecular Biology in 2009 [a]. During this time, I was also the lead analyst for replication and a member of the Integrated Analysis and Manuscript Preparation group for the ENCODE Nature publication [b]. We also published other aspects of this work in Genome Research [c] and Molecular Biology of the Cell [d]. This period of my research career was critical at introducing me to the analysis of genomic data as I developed my own algorithms for interrogating genome tiling microarrays, laying the groundwork for my future work in analysis and visualization of high-throughput sequencing data.
   a. Karnani N, **Taylor CM**, Dutta A. Microarray analysis of DNA replication timing. Methods Mol Biol. 2009;556:191-203. doi: 10.1007/978-1-60327-192-9_14. PMID: 15499007. PMCID: PMC4201590.
   b. ENCODE Project Consortium, Birney E, Stamatoyannopoulos JA, Dutta A, Guigó R, Gingeras TR, Margulies EH, Weng Z, Snyder M, Dermitzakis ET, Thurman RE, Kuehn MS, **Taylor CM** et al. Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project. Nature. 2007 Jun;447(7146),799-816. PMCID: PMC2212820.
   c. Karnani N, **Taylor C**, Malhotra A, Dutta A. Pan-S replication patterns and chromosomal domains defined by genome-tiling arrays of ENCODE genomic areas. Genome Research. 2007 Jun;17(6), 865-876. PMCID: PMC1891345.
   d. Karnani N, **Taylor CM**, Malhotra A, Dutta A. (2010). Genomic study of replication initiation in human chromosomes reveals the influence of transcription regulation and chromatin structure on origin selection. Mol Biol Cell. 2010 Feb 1;21(3):393-404. doi: 10.1091/mbc.E09-08-0707. PMCID: PMC2814785.
2. I shifted my research focus in 2009 to the field of RNA Sequencing and began a very fruitful collaboration with a virologist in Tulane's Cancer Center named Erik Flemington. My laboratory developed RNA

Sequencing analysis tools that would interrogate the reads that didn't map to the host genome which were typically discarded in other analysis pipelines at this time. We instead followed up on these reads by mapping them to other potential databases in succession and assembled transcripts to discover what exogenous agents may be found within RNA-Sequencing data of a host. This software system was called PARSES: Pipeline for Analysis of RNA-Seq Exogenous Sequences [a]. Using this approach we discovered murine leukemia virus in an EBV positive human B-cell line [a]. This technology was then integrated into a full-featured software system called RNA CoMPASS: RNA Comprehensive Multi-Processor Analysis System for Sequencing [b]. This system performed both the typical endogenous analysis and our exogenous analysis from PARSES in tandem and was distributable over a cluster to parallelize the computation. This process of dual analysis of RNA-Sequencing data led to many interesting findings [c,d] and established a strong collaboration between my lab and Erik Flemington's lab that exists to this day. We also helped Erik to establish the Cancer Crusaders Bioinformatics Lab which was an initial testing ground for the model of collaborative research that I have subsequently built my own lab around.

a. Lin Z, Puetter A, Coco J, Xu G, Strong MJ, Wang X, Fewell C, Baddoo M, **Taylor C**, Flemington EK. Detection of murine leukemia virus in the Epstein-Barr virus-positive human B-cell line JY, using a computational RNA-Seq-based exogenous agent detection pipeline, PARSES. J Virol. 2012 Mar;86(6):2970-7. doi: 10.1128/JVI.06717-11. PMID: 22238296; PMCID: PMC3302299.
b. Xu G, Strong MJ, Lacey MR, Baribault C, Flemington EK, **Taylor CM**. RNA CoMPASS: a dual approach for pathogen and host transcriptome analysis of RNA-seq datasets. PLoS One. 2014 Feb 25;9(2):e89445. doi: 10.1371/journal.pone.0089445. PMID: 24586784; PMCID: PMC3934900.
c. Strong MJ, Xu G, Coco J, Baribault C, Vinay DS, Lacey MR, Strong AL, Lehman TA, Seddon MB, Lin Z, Concha M, Baddoo M, Ferris M, Swan KF, Sullivan DE, Burow ME, **Taylor CM**, Flemington EK. Differences in gastric carcinoma microenvironment stratify according to EBV infection intensity; implications for possible immune adjuvant therapy. PLoS Pathog. 2013;9(5):e1003341. doi: 10.1371/journal.ppat.1003341. PMID: 23671415; PMCID: PMC3649992.
d. Strong MJ, O'Grady T, Lin Z, Xu G, Baddoo M, Parsons C, Zhang K, **Taylor CM**, Flemington EK. Epstein-Barr virus and human herpesvirus 6 detection in a non-Hodgkin's diffuse large B-cell lymphoma cohort by using RNA-seq. J Virol. 2013 Dec;87(23):13059-62. PMID: 24049168; PMCID: PMC3838131.

3. The major focus of my current research began in 2010 with the application of high-throughput sequencing to analyze microbial communities through sequencing of the 16S rRNA. My group developed a software framework for analysis of this data called Viamics [a]. This system was intended to be easy to use for biologists who had limited experience with command line tools such as Mothur. It provided a graphical user interface that allowed our collaborators to easily analyze and interact with their sequencing data and to produce publication quality figures at the push of a button. We also developed a novel method for looking at subtle nucleotide variation in the 16S reads called oligotyping [b]. This method allowed us to analyze 16S data down to a sub-species level and was applied to the analysis of genitourinary tract microbiota in monogamous couples. Shockingly, we were able to see strong enough correlations between oligotypes of gardnerella vaginalis in a woman's vaginal microbiota and her male sexual partner's penile skin microbiota that we were able to predict which males and females in our study were sexual partners with a high degree of accuracy. We have recently published a follow up study to [b] where we applied the oligotyping method to additional couples from the paired sexual partner cohort [d] and we continue to collaborate with researchers throughout our region on analysis and visualization of the human vaginal microbiome.
   a. Murat Eren A, Ferris MJ, **Taylor CM**. A framework for analysis of metagenomic sequencing data. Pac Symp Biocomput. 2011:131-41. PMID: 21121041.
   b. Eren AM, Zozaya M, **Taylor CM**, Dowd SE, Martin DH, Ferris MJ. Exploring the diversity of Gardnerella vaginalis in the genitourinary tract microbiota of monogamous couples through subtle nucleotide variation. PLoS One. 2011;6(10):e26732. PMID: 22046340; PMCID: PMC3201972.
   c. Zozaya M, Ferris MJ, Siren JD, Lillis R, Myers L, Nsuami MJ, Eren AM, Brown J, **Taylor CM**, Martin DH. Bacterial communities in penile skin, male urethra, and vaginas of heterosexual couples with and without bacterial vaginosis. Microbiome. 2016 Apr 19;4:16. doi: 10.1186/s40168-016-0161-6. PMID: 27090518; PMCID: PMC4835890.

4. Our early work in the vaginal microbiome and studies of Bacterial Vaginosis led to an interest in studying the newborn infant gut microbiota due to the intimate association between a mother's vaginal microbiota and the newborn infant's gut microbiota. We developed a collaboration with a clinician (Duna Penn) who was collecting fecal samples from premature infants and sequenced the gut microbiota of these infants. We found an association between H2 receptor blockers and the fecal microbiota and our article appeared on the cover of the issue of the Journal of Pediatric Gastroenterology Nutrition in which it appeared [a]. This study was followed up with an investigation of the development of necrotizing enterocolitis in premature infants. We found that both overall bacterial diversity and Clostridia abundance decreased in the infant gut microbiome with increasing severity of necrotizing enterocolitis [b]. We have recently reported a similar study describing changes in the gut microbiome of pediatric patients with end stage renal disease [c]. This work has all seeded an interest in understanding the drivers of initial colonization of the infant gut and we have recently secured funding to perform environmental sampling of Neonatal Intensive Care Units and the gut microbiome of newborn infants housed within them to look for associations between environmental bacteria and colonizers of the newborn infant gut.
    a. Gupta RW, Tran L, Norori J, Ferris MJ, Eren AM, **Taylor CM**, Dowd SE, Penn D. Histamine-2 receptor blockers alter the fecal microbiota in premature infants. J Pediatr Gastroenterol Nutr. 2013 Apr;56(4):397-400. doi: 10.1097/MPG.0b013e318282a8c2. PMID: 23254444.
    b. McMurtry VE, Gupta RW, Tran L, Blanchard EE 4th, Penn D, **Taylor CM**, Ferris MJ. Bacterial diversity and Clostridia abundance decrease with increasing severity of necrotizing enterocolitis. Microbiome. 2015 Mar 23;3:11. doi: 10.1186/s40168-015-0075-8. PMID: 25810906; PMCID: PMC4373520.
    c. Crespo-Salgado J, Vehaskari VM, Stewart T, Ferris M, Zhang Q, Wang G, Blanchard EE, **Taylor CM**, Kallash M, Greenbaum LA, Aviles DH. Intestinal microbiota in pediatric patients with end stage renal disease: a Midwest Pediatric Nephrology Consortium study. Microbiome. 2016 Sep 17;4(1):50. doi: 10.1186/s40168-016-0195-9. PMID: 27640125; PMCID: PMC5027112.

5. Because of our interest in human health and the difficulty and ethical issues associated with performing mechanistic studies in human patients, we have embarked on a large number of model organism studies investigating the association of gut microbiota with obesity and the ability to modulate the gut microbiota. We began with a study looking at the influence of a series of botanical extracts on the mucosal and luminal microbiota in diet-induced obese mice [a]. We found that the botanical supplements differentially affected the mucosal and luminal microbiota and hence that it was important to include both types of samples in future studies. Once this model was developed, we performed an adoptive transfer of gut microbiota in mice and showed that we could induce neurobehavioral changes in the absence of obesity by transplanting microbiota from obese mice into lean mice that are maintained on a standard chow diet [b]. We have since investigated the host response to infection with Pneumocystis pneumonia and how it changes based on differences in the intestinal microbiota [c]. We have recently used a probiotic, Lactobacillus reuteri, to inhibit immune deficiencies by modulating the gut microbiota in mice [d]. These studies have all established the models and ability for us to modulate the gut microbiota in mice via antibiotics, probiotics, botanicals and adoptive transfer in order to mechanistically study changes in response to pathogen challenges. Ultimately we aim to translate these findings to bear on the human condition.
    a. Wicks S, **Taylor CM**, Luo M, Blanchard IV E, Ribnicky D, Cefalu WT, Mynatt RL, Welsh DA. Artemisia supplementation differentially affects the mucosal and luminal ileal microbiota of diet-induced obese mice. Nutrition. 2014 Jul-Aug;30(7-8 Suppl):S26-30. doi:10.1016/j.nut.2014.02.007. PMID: 24985102.
    b. Bruce-Keller AJ, Salbaum JM, Luo M, Blanchard E 4th, **Taylor CM**, Welsh DA, Berthoud HR. Obese-type gut microbiota induce neurobehavioral changes in the absence of obesity. Biol Psychiatry. 2015 Apr 1;77(7):607-15. doi: 10.1016/j.biopsych.2014.07.012. PMID: 25173628; PMCID: PMC4297748.
    c. Samuelson DR, Charles TP, de la Rua NM, **Taylor CM**, Blanchard EE, Luo M, Shellito JE, Welsh DA. Analysis of the intestinal microbial community and inferred functional capacities during the host response to Pneumocystis pneumonia. Exp Lung Res. 2016 Oct – Dec;42(8-10):425-439. doi:10.1080/01902148.2016.1258442. PMID: 27925857; PMCID: PMC5304582.
    d. He B, Hoang TK, Wang T, Ferris M, **Taylor CM**, Tian X, Luo M, Tran DQ, Zhou J, Tatevian N, Luo F, Molina JG, Blackburn MR, Gomez TH, Roos S, Rhoads JM, Liu Y. Resetting microbiota by Lactobacillus reuteri inhibits T reg deficiency-induced autoimmunity via adenosine A2A receptors. J Exp Med. 2017 Jan;214(1):107-123. doi: 10.1084/jem.20160961. PMID: 27994068; PMCID: PMC5206500.

Complete List of PublishedHere Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/christopher.taylor.1/bibliography/43101263/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

1R01AI118860-01A1 **Taylor/Quayle/Aiyar(MPIs)** 08/08/17 – 07/31/21
NIH/NIAID
Consequences of vaginal microbiota on IFN-gamma-mediated clearance of Chlamydia trachomatis
The goal of this award is to characterize the vaginal microbiota that is associated with spontaneous clearance of Chlamydia infection. My role is as multi-principal-investigator leading the sequencing and bioinformatics analysis of the vaginal microbiome data.
Role: Multi-Principal-Investigator

1UH2AA026226-01 **Welsh(PI)** 09/15/17 – 08/31/19
NIH/NIAAA
Precision Medicine Approaches for Alcohol and HIV-associated Dysbiosis, Immune Activation and Cardiometabolic Syndrome
The goal of this project is to assess the dysbiosis of microbiota caused by alcohol usage in an HIV-positive population and to investigate possible personalized approaches to treating the dysbiosis.
Role: Co-I

P20GM103424 **Kousoulas(PI)** 05/01/16 – 04/30/20
NIH/NIGMS
Louisiana Biomedical Research Network
The goal of this funding is to unite the LSU system bioinformatics, biostatistics and computational biology resources. My role is as co-investigator and director of the bioinformatics, biostatistics and computational biology core.
Role: Co-Investigator

5R21AI111058-02 **Aly(PI)** 07/01/16 – 06/30/18
NIH/NIAID (Subcontract # HSC-554475-16/17)
Selection of the Determinants of Plasmodium Sporozoite Infectivity and Motility
The goal of this project is to use RNA sequencing to determine the mechanisms of mosquito plasmodium infection and possible deterrents to motility. My role is as co-investigator and bioinformatics expert.
Role: Co-Investigator

U54-TR-001368-01 **Kimberly(PI)** 09/01/15 – 08/31/19
NIH/NCATS
UAB Center for Clinical and Translational Science (CCTS)
The goal of this center is to promote clinical and translational science across the southern region. UAB, LSU, and Tulane are members of the CCTS. My role in this project is as co-investigator and bioinformatics expert.
Role: Co-Investigator

Completed Research Support

N01-A1-2014-00003 [HHSN272201400003C] **Wilson(PI)** 05/23/14 – 10/31/16
NIH/NIAID (Subcontract #CTR-FF3-N1006, Autoimmune Technologies, LLC)
Development of Therapeutic Medical Countermeasures for Biodefense and Emerging Infectious Diseases
The goal of this project is to identify and characterize influenza virus mutants that are resistant to Flufirvitide-3, a small peptide that has been shown to be highly effective as an entry inhibitor that blocks infection with influenza virus. This project is part of FDA approval of the drug as a treatment for influenza.
Role: Co-Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Muzny, Christina A.**

eRA COMMONS USER NAME (credential, e.g., agency login): **CMUZNY**

POSITION TITLE: **Associate Professor of Medicine**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Texas at Austin; Austin, TX	B.A.	05/1998	Biology
Texas A&M College of Medicine; College Station, TX	M.D.	05/2003	Medicine
University of Mississippi Medical Center; Jackson, MS	Postdoctoral	12/2006	Internal Medicine
University of Mississippi Medical Center; Jackson, MS	Postdoctoral	12/2009	Infectious Diseases
University of Alabama at Birmingham School of Public Health, Birmingham, AL	MSPH Epi	12/2017	Clinical and Translational Science

A. Personal Statement

Christina A. Muzny, MD, is an infectious diseases physician at the University of Alabama, Birmingham, with expertise in translational research related to the vaginal biome and the pathogenesis of bacterial vaginosis (BV). Her clinical and research interests over the past 12 years have focused on sexually transmitted infections (STIs) (specifically vaginal infections including BV and trichomoniasis) and HIV among difficult-to-reach populations of women, including lesbian and bisexual women. Dr. Muzny's current NIH/NIAID K23-funded vaginal microbiome research focuses on investigating the pathogenesis of incident BV among African American women who have sex with women. She also serves as the UAB Site Principal Investigator on an NIH/NIAID R01- funded study to compare different dosing regimens of metronidazole for vaginal trichomoniasis among HIV- negative women.

Dr. Muzny is a teaching faculty for the AL-NC STD/HIV Prevention Training Center, an Associate Scientist for the UAB Center for AIDS Research, and a research mentor to junior faculty members in infectious diseases and a biology master's graduate student. Her infrastructure at UAB includes an experienced team of 2 research nurses, 2 laboratory technologists, a study coordinator, and two bioinformatics experts. She regularly collaborates with Drs. Taylor and Talluri on her vaginal microbiome research in addition to other experts.

For the purposes of this R01, Dr. Muzny will provide vaginal microbiome expertise related to the study activities described in Aim 3.

Related Publications:

a. Muzny CA, Schwebke JR. Pathogenesis of Incident Bacterial Vaginosis – Review of Current Hypotheses. J Infect Dis 2016; 214 (S1): S1-5. PMID: 27449868.
b. Schwebke JR, Muzny CA, Josey W. Role of Gardnerella vaginalis in the Pathogenesis of Bacterial Vaginosis – A Conceptual Model. J Infect Dis 2014; 210(3): 338-343. PMID: 24511102.
c. Muzny CA, Rivers CA, Austin EL, et al. Trichomonas vaginalis Infection among Women Receiving Gynecological Care at an Alabama HIV Clinic. Sex Transm Inf 2013; 89: 514-518. PMID: 23449600
d. Muzny CA, Rivers CA, Mena LA, et al. Genotypic Characterization of Trichomonas vaginalis Isolates among WSW in Sexual Partnerships. Sex Transm Dis 2012; 39: 556- 558. PMID: 22706219.

B. Positions and Honors

Positions and Employment:

2005-2009 Medical Service, G.V. (Sonny) Montgomery Veterans Affairs Medical Center; Jackson, MS
2009-2010 Assistant Professor of Medicine, Infectious Diseases, Univ. of Mississippi Medical Center
2010-Present Assistant Professor of Medicine, Infectious Diseases, Univ. of Alabama at Birmingham
2017-Present Associate Professor of Medicine, Infectious Diseases, Univ. of Alabama at Birmingham

Selected Honors and Awards:

1995-1998 Univ. of Texas at Austin College of Natural Sciences Dean's List
1997-1998 Univ. of Texas at Austin College Scholar
1999-2003 Honors Graduate, Texas A&M College of Medicine
2012-13,15-16 Univ. of Alabama at Birmingham Department of Medicine Research Supplement Award
2012 Univ. of Alabama at Birmimgham Department of Medicine Clinician Educator Award
2012 Travel Scholarship; 39th Annual Meeting of the Infectious Diseases Society of Gynecology
2014 Young Investigator Award; American Sexually Transmitted Diseases Association
2017 Inspirational Physician Honoree; American Medical Association Women Physician's Section

Extramural Offices:

2007-2009 Graduate Medical Education Committee, Sub-Specialty Representative, Univ. of Mississippi
2014-Present Member, Institutional Review Board 02, Univ. of Alabama at Birmingham
2015-Present Department of Medicine Peer Mentorship Committee, Univ. of Alabama at Birmingham
2015-Present Department of Medicine Research Development Group, Univ. of Alabama at Birmingham
2016-Present Department of Medicine Scientific Review Committee, Univ. of Alabama at Birmingham

Selected Professional Societies:

2004-Present American College of Physicians
2006-Present Infectious Diseases Society of America
2007-Present American Society of Microbiology
2007-Present American Sexually Transmitted Diseases Society
2015-Present Southern Society for Clinical Investigation
2016-Present Infectious Diseases Society of Gynecology

C. Contributions to Science

1. My current research focuses on the epidemiology and pathogenesis of incident BV, the most common vaginal infection. It remains controversial whether BV is a sexually transmitted infection. With my K23 NIH/NIAID mentored career development award, I am investigating the hypothesis that sexual exposure to *Gardnerella vaginalis* (present in 95%-100% of cases of clinically diagnosed BV) is the inciting event leading to the complex vaginal flora associated with BV. A better understanding of the pathogenesis of incident BV is essential for the prevention of this common vaginal infection and its adverse public health consequences.

a. Muzny CA, Schwebke JR. Gardnerella vaginalis: Still a Prime Suspect in the Pathogenesis of Bacterial Vaginosis. **Curr Infect Dis Rep 2013; 15: 130-5.** PMID: 23371405.
b. Muzny CA, Sunesara IR, Kumar R, et al. Characterization of the Vaginal Microbiota Among Sexual Risk Behavior Groups of Women with BV. **PLoS One 2013; 8(11): e80254.** PMCID: PMC3827412.
c. Muzny CA, Sunesara IR, Griswold M, et al. Association Between BVAB1 and High Nugent Scores among Women with BV. **Diagn Microbiol Infect Dis 2014; 80: 321-323.** PMCID: PMC4326426.
d. Muzny CA, Schwebke JR. Biofilms: An Underappreciated Mechanism of Treatment Failure and Recurrence in Vaginal Infections. **Clin Infect Dis 2015, e-pub May 1, 2015.** PMID: 25935553.

2. I have performed multiple studies of trichomoniasis among HIV+ and HIV- women in high-risk clinical settings from a microbiologic and epidemiologic perspective. I am also currently working on a multi-site NIH/NIAID R01 funded clinical trial to compare different dosing regimens for vaginal trichomoniasis among HIV- women.

a. Cornelius DC, Robinson DA, Muzny CA, et al. Multilocus Sequence Typing for Genetic Characterization of Trichomonas vaginalis. **J Clin Microbiol 2012; 50: 3293-3000.** PMCID: PMC3457461.

b. Muzny CA, Schwebke JR. The Clinical Spectrum of *Trichomonas vaginalis* Infection and Challenges to Management. **Sex Transm Inf 2013; 89: 423-425.** PMID: 23543252.
c. Muzny CA, Blackburn RJ, Sinsky RJ, et al. Added Benefit of Nucleic Acid Amplification Testing for the Diagnosis of *Trichomonas vaginalis* among Men and Women Attending a Sexually Transmitted Diseases Clinic. **Clin Infect Dis 2014; 59(6): 834-841.** PMID: 24928292.
d. Backus K, Muzny CA, Beauchamps L. *Trichomonas vaginalis* Successfully Treated with Boric Acid in a Metronidazole-Allergic Female. **Sex Transm Dis 2017; 44(2): 120**. PMID: 27984554.

3. My research efforts also focus on the sexual health of African American lesbian and bisexual women in the Southern U.S. I have successfully developed two cohorts of these women studied for sexual behavior and sexual risks at the Mississippi State Department of Health STD clinic and the Jefferson County Health Department STD clinic. These studies found that women were at high risk for STIs, particularly *T. vaginalis*. Results from these studies have helped to tailor sexual health services provided to African American lesbian and bisexual women.

a. Muzny CA, Sunesara IR, Martin DH, et al. Sexually Transmitted Infections among African American Women Who Have Sex with Women: Does Sex with Men Make a Difference? **Sex Transm Dis 2011; 38: 1118-1125.** PMID: 22082722.
b. Muzny CA, Harbison HS, Pembleton ES, et al. Sexual Risk Behaviors, Perception of Sexually Transmitted Infection Risk, and Practice of Safe Sex among African American Women Who Have Sex with Women. **Sex Transm Dis 2013; 40: 395-400.** PMID: 23588129.
c. Muzny CA, Austin EL, Harbison HS, et al. Sexual Partnership Characteristics of African American Women Who Have Sex with Women; Impact on Sexually Transmitted Infection Risk. **Sex Transm Dis 2014; 41: 611-617.** PMID: 25211257.
d. Muzny CA, Kapil R, Austin EL, B. Chlamydia trachomatis Infection Prevalence and Serum Immunoglobulin Responses Among African American Women Who Have Sex with Women. **Int J STD & AIDS 2016; 27(11): 978-983.** PMID: 26384942.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1Dq0c42rn4QN/bibliography/47636050/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing

UAB Center for AIDS Research Developmental Award (Eaton, PI) 3/1/17 – 2/28/18
Identifying Patient-Centered Sexually Transmitted Infection Testing Services to Reduce HIV/STI Transmission in Young African American Men Who Have Sex with Men
The goal of this award is to develop a set of patient-centered STI testing option attributes for young African American MSM using qualitative research to inform a quantitative study
Role: Co-Investigator (Research Mentor to Dr. Eaton)

University of Alabama at Birmingham IMPACT Award (Muzny: PI) 7/1/15 – 6/30/18
Pathogenesis of Bacterial Vaginosis among Women Who Have Sex with Women
The goal of this award is to provide supplemental funds to conduct K23-related research activities.
Role: Principal Investigator

K23AI106957 (Muzny: PI) 6/1/14 – 5/31/19
NIH/NIAID
Pathogenesis of Bacterial Vaginosis among Women Who Have Sex with Women
The goal of this award is to use cultivation-independent molecular methods to determine the sequence of microbiological events culminating in BV among sexually active African American WSW.
Role: Principal Investigator

R01AI097080 (Kissinger: PI; Muzny UAB Site PI) 8/15/13 – 1/15/18

NIH/NIAID
Trichomonas vaginalis Repeat Infections among HIV-Negative Women

The goal of this multi-center study is to compare different dosing regimens for vaginal trichomoniasis.
Role: Co-Investigator (UAB Site Principal Investigator)

R01AI097080 Supplement (Kissinger: PI; Muzny UAB Site PI) 6/30/16 – 1/15/18

NIH/NIAID
Trichomonas vaginalis DNA Clearance and Specimen Repository Study
This study aims to determine how long *T. vaginalis* nucleic acid is detectable post-treatment and to enhance a specimen repository for a vaginal microbiome study post-*T. vaginalis* treatment
Role: Co-Investigator (UAB Site Principal Investigator)

HHSN272201100034C (Kimberlin: PI) 9/28/11 – 8/15/18
Identification of Herpes Simplex Virus (HSV) Shedding in the Female Genital Tract of Pregnant and Non-Pregnant Women by the Xpert HSV ½ Assay, Routine PCR, and Culture
The goals of this study are to estimate the sensitivity of the Xpert HSV 1/2 Assay relative to culture for detecting HSV DNA in the genital tract of pregnant and non-pregnant women in STI clinics.
Role: Co-Investigator

Completed

UL1TR001417; CCTS Multidisciplinary Network Pilot Program Award (Muzny: PI) 4/1/16 – 3/31/17
NIH/NCATS
Genital Microbiomes of Women with Recurrent BV and their Regular Male Sexual Partners
The goal of this award is to compare the genital microbiota of women with recurrent BV and their regular male sexual partner in order to study the hypothesis that BV is an STI.
Role: Principal Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Cleary, Susan May

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Associate Professor in Health Economics

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Rhodes University, Grahamstown, South Africa	BA	12/1996	English and Economics
University of Cape Town, South Africa	BA Honours	12/1999	Economics
University of Cape Town, South Africa	Masters	12/2001	Economics
University of Cape Town, South Africa	PhD	12/2007	Health Economics

A. Personal Statement

Susan Cleary, PhD, is an Associate Professor in Health Economics in the School of Public Health and Family Medicine at the University of Cape Town. She has more than 15 years' experience in cost-effectiveness analysis and decision analytic modeling. She (co)authored the first CEAs of HIV-treatment in South Africa from clinical trials, routine public primary health care settings and private practice. Since then, Dr. Cleary has conducted and supervised CEAs across a diverse set of disease and programme areas including cryptococal antigen screening, HPV vaccination, interventions to improve quality of care for children and models of care for antiretroviral treatment, amongst others. Current projects include the cost-effectiveness of GeneXpert for TB diagnosis and behavioural interventions for mental illness in patients with HIV or Diabetes. She has given extensive policy input over the years, including (co-)leading the economics and financing components of the South African National Strategic Plans for HIV, STIs and TB covering the periods 2007-2011 and 2012-2016.

Dr. Cleary has considerable experience in studies assessing the affordability and accessibility of interventions from the patient perspective. For this project, she will oversee all cost/cost-effectiveness related activities (Aim 2).

B. Positions and Honors

2001-2004: Junior Researcher, Health Economics Unit, School of Public Health and Family Medicine, UCT
2004-2007: Researcher, Health Economics Unit, School of Public Health and Family Medicine, UCT
2008-2010: Senior Lecturer, Health Economics Unit, School of Public Health and Family Medicine, UCT
2007-2011: Director, Health Economics Unit, School of Public Health and Family Medicine, UCT
2011 to date: Associate Professor, Health Economics Unit, School of Public Health and Family Medicine, UCT

C. Contributions to Science

1. Cost-effectiveness of HIV-treatment

When I started working as a health economist in 2001, the HIV-epidemic was arguably the most critical challenge facing the South African health system. At this stage, there were no data available on the cost-effectiveness of HIV-treatment within our setting. To fill this gap, I collected primary data from antiretroviral services, HIV wellness services and within hospitals and developed Markov modeling expertise in order to

ultimately assess the full costs of HIV care and the cost-effectiveness of Antiretroviral Treatment (ART). This work has continued over time to include evaluations of alternative models of care for ART and approaches to managing common opportunistic infections, amongst others.

1. Jarvis JN, Harrison TS, Lawn SD, Meintjes G, Wood R, Cleary S. Cost effectiveness of cryptococcal antigen screening as a strategy to prevent HIV-associated cryptococcal meningitis in South Africa. *PLoS One*. 2013;8(7):e69288. doi:10.1371/journal.pone.0069288. PMID: 23894442 PMCID: PMC3716603.
2. Bango F, Ashmore J, Wilkinson L, van Cutsem G, Cleary S. Adherence clubs for long-term provision of antiretroviral therapy: cost-effectiveness and access analysis from Khayelitsha, South Africa. *Trop Med Int Heal*. 2016;21(9):1115-1123. doi:10.1111/tmi.12736. PMID: 27300077.
3. Cleary SM, McIntyre D, Boulle AM. Assessing efficiency and costs of scaling up HIV treatment. *AIDS*. 2008;22 Suppl 1:S35-42. doi:10.1097/01.aids.0000327621.24232.71. PMID: 18664951.
4. Cleary SM, McIntyre D, Boulle AM. The cost-effectiveness of antiretroviral treatment in Khayelitsha, South Africa--a primary data analysis. *Cost Eff Resour Alloc*. 2006;4:20. doi:10.1186/1478-7547-4-20. PMID: 17147833 PMCID: PMC1770938.

2. Affordability of HIV-treatment

In addition to understanding cost-effectiveness, it was essential to understand the affordability of HIV-related treatment, given the large and new burden of disease, the relatively high cost of treatment, and the potentially long duration of ART. I therefore developed cost modeling expertise, which enables me to provide extensive policy input, including chairing or co-chairing the costing and financing components of the government's National Strategic Plans for HIV/AIDS and STIs covering the periods 2007-2011 and 2012-2016. In addition, I was part of a team that developed costing models that were used by UNAIDS, WHO and low and middle income countries seeking to cost their national strategic plans. From a conceptual perspective, I developed a mathematical programming approach that is capable of simultaneously assessing cost-effectiveness and affordability.

1. Cleary S, McIntyre D. Financing equitable access to antiretroviral treatment in South Africa. *BMC Health Serv Res*. 2010;10(Suppl 1):S2. doi: 10.1186/1472-6963-10-S1-S2. PMID: 20594368 PMCID: PMC2895746.
2. Cleary S, Mooney G, McIntyre D. Equity and efficiency in HIV-treatment in South Africa: the contribution of mathematical programming to priority setting. *Health Econ*. 2010;19(10):1166-1180. doi: 10.1002/hec.1542. PMID: 19725025.
3. Cleary SM, Mcintyre D. Affordability - the forgotten criterion in health-care priority setting. *Health Econ*. 2009;18:373-375. doi:10.1002/hec. PMID: 19267322.

3. Costs and cost-effectiveness of HIV-treatment in other populations

While my initial passion was to work towards the provision of HIV-treatment to South Africans dependent on our public health system, I also contributed towards the understanding of costs and cost-effectiveness within the South African private health system, both on its own, and in comparison to public sector care. Similarly, I supported work related to the economic evaluation of HIV-treated within other low and middle income settings.

1. Leisegang R, Maartens G, Hislop M, Sargent J, Darkoh E, Cleary S. A novel Markov model projecting costs and outcomes of providing antiretroviral therapy to public patients in private practices versus public clinics in South Africa. *PLoS One*. 2013;8(2):e53570. doi:10.1371/journal.pone.0053570. PMID: 23405073 PMCID: PMC3566152.
2. Nachega JB, Leisegang R, Bishai D, et al. Association of Antiretroviral Therapy Adherence and Health Care Costs. *Ann Intern Med*. 2010;152:18-25. doi: 10.7326/0003-4819-152-1-201001050-00006. PMID: 20048268.
3. Leisegang R, Cleary S, Hislop M, et al. Early and Late Direct Costs in a Southern African Antiretroviral Treatment Programme: A Retrospective Cohort Analysis. Rosen S, ed. *PLoS Med*. 2009;6(12):11. doi: 10.1371/journal.pmed.1000189. PMID: 19956658 PMCID: PMC2777319.

4. Jouquet G, Bygrave H, Kranzer K, et al. Cost and cost-effectiveness of switching from d4T or AZT to a TDF-based first-line regimen in a resource-limited setting in rural Lesotho. *J Acquir Immune Defic Syndr*. 2011;58(3):e68-74. doi:10.1097/QAI.0b013e31822a9f8d. PMID: 21765366.

4. The patient perspective within economic evaluation

While the abovementioned work on the costs and affordability of HIV-treatment and other health care interventions is key to understanding health systems efficiency and the financing of interventions at scale, I also have a keen interest in understanding the patient perspective in accessing needed interventions. To this end, I have been involved in multiple studies investigating patient access barriers to care, including barriers related to affordability, availability and the acceptability of the health service. This, in addition to the work on efficiency, provides me with insight into the key barriers that patients experience when accessing care, which is essential to consider when designing the implementation of new programmes.

1. Cleary SM, Birch S, Moshabela M, Schneider H. Unequal access to ART: exploratory results from rural and urban case studies of ART use. *Sex Transm Infect*. 2012;88(2):141-146. doi:10.1136/sextrans-2011-050136. PMID: 22345029.
2. Moshabela M, Schneider H, Silal SP, Cleary SM. Factors associated with patterns of plural healthcare utilization among patients taking antiretroviral therapy in rural and urban South Africa: a cross-sectional study. *BMC Health Serv Res*. 2012;12(1):182. doi:10.1186/1472-6963-12-182. PMID: 22747971.
3. Cleary S, Birch S, Chimbindi N, Silal S, Mcintyre D. Investigating the affordability of key health services in South Africa. *Soc Sci Med*. 2013;80:37-46. PMID: 23415590.
4. Foster N, Vassall A, Cleary S, Cunnama L, Churchyard G, Sinanovic E. The economic burden of TB diagnosis and treatment in South Africa. *Soc Sci Med*. 2015;130:42-50. doi:10.1016/j.socscimed.2015.01.046. PMID: 25681713.

5. Costing inpatient care

A final area of expertise that is of relevance to this grant is my work on assessing the costs of inpatient care. Without an electronic patient information system, costing inpatient care in South African public hospitals is challenging and time consuming. However, these estimates are essential in that new technologies often avert inpatient care, making them relatively more cost-effective or even cost saving.

1. Pepper D, Burch V, Levitt N, Cleary S. Hyperglycaemic emergency admissions to a secondary-level hospital – an unnecessary financial burden. S Afr Med J. 2007;12(2):56–60.
2. Cleary, S., Boulle, A., Castillo-Riquelme, M. & McIntyre, D. The burden of HIV/AIDS in the public healthcare system. South Afr. J. Econ. 76, 3–14 (2008). No PMID
3. de Cherif TKS, Schoeman JH, Cleary S, Meintjes G a, Rebe K, Maartens G. Early severe morbidity and resource utilization in South African adults on antiretroviral therapy. BMC Infect Dis. 2009 Dec 15;9:205. doi: 10.1186/1471-2334-9-20. PMID: 20003472 PMCID: PMC2803481.
4. Kevany S, Meintjes G, Rebe K, Maartens G, Cleary S. Clinical and financial burdens of secondary level care in a public sector antiretroviral roll-out setting (G. F. Jooste Hospital). South African Med J SuidAfrikaanse Tydskr vir Geneeskd [Internet]. 2009;99(5):320–5. PMID: 19588792

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing research projects

Wellcome Trust PI Sorsdahl and Myers 01/01/2015 – 12/31/2019
Strengthening South Africa's health system through integrating treatment for mental illness into chronic disease care (Project MIND)
Goal: To understand the effectiveness and cost-effectiveness of models of care and task shifting for mental illness within chronic disease care.
Role: Co-investigator

United Kingdom DFID RDs Gilson and Hanson 01/01/2011 – 12/31/2018
Responsive and Resilient Health Systems (RESYST)
Goal: An eight year research programme consortium addressing issues of financing, human resources and governance in Africa and Asia.
Role: Management team member

Atlantic Philanthropies PI Gilson and Lehman 01/01/2010 – 12/31/2017
District Innovation and Action Learning for Health Systems (DIALHS)
Goal: An action-learning project supporting district health system development in South Africa.
Role: Co-investigator

Doris Duke Charitable Foundation PI Gilson 01/01/2013 – 12/31/2017
Implementing large-scale health system strengthening intervention: experience from the DDCF's African health Initiative
Goal: A four year programme of work to understand the factors influencing implementation practice in large-scale health system strengthening projects.
Role: Co-investigator

Completed research projects

None in the last three years.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Tracy Leonora Meiring, Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: NRF Research Career Award Fellow, University of Cape Town

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Pretoria, South Africa	B.S	12/1996	Genetics
University of Pretoria, South Africa	B.S (Hons)	04/1998	Genetics
University of Pretoria, South Africa	M.S	04/2002	Genetics
University of Pretoria, South Africa	Ph.D.	09/2009	Genetics
University of the Western Cape, South Africa	Postdoctoral	12/2010	Molecular Microbiology
University of Cape Town (UCT), South Africa	Postdoctoral	06/2014	Molecular Virology

A. Personal Statement

Tracy Leonora Meiring, PhD, is a geneticist with experience and interest in metagenomics and viromics, and specific expertise in the vaginal microbiome and virome. As a postdoctoral fellow at the Institute for Microbial Biotechnology and Metagenomics (IMBM, UWC) she gained experience in the analysis and interpretation of metagenomic data generated on the Illumina and Roche 454 platforms. From 2011-2014, Dr. Meiring held a postdoctoral fellow position at the Division of Medical Virology and Institute for Infectious Diseases and Molecular Medicine (IDM) at UCT. During this time, she undertook a metagenomic study of Human papillomavirus (HPV) genetic diversity in cervical specimens from HIV-infected South African women; she was among the first to use next generation sequencing to characterize human papillomaviruses in clinical specimens. In this position she attained the skills required to analyze large sequence data sets, including the assembly of viral genomes from complex metagenomic data.]

In 2012, she visited the laboratory of Dr Eoin Brodie (Lawrence Berkeley National Laboratory, Berkeley, California) where she received training in preparing Illumina 16S amplicon libraries from clinical samples and in microbiome data analysis. In 2014, Dr. Meiring was appointed as a National Research Foundation Research Career Advancement Fellow at UCT. Her current research activities include characterizing the vaginal microbiomes of South African women, with the aim of determining associations with HPV and HIV infection. As an early-career investigator establishing my research group, she currently supervises two PhD students and co-supervises one PhD and one MSc student.

For this proposal, Dr. Meiring will serve as co-investigator and be responsible for the microbiome profiling of the vaginal specimens at the University of Cape Town.

Related Publications:

a. Adler DH, Wallace M, Bennie T, Mrubata M, Abar B, **Meiring TL**, Williamson AL, Bekker LG. Cervical dysplasia and high-risk human papillomavirus infections among HIV-infected and HIV-uninfected adolescent females in South Africa. Infect Dis Obstet Gynecol. 2014;2014:498048. doi: 10.1155/2014/498048. PMCID: PMC4217359.
b. Adler D, Wallace M, Bennie T, Abar B, Sadeghi R, **Meiring T**, Williamson AL, Bekker LG. High risk

human papillomavirus persistence among HIV-infected young women in South Africa. Int J Infect Dis. 2015 Apr;33:219-21. doi: 10.1016/j.ijid.2015.02.009. PMCID: PMC4397173.

B. Positions and Honors

Positions and Employment

2005-2006	Technical Assistant, Department of Genetics, University of Pretoria, South Africa
2006-2007	Training Manager, WITS Health Consortium, Johannesburg, South Africa
2007-2008	Senior Technical Assistant, Department of Genetics, University of Pretoria, South Africa
2009-2010	Postdoctoral Research Fellow, Institute for Microbial Biotechnology and Metagenomics, University of the Western Cape, South Africa
2011-2014	Postdoctoral Research Fellow, Division of Medical Virology and Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, South Africa
2014-present	NRF Research Career Award Fellow, Division of Medical Virology and Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, South Africa

Honors

1998	Best BSc Honors student in Genetics, University of Pretoria, South
Africa 2010	Claude Leon Foundation Fellowship
2013	Carnegie Foundation Fellowship
2014	Clinical Infectious Disease Research Initiative (Wellcome Trust) Fellowship

C. Contributions to Science

1. Vaginal microbiome and human papillomavirus (HPV)

   Persistent infection with high risk HPVs is causally associated with the development of cervical intraepithelial lesions and cervical cancer. In South Africa cervical cancer is the leading cause of cancer related mortality in women. Co-infection with HIV in the region is high. The burden of HPV-associated disease is significantly higher in HIV-positive individuals even if they are receiving anti-retroviral therapy. The role of the vaginal microbiome in the acquisition and persistence of HPV, as well as the development of cervical lesions and cervical cancer is an active area of research. I am currently undertaking several studies examining this in a longitudinal study of a cohort of HIV-uninfected and HIV-infected South African women from Gugulethu, Cape Town. To date we have completed the analysis of the microbiome in baseline vaginal specimens and found that the majority of the women did not have *Lactobacilli* spp. dominated vaginal microbiotas considered to be protective. We further identified bacterial biomarkers for prevalent HPV infection. We are currently preparing a manuscript to disseminate these results and expanding on the study.

2. Next generation sequencing to detect HPV infection

   Several studies have indicated that many current commercial HPV typing methods are not able to reliably identify all genotypes present in complex multiple infections. This is of particular concern in HIV-infected individuals who have a high burden of multiple HPV type infections. I carried out a study that was the first to demonstrate the use of shotgun Illumina sequencing of cervical specimens for genome sequencing and genotyping of HPV in complex multiple infections in an unbiased manner. In collaboration with Prof Ulf Gyllensten (Uppsala University, Sweden) we applied a similar shotgun sequencing method using the Ion Proton platform. This demonstrated the applicability of the method to both HPV detection and metagenomic characterization of clinical vaginal samples. I additionally developed a HPV detection method based on NGS of HPV L1 FAP amplicons. Application of this method to penile samples from HIV-infected and HIV- uninfected men detected 181 different HPV genotypes (45 α-HPV types, 45 β-HPV types, and 91 γ-HPV types) in a cohort of 218 HPV-positive men. This represents an extremely broad range of HPV types to be

reported in a single study and is the first study using NGS technology on penile samples from Africa.

a. **Meiring TL**, Mbulawa ZZA, Lesosky M, Coetzee D, Williamson AL. High diversity of alpha, beta and gamma human papillomaviruses in genital samples from HIV-negative and HIV-positive heterosexual South African men. Papillomavirus Res. 2017 Jun;3:160-167. doi: 10.1016/j.pvr.2017.05.001.
PMID: 28720451
b. Ameur A, **Meiring TL**, Bunikis I, Haggqvist S, Lindau C, et al. Comprehensive profiling of the vaginal microbiome in HIV positive women using massive parallel semiconductor sequencing. Sci Rep. 2014 Mar 18;4:4398. doi: 10.1038/srep04398. PMCID: PMC3957130
c. **Meiring TL**, Salimo AT, Coetzee B, Maree HJ, Moodley J, et al. Next-generation sequencing of cervical DNA detects human papillomavirus types not detected by commercial kits. Virol J. 2012 Aug 16;9:164. doi: 10.1186/1743-422X-9-164. PMCID: PMC3493284.

3. HPV testing in South Africa

In South Africa cervical cancer is still at an unacceptable incidence despite the Cervical Cancer Screening Programme Guidelines recommending three Papanicolaou (Pap) smears in a lifetime at ten year intervals starting at age 30. In recent years there has been discussion of modifying the South African guidelines to include algorithms with HPV testing. There is now good evidence that HPV testing could replace or complement cytology. In Sweden the National Board of Health and Welfare recommend primary screening by HPV testing from 2017. I am a co-investigator on a South African Medical Research Council funded study (Williamson, PI) that will target cervical cancer screening and management in the Eastern Cape Province of South Africa by assessing a relatively economical and high-resolution HPV test (hpVIR) for HPV detection in self-collected vaginal specimens developed and utilized in clinical screening in Sweden. I am responsible for the transfer and implementation of the hpVIR test at UCT.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/tracy.meiring.1/bibliography/45433578/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

NRF RCA 13100150715/91478 Meiring (PI) 07/01/2014 – 06/30/2019
Title: South African Vaginal Microbiome: Composition and Associations with Sexually Transmitted Diseases Role: PI
Goals: 1) To investigate the associations between the cervicovaginal microbiome and human papillomavirus (HPV) infection in South African women
2) To investigate the impact of HIV status and CD4+ cell count on the composition of the cervical virome.

SAMRC/FORTE RFA01-2016 Williamson (PI) 06/01/2016 – 05/31/2019
Title: A study of the feasibility of the introduction of a Swedish HPV test for the management and prevention of cervical disease in the Eastern Cape
Role: Co-Investigator responsible for transfer and implementation of the hpVIR test at UCT and collaborate on the metagenomics project
Goals: 1) Transfer technology for *hpVIR* test from Sweden to UCT
2) To screen self-collected and clinician obtained cervical specimens collected in Eastern Cape for HPV using *hpVIR* test and compare it to Hybrid Capture 2 (HC2) test.
3) To determine the acceptability of self-collection of samples for HPV in women from the Eastern Cape.

4) To identify potential challenges and opportunities for the introduction of the new hpVIR test into the public sector health system.
5) To study metagenomics in clinician taken samples from women recruited at the colposcopy clinic and primary health care clinics in order to determine which viruses are present on the cervix of women with normal cytology and abnormal cervical cytology. This includes a comparison of the metagenomics in HIV-1 positive and HIV-1 negative women with HPV infections.

Poliomyelitis Research Foundation PRF15/32 Williamson (PI) 08/01/2015-07/31/2018 Title: Characterization of genital human papillomaviruses (HPVs) in men and women recruited as couples. Role: Co-Investigator

Goals: 1) To clone and sequence novel Beta and Gamma HPVs from male genital samples
2) To establish the prevalence of the Beta- and Gamma papillomaviruses in female genital samples
3) To compare the HPVs in the women and their male partners to look at combinations of multiple HPV infection, sharing of viruses in couples, association with HIV infection, CD4 count as well as abnormal cervical cytology

Recently Completed Research Support

None.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Robert Clive Pattinson, M.D.

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Director, MRC Maternal and Infant Health Care Strategies Research Unit

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of the Witwatersrand Johannesburg, South Africa	BSc	06/1973	Microanatomy, Biochemistry
University of the Witwatersrand	MB BCh	06/1977	
University of Stellenbosch, Western Cape, Africa	M.Med	06/1985	Obstetrics/Gynecology
South African College of Obstetricians and Gynecologists	FCOG (SA)	06/1985	Obstetrics/Gynecology
Royal College of Obstetricians/Gynecologists London, England	M.D.	06/1992	Doppler Velocimetry
Fellow Royal College Obstetricans Gynaecologists	FRCOG	06/2008	Obstetrics/gynaecology

A. Personal Statement

Professor Bob Pattinson is the director of the South African Medical Research Council's Maternal and Infant Health Care Strategies Research Unit, clinical Head of the Department of Obstetrics and Gynaecology at the University of Pretoria, and an internationally recognized expert in perinatology. He serves on the National Committee for the Confidential Enquiries into Maternal Deaths and the National Perinatal Morbidity and Mortality Committee in South Africa and compiled and edited their reports. He also is responsible for the perinatal care and child health care surveys in South Africa. His main research interests are in obstetrics, medical audits, health systems and effective methods of outreach. His main research focus is on determining the most effective means of implementing new health care strategies and improving current programmes, in other words how to effectively complete the audit cycle. Recently the scale-up of the Essential Steps in Managing Obstetric Emergencies (ESMOE) and Emergency Obstetric Simulation Training (EOST) programme has been completed. This programme demonstrated a 29.3% reduction in maternal mortality before and after its implementation in 12 districts in South Africa. Current clinical research is focusing on predicting and preventing stillbirths.

Dr. Pattinson also served as chairperson of WHO's trial Data Management Committee for Active Management of the Third Stage of Labour from 2008 until 2011. For this study he will oversee the collection of specimens from mother-infant pairs admitted to hospital during and after delivery, the abstraction of medical records and discharge summaries for birth and pregnancy outcomes, and support data analysis and manuscript development relating to adverse pregnancy and birth outcomes.

a. **Pattinson RC**, Hulsbergen MH, Van Hoorick L. The effect of maternal HIV infection on maternal conditions and perinatal deaths in southwest Tshwane. Facts Views Vis Obgyn 2010, 2(4): 227-31.

b. **Pattinson RC**, Kerber K, Waiswa P, Day LT, Mussell F, Asiruddin SK, Blencowe H, Lawn JE. Perinatal mortality audit: Counting, accountability and overcoming challenges in scaling up in low- and middle-income countries. Int J Gynaecol Obstet. 2009 Oct;107 Suppl 1:S113-21, S121-2. doi: 10.1016/j.ijgo.2009.07.011

c. South Africa Every Death Counts Writing Group, Bradshaw D, Chopra M, Kerber K, Lawn JE, Bamford L, Moodley J, **Pattinson R**, Patrick M, Stephen C, Velaphi S. Every death counts: use of mortality audit data for decision making to save the lives of mothers, babies and children in South Africa. Lancet. 2008 Apr 12;371(9620):1294-304. doi: 10.1016/S0140-6736(08)60564-4.

d. Lawn JE, Lee AC, Kinney M, Sibley L, Carlo WA, Paul VK, **Pattinson RC**, Darmstadt GL. Two million intrapartum stillbirths and neonatal deaths: where, why, and what can we do? Int J Gynaecol Obstet. 2009 Oct;107 Suppl 1:S5-18, S19. doi: 10.1016/j.ijgo.2009.07.016.

B. Positions and Honors

Positions and Employment

1981 – 1985 Clinical Assistant, Department Obstetrics & Gynecology, Stellenbosch University Tygerberg Hospital, Parawvallei, RSA
1985 – 1988 Consultant, Department Obstetrics & Gynecology, Stellenbosch University
1988 – 1991 Senior Consultant, Department Obstetrics & Gynecology, Stellenbosch University
1991 – 1992 Principal Consultant, Department Obstetrics & Gynecology, Kalafong Hospital and Pretoria University
1991 - Professor and Clinical Head, Department Obstetrics and Gynecology, Pretoria University and Chief Specialist, Kalafong Hospital
1997 - Director, Maternal and Infant Health Care Strategies Research Unit

Other Experiences and Professional Memberships

1992 – 1997 Ethics Committee of the University of Pretoria Medical School
1993 - School of Primary Health Care, University of Pretoria: member of the management board
1994 – 1996 Chairperson, Maternal and Child Health Care and Nutrition Task Group, Pretoria Region, Gauteng Provincial Administration
1995 – 1999 Member Academic Advisory Group to Dr C Marshall, Director Maternal and Child Health and Nutrition, Gauteng Provincial Administration
1995 – 2000 Executive Member Priorities in Perinatal Care Association,
1995 – 2001 Chairperson - “Pregnancy, neonatology and child growth and development” block for new curriculum, Faculty of Medicine, University of Pretoria,
1997-1999 Chairman: Maternal and Fetal Society of South Africa –
1997 - Member National Committee for Confidential Enquiries into Maternal Deaths and Editor or all reports
1999 - Member South African College of Medicine Committee (Obstetrics and Gyneacology)
2002 - Chairperson Priorities in Perinatal Care Association
2005 - Member the PhD Committee of the Faculty of Health Sciences, University of Pretoria
2008 - 2011 Chairperson of the WHO AMSTL trial Data Management Committee
2009 - Member of WHO Global Survey Steering Committee
2009 Chairperson of the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) – Facility Based Strategies & Constraints
2008 - Member of National Perinatal Morbidity and Mortality Committee (NaPeMMCo)
2008 - 2010 Brazilian Network for Surveillance of Severe Maternal Morbidity
2009 - Member of Maldives Steering Committee of Maternal and Perinatal Morbidity and Mortality Audit System
2009 Technical advisor – Zimbabwean Confidential Enquiry into Maternal Deaths
2009 - Member of the Programme Advisory Committee, DFID funded Zimbabwe Maternal and Newborn Health Programme
2006 Technical Advisor, WHO on Monitoring and Evaluation for Maternal and Newborn Health and Services at District Level
2007 - 2010 Member of WHO Working Group on Maternal Mortality and Morbidity classifications
2010 - Member of WHO Working Group on Perinatal Mortality and Morbidity classifications
2010 Member of Royal College Study Group on accelerating progress for reaching Millennium Goals 4 & 5
2009 - Member of the Essential Steps in Managing Obstetric Emergency (ESMOE) Board, South Africa

2009 - Lancet Working Group – Stillbirth series

Honors

1987 – 1988 South African Medical Research Council Post Graduate Bursary
1999 – 2002 Scientific Merit Award, University of Pretoria
2000 Certificate for Innovation in Education, University of Pretoria
2015 GSK Save the Children 2015 Health Care Innovation Award
2016 Havenga Medal from Suid Afrikaanse Wetenskap en Kuns for contribution to Health
2017 Exceptional Academic Achievement award, University of Pretoria
2017 Discovery Foundation Excellence award

1. C. Contributions to Science

Developing an international classification system for perinatal and maternal deaths: Part of the frustration of working in maternal and perinatal audit systems has been the multiple classification systems used to classify deaths. This has meant communication between countries and scientists was often confused. I was a member of the WHO ICD Maternal Mortality and the WHO ICD Perinatal Mortality working groups that developed standardized classification systems for maternal and perinatal deaths.

a. Allanson ER, Tunçalp Ö, Gardosi J, **Pattinson RC**, Francis A, Vogel JP, Erwich JJHM, Flenady VJ, Frøen JF, Neilson J, Quach A, Chou D, Mathai M, Say L, Gülmezoglu AM. The WHO application of ICD-10 to deaths during the perinatal period: ICD-PM: results from pilot database testing in South Africa and United Kingdom. BJOG 2016 Nov;123(12):2019-2028 doi: 10.1111/1471-0528.14244. PMID: 27527122

b. Say L, Souza JP, **Pattinson RC**. Maternal near miss towards a standard tool for monitoring quality of maternal health care. Best Pract Res Clin Obstet Gynaecol. 2009 Jun; 23(3): 287-296. doi: 10.1016/j.bpobgyn.2009.01.007. PMID: 19303368.

2. Identifying problems and developing solutions: Improving maternal and perinatal care can only be performed in one has clearly identified the problems. I have developed audit systems for South Africa and used the audit results to develop interventions and assess their impact. This has helped to develop implementation science.

a. Allanson ER and **Pattinson RC**. Quality-of-care audits and perinatal mortality in South Africa. Bull World Health Organ. 2015 Jun;93(6), pp.424-8. doi: 10.2471/BLT.14.144683. PMID: 26240464 PMCID: PMC4450707.

b. Allanson ER, Muller M, and **Pattinson RC**. Causes of perinatal mortality and associated maternal complications in a South African province: challenges in predicting poor outcomes. BMC Pregnancy and Childbirth. 2015 Feb 15;15:37. doi: 10.1186/s12884-015-0472-9. PMID: 25880128 PMCID: PMC4339432.

c. **Pattinson RC**, Makin JD, Say L, Bastos M. Critical incident audit and feedback to improve perinatal and maternal mortality and morbidity. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD002961 (update published in first edition 2011). PMID: 16235307 PMCID: PMC4171456.

d. De Knijf A, **Pattinson RC**. Confidential enquiries into quality of care of women in labour using Hypoxic Ischemic Encephalopathy as a marker. Facts Views Vis Obgyn. 2010;2(4):219-25. PMID: 25009710 PMCID: PMC4086007

3. Reducing stillbirths: Stillbirths are increasingly being recognized as an un-researched and under-appreciated area. I have been involved with research to bring this to the fore.

a. Frøen JF, Friberg IK, Lawn JE, Bhutta ZA, **Pattinson RC**, Allanson ER, Flenady V, McClure EM, Franco L, Goldenberg RL and Kinney MV. Stillbirths: progress and unfinished business. Lancet. 2016 Feb 6;387(10018):574-86. doi: 10.1016/S0140-6736(15)00818-1. PMID: 26794077.

b. Graham W, Wood S, Byass P, Filippi V, Gon G, Virgo S, Chou D, Hounton S, Lozano R, **Pattinson R** and Singh S. Diversity and divergence: the dynamic burden of poor maternal health. Lancet. 2016 Oct 29;388(10056):2164-2175. doi: 10.1016/S0140-6736(16)31533-1. PMID: 27642022.

c. Lawn JE, Blencowe H, **Pattinson R**, Cousens S, Kumar R, Ibiebele I, Gardosi J, Day L, Stanton C, for the Lancet Stillbirth Series steering team. Stillbirth - Where? When? Why? How to make the data count? Lancet. 2011 Apr 23;377(9775):1448-63. doi: 10.1016/S0140-6736(10)62187-3. PMID: 21496911

d. **Pattinson R**, Kerber K, Buchmann E, Friberg IK, Belizan M, Lansky S, Weissman E, Mathai M, Rudan I, Walker N, Lawn JE, for The Lancet's Stillbirths Series steering team. Stillbirths: how can health systems deliver for mothers and babies? Lancet. 2011 May 7;377(9777):1610-23. doi: 10.1016/S0140-6736(10)62306-9. PMID: 21496910.

4. Implementing strategies to reduce deaths: Identifying the problem is not enough and research into methods of implementation are critical. I have been involved with investigating this for some time.

a. Bergh, AM, Allanson E and **Pattinson RC**. 2015. What is needed for taking emergency obstetric and neonatal programmes to scale? Best Pract Res Clin Obstet Gynaecol. 2015 Nov;29(8):1017-27. doi: 10.1016/j.bpobgyn.2015.03.015. PMID: 25921973.

b. Bergh AM, Baloyi S and **Pattinson RC**. What is the impact of multi-professional emergency obstetric and neonatal care training? Best Pract Res Clin Obstet Gynaecol. 2015 Nov;29(8):1028-43. doi: 10.1016/j.bpobgyn.2015.03.017. PMID: 25937554.

c. Bergh A-M, Van Rooyen E, **Pattinson RC**. (2008). 'On-site' versus 'off-site' facilitation: a randomised trial of outreach strategies for scaling up kangaroo mother care. Human Resources for Health. 2008 Jul 23;6:13. No PMID.

d. Odendaal HJ**, Pattinson RC**, Bam R, Kotze TJ. Aggressive versus expectant management in women with severe preeclampsia between 28 and 34 weeks gestation: A randomized clinical trial. Obstet Gynecol 1990;76:1070-1075. No PMID.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

European Union 1/1/2015 – 12/31/2018
Title: Scale-up Essential Steps in Managing Obstetric Emergencies
Role: PI

SAMRC/CSIR SHIP 1/1/2015 – 12/31/2018
Title: The role of continuous wave ultrasound of the umbilical artery in predicting and preventing stillbirths
Role: PI

Recently Completed Research Support

Department for International Development (DFID) 1/1/2012 – 12/31/2016
Title: Scale-up Essential Steps in Managing Obstetric Emergencies
Role: PI

Centers for Disease Control U2GPS001053 1/1/2006 – 12/31/2014
Title: Use of Child Healthcare Problem Identification Program and Perinatal Problem Identification
Role: PI
Goal: Hospital-based child health care surveys using the Child Healthcare Problem Identification Programme (Child PIP) and the Perinatal Problem Identification Programme (PPIP) to monitor the impact of the prevention of mother to child transmission (PMTCT) of HIV and improve the quality of care of PMTCT delivery as well as overall quality of care

DFID 1/1/2012-12/31/2016
Title: Scale-up ESMOE and EOST
Role PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Koleka P Mlisana

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Associate Professor in Medical Microbiology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Natal	MB ChB	12/1986	Medicine
University of Natal	MMed Path(Microbiology	12/1993	Medical Microbiology
University of KwaZulu Natal	PhD	12/2014	Medical Microbiology

A: Personal Statement

Dr. Koleka P. Mlisana is a medical microbiologist and currently head the Department of Medical Microbiology at the University of KwaZulu Natal and the National Health Laboratory Service in Durban, South Africa, and leads NHLS's GeneXpert Working Committee. She has worked in HIV research at the Centre for the AIDS Programme of Research in South Africa (CAPRISA) for over 10 years, focusing on HIV-1 subtype C pathogenesis and prevention in young women as well as doing HIV vaccine trials in KwaZulu Natal. Her work included looking at the impact of sexually transmitted infections (STIs) and genital tract inflammation on HIV-1 acquisition and rate of disease progression in subtype C infected women wherein similar levels of inflammation were shown in both symptomatic and asymptomatic STIs resulting in increased risk of HIV acquisition.

In the past 5 years, Dr. Mlisana's research focus has broadened to general microbiology, specifically TB diagnostics and drug resistance as well as establishing a molecular diagnostic platform for STIs. She is the UKZN representative and investigator on the DST-NRF Centre of Excellence in HIV Prevention grant in South Africa providing STI laboratory diagnosis and research for the programme. She is also the principal investigator for an NHLS Trust funded grant exploring rapid diagnostic methods in TB meningitis. Her group is also working on laboratory detection of rifampicin low level resistance in MTB using both phenotypic and genotypic techniques.

Dr. Mlisana has worked with Dr Neel Gandhi as the South African PI on his NIH funded study determining clinical outcomes in patients concurrently treated for MDR TB and HIV and a co-investigator in the study examining the transmission dynamics of XDR TB.

For this project, Dr Mlisana will provide expert support for the implementation and operations of the GeneXpert diagnostic platform in all study clinics, ensure access to and abstraction of additional ANC and HIV-related laboratory test results from NHLS's laboratory information system, and facilitate data collection.

a. Shah NS, Auld SC, Brust JCM, Mathema B, Ismail N, Moodley P, **Mlisana K,** Allana S, Campbell A, Mthiyane T, Morris N, Mpangase P, van der Meulen H, Omar SV, Brown TS, Narechania A, Shaskina E, Kapwata T, Kreiswirth B, Gandhi NR. Transmission of Extensively Drug-resistant Tuberculosis in South Africa. N Engl J Med. 2017 Jan 19;376(3):243-253. doi: 10.1056/NEJMoa1604544. PMCID: PMC5330208.

b. Desjardins CA, Cohen KA, Munsamy V, Abeel T, Maharaj K, Walker BJ, Shea TP, Almeida DV, Manson AL, Salazar A, Padayatchi N, O'Donnell MR, **Mlisana KP,** Wortman J, Birren BW, Grosset J, Earl AM, Pym AS. Genomic and functional analyses of Mycobacterium tuberculosis strains implicate ald in D-cycloserine resistance. Nat Genet. 2016 May;48(5):544-51. doi: 10.1038/ng.3548. PMCID: PMC4848111.

c. Cohen KA, Abeel, T, McGuire AM, Desjardins CA, Munsamy V, Shea TP, Walker BJ, Bantubani N, Almeida DV, Alvarado L, Chapman SB, Mvelase NR, Duffy EY, Fitzgerald MG, Govender P, Gujja S, Hamilton S, Howarth C, Larimer JD, Maharaj K, Pearson MD, Priest ME, Zeng Q, Padayatchi N, Grosset J, Young SK, Wortman J, **Mlisana KP,** O'Donnell MR, Birren BW, Bishai WR, Pym AS and Earl AM. Evolution of Extensively Drug-Resistant Tuberculosis over Four Decades: Whole Genome Sequencing and Dating Analysis of Mycobacterium tuberculosis Isolates from KwaZulu-Natal. PLoS Med. 2015 Sep 29;12(9):e1001880. doi: 10.1371/journal.pmed.1001880.PLoS Med 12, no. 9 (2015): e1001880. PMCID: PMC4587932.

d. Niehaus AJ, **Mlisana, K**, Gandhi NR, Mathema B, and Brust JCM. High Prevalence of inh A Promoter Mutations among Patients with Drug-Resistant Tuberculosis in KwaZulu-Natal, South Africa. PLoS One. 2015 Sep 2;10(9):e0135003. doi: 10.1371/journal.pone.0135003. PMCID: PMC4557915.

B. Positions and Honors

Positions & Employment:

1987	Intern, King Edward VIII Hospital, Durban, SA
1988	Medical Officer, Paediatrics Department at King Edward Hospital
1898 - 1993	Registrar in training, Department of Medical Microbiology, KEH VIII
1994 - 1995	Specialist Lecturer, Univ of Natal Medical School, Dept of Microbiology, Durban
1995 - 2002	Private pathology practice as a Microbiologist at Drs N.L. Pillay, Mackintosh & Partners Laboratory, now Lancet Laboratories.
2003 – 2009	Project Director, Centre for the AIDS Programme of Research in South Africa (CAPRISA)
2006 – 2009	Site Principal Investigator for South African AAIDS Vaccine Initiativ (SAAVI)
2007	National representative Principal Investigator for HIV Vaccine trial PAVE 100, HVTN
2007 – 2009	Head: CAPRISA HIV Vaccine Unit
2009 – 2011	Head: CAPRISA Pathogenesis and HIV Vaccine Programme
Sep 2011 – to date	Head: Department of Medical Microbiology, NHLS & UKZN

Committee appointments:

2003	Scientific Committee - Co-ordinator for the HIV track: International Chemotherapy Congress
2007 – 2008	Member of the HVTN Efficacy Trials Design Working Group (ETDWG)
2007	Co-Chair of Basic and Clinical Sciences Track for SA AIDS 2007 Conference
2008	Co-Chair of the international AIDS Vaccine 2008 Conference
2008 – 2010	Member of the SA Medical Research Council Board Committee
2011 – 2015	Member of National Advisory Group on Immunisation Committee
2012 – 2014	Member of National Health Laboratory Service (NHLS) Board
2013	Conference Chair of the 6th SA AIDS 2013 Conference
2015 – present	Member of the Board of Trustees for South African National AIDS Council (SANAC)
2016	Co-chair of the Scientific Programme Committee for AIDS 2016 Conference
2016 – 2018	Member of the Ministerial Advisory Committee on Antimicrobial Resistance
Current	Protocol co-Chair of HVTN086/SAAVI103 Trial

Professional Memberships:

Health Professions Council of South Africa
South African Medical Association
Southern African HIV/AIDS Clinician's Society
Infectious Disease Society of South Africa
South African Society for Clinical Microbiologists

Honors:

2006 – 2007	Member of the Women's Global Health Scholars' Program, Fogarty International Center and Office of Women's Health, National Institutes of Health
2008 – 2009	International Advisory Board member of the University of Rochester Centre for AIDS Research (CFAR)

C. Contributions to Science

1. Drug resistant TB in South Africa: Some of our preliminary work has been to define the prevalence of both rifampicin and isoniazid resistance in the KZN province which is known to have the highest prevalence of MDR-TB in SA. With the recent roll-out of GeneXpert for diagnosis of TB in the country, it is critical to establish the prevalence of Rif monoresistance as Rif resistance is used as a surrogate for MDR-TB.

    a. Allana S, Shashkina E, Mathema B, Bablishvili N, Tukvadze N, Shah NS, Kempker RR, Blumberg HM, Moodley P**, Mlisana K**, Brust JC. pncA Gene Mutations Associated with Pyrazinamide Resistance in Drug-Resistant Tuberculosis, South Africa and Georgia. Emerging Infectious Diseases. Emerg Infect Dis. 2017 Mar;23(3):491-495. doi: 10.3201/eid2303.161034. PMCID: PMC5382742.

    b. O'Donnell MR, Pillay M, Pillay M, Werner L, Master I, Wolf A, Mathema B, Coovadia Y, **Mlisana K,** Horsburgh R, and Padayatchi N. Primary capreomycin resistance is common, and associated with early mortality in extensively drug-resistant tuberculosis (XDR-TB) patients in KwaZulu-Natal, South Africa. J Acquir Immune Defic Syndr. 2015 Aug 15;69(5):536-43. doi: 10.1097/QAI.0000000000000650. PMCID: PMC4501864.

    c. Dlamini-Mvelase NR, Werner L, Phili R, Cele LP, and **Mlisana, KP.** Effects of introducing Xpert MTB/RIF test on multi-drug resistant tuberculosis diagnosis in KwaZulu-Natal South Africa. BMC Infect Dis. 2014 Aug 16;14:442. doi: 10.1186/1471-2334-14-442. PMCID: PMC4141089.

    d. Coovadia YM, Mahomed S, Pillay M, Werner L, and **Mlisana, K.** Rifampicin mono-resistance in Mycobacterium tuberculosis in KwaZulu-Natal, South Africa: a significant phenomenon in a high prevalence TB-HIV region. PLoS One. 2013 Nov 6;8(11):e77712. doi: 10.1371/journal.pone.0077712. PMCID: PMC3819362.

2. The role of transmission in the spread of Drug-Resistant TB and the evolution of MDR-TB in South Africa: The development of drug resistant TB has always been thought to be as a result of poor or non-adherence to anti-TB treatment in patients with susceptible TB. The increase in patients diagnosed with MDR-TB without a previous history of TB challenged this dogma. As a result, we participated in a study that attempted to determine and quantify the role of transmission of MDR-TB in patients with no prior exposure to TB in the province of KwaZulu Natal in South Africa. Using whole genome sequencing, in collaboration with other researchers, we defined the evolution of XDR-TB over four decades showing isoniazid resistance as overwhelmingly the initial resistance mutation to be acquired.

    a. Shah NS, Auld SC, Brust JC, Mathema B, Ismail N, Moodley P, **Mlisana K**, Allana S, Campbell A, Mthiyane T, Morris N. Transmission of Extensively Drug-Resistant Tuberculosis in South Africa. N Engl J Med. 2017 Jan 19;376(3):243-253. doi: 10.1056/NEJMoa1604544. PMCID: PMC5330208.

    b. Cohen KA, Abeel T, McGuire AM, Desjardins CA, Munsamy V, Shea TP, Walker BJ, Bantubani N, Almeida DV, Alvarado L, Chapman SB, Mvelase NR, Duffy EY, Fitzgerald MG, Govender P, Gujja S, Hamilton S, Howarth C, Larimer JD, Maharaj K, Pearson MD, Priest ME, Zeng Q, Padayatchi N, Grosset J, Young SK, Wortman J, **Mlisana KP**, O'Donnell MR, Birren BW, Bishai WR, Pym AS and Earl AM. Evolution of Extensively Drug-Resistant Tuberculosis over Four Decades: Whole Genome Sequencing and Dating Analysis of Mycobacterium tuberculosis Isolates from KwaZulu-Natal. PLoS Med. 2015 Sep 29;12(9):e1001880. doi: 10.1371/journal.pmed.1001880. PMCID: PMC4587932.

    c. Lim JR, Gandhi NR, Mthiyane T, **Mlisana K**, Moodley J, Jaglal P, Ramdin N, Brust JC, Ismail N, Rustomjee R, Shah NS. Incidence and Geographic Distribution of Extensively Drug-Resistant Tuberculosis in KwaZulu-Natal Province, South Africa. PLoS One. 2015 Jul 6;10(7):e0132076. doi: 10.1371/journal.pone.0132076. PMCID: PMC4493033.

3. Impact of STIs and Genital inflammation on HIV-1 acquisition and rate of disease progression:
Management of STIs for most inadequately resourced countries continues to be syndromic despite the high prevalence asymptomatic infections. We assessed the adequacy of syndromic diagnosis of STIs and evaluated the association between STI diagnosis and the risk of HIV acquisition in high risk women in SA. Establishing an acute HIV infected cohort also allowed us to investigate rates of HIV disease progression in this community.

    a. Masson L, Salkinder AL, Olivier AJ, McKinnon LR, Gamieldien H, **Mlisana K**, Scriba TJ, Lewis DA, Little F, Jaspan HB, Ronacher K. Relationship between female genital tract infections, mucosal interleukin-17 production and local T helper type 17 cells. Immunology. 2015 Dec;146(4):557-67. doi: 10.1111/imm.12527. PMCID: PMC4693890.

    b. **Mlisana K,** Werner L, Garrett NJ, McKinnon LR, van Loggerenberg F, Passmore JS, Gray CM, Morris L, Williamson C, and Abdool Karim SS. Rapid disease progression in HIV-1 subtype C infected South African women. Clin Infect Dis. 2014 Nov 1;59(9):1322-31. doi: 10.1093/cid/ciu573. PMCID: PMC4271037.

    c. **Mlisana K,** Sobieszczyk M, Werner L, Feinstein A, van Loggerenberg F, Naicker N, Williamson C, and Garrett N. Challenges of Diagnosing Acute HIV-1 Subtype C Infection in African Women: Performance of a Clinical Algorithm and the Need for Point-of-Care Nucleic-Acid Based Testing. PLoS One. 2013 Apr 30;8(4):e62928. doi: 10.1371/journal.pone.0062928. PMCID: PMC3639937.

    d. **Mlisana K**, Naicker N, Werner L, Roberts L, van Loggerenberg F, Baxter C, Passmore JS, Grobler AC, Sturm AW, Williamson C, Ronacher K, Walzl G, Abdool Karim SS. Symptomatic vaginal discharge is a poor predictor of sexually transmitted infections and genital tract inflammation in high-risk women in South Africa**.** J Infect Dis. 2012 Jul 1;206(1):6-14. doi: 10.1093/infdis/jis298. PMCID: PMC3490689.

Complete list of published work:
http://www.ncbi.nlm.nih.gov/sites/myncbi/koleka.mlisana.1/bibliography/45099467/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

Active Research Support:

DST-NRF Centre of Excellence in HIV Prevention
UID 96354 **PI: Salim Abdool Karim** 03/01/2015 – 02/28/2020
University of KwaZulu Natal: Subcontract co-investigator
Title: Laboratory diagnosis and susceptibility testing of sexually transmitted pathogens.
Role: **UKZN Investigator**

Completed Research Support:

NHLS Research Trust
National Health Laboratory Service: **PI: Koleka Mlisana** 03/01/2015 – 02/28/2017
Title: Rapid Diagnosis of Tuberculous Meningitis: Detection of Tuberculostearic acid in Cerebrospinal Fluid.
Goal: To determine various diagnostic techniques (phenotypic and genotypic) for TBM as well as to develop and optimize a method for the detection of tuberculostearic acid for diagnosing TB meningitis.
Role: **Principal Investigator**

1R01AI089349 – 01 **PI: Gandhi** 4/1/2010 – 06/30/2016
NIH/NIAID R01 grant
Title: Transmission of HIV-associated XDR TB in Rural South Africa.
Goal: The goal of this study is to determine the proportion of XDR TB cases which arise from transmission and to identify locations and networks where transmission is occurring.
Role: **co- Investigator**

1R01AI087465 - 01A1 **PI: Gandhi** 07/01/2010 – 06/30/2016
NIH/NIAID R01 grant
Title: Impact of HIV, Antiretroviral Therapy and TB Genotype on Survival in MDR TB.
Goal: The goal of this study is to examine the impact of concurrent treatment of MDR TB and HIV on survival, treatment outcomes, adverse events and adherence in co-infected patients.
Role: **UKZN Principal Investigator**

Einstein Global Health Center pilot grant **PI: Brust** 03/01/2013–02/28/2015
Title: Prevalence of inhA Promoter Mutations in Patients with Drug-Resistant TB in KwaZulu-Natal, South Africa
Goal: The goal of this study is to determine the proportion of drug-resistant TB cases which are due to *inhA* promoter mutations in Kwa-Zulu Natal province, South Africa
Role: **UKZN co-Investigator**

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)	
Section A, Senior/Key Person		**236,803.00**
Section B, Other Personnel		**1,069,339.00**
Total Number Other Personnel	86	
Total Salary, Wages and Fringe Benefits (A+B)		**1,306,142.00**
Section C, Equipment		**11,538.00**
Section D, Travel		**66,180.00**
1. Domestic		
2. Foreign	66,180.00	
Section E, Participant/Trainee Support Costs		**57,376.00**
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence	40,424.00	
5. Other	16,952.00	
6. Number of Participants/Trainees		
Section F, Other Direct Costs		**440,477.00**
1. Materials and Supplies	263,251.00	
2. Publication Costs	34,000.00	
3. Consultant Services	129,714.00	
4. ADP/Computer Services		
5. Subawards/Consortium/Contractual Costs		
6. Equipment or Facility Rental/User Fees		
7. Alterations and Renovations	6,154.00	
8. Other 1	7,198.00	
9. Other 2	160.00	
10. Other 3		
Section G, Direct Costs (A thru F)		**1,881,713.00**
Section H, Indirect Costs		**149,614.00**
Section I, Total Direct and Indirect Costs (G + H)		**2,031,327.00**
Section J, Fee		

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1. Human Subjects Section

Clinical Trial?	[X] Yes	[ ] No
*Agency-Defined Phase III Clinical Trial?	[ ] Yes	[X] No

2. Vertebrate Animals Section

Are vertebrate animals euthanized?	[ ] Yes	[ ] No
If "Yes" to euthanasia Is method consistent with American Veterinary Medical Association (AVMA) guidelines?	[ ] Yes	[ ] No
If "No" to AVMA guidelines, describe method and provide scientific justification		

3. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

[ ] Yes [X] No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount ($)	*Source(s)

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4. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ☐ Yes ☒ No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://stemcells.nih.gov/research/registry/. Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

Cell Line(s): ☐ Specific stem cell line cannot be referenced at this time. One from the registry will be used.

5. Inventions and Patents Section (RENEWAL)

*Inventions and Patents: ☐ Yes ☐ No

If the answer is "Yes" then please answer the following:

*Previously reported: ☐ Yes ☐ No

6. Change of Investigator / Change of Institution Section

☐ Change of Project Director / Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

☐ Change of Grantee Institution

*Name of former institution:

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 10/31/2018

Introduction	
1. Introduction to Application (Resubmission and Revision)	
Research Plan Section	
2. Specific Aims	Specific_Aims1047970068.pdf
3. Research Strategy*	Research_Strategy1047970069.pdf
4. Progress Report Publication List	
Human Subjects Section	
5. Protection of Human Subjects	Human_Subjects_rev1047970070.pdf
6. Data Safety Monitoring Plan	DSMP_rev1047970071.pdf
7. Inclusion of Women and Minorities	Inclusion_of_Women_and_Minorities1047818687.pdf
8. Inclusion of Children	Inclusion_of_Children1047818688.pdf
Other Research Plan Section	
9. Vertebrate Animals	
10. Select Agent Research	
11. Multiple PD/PI Leadership Plan	Multi_PI_Plan1047818690.pdf
12. Consortium/Contractual Arrangements	Consortium_Agreement_rev1047970809.pdf
13. Letters of Support	Letters_of_support1047818682.pdf
14. Resource Sharing Plan(s)	Resource_sharing_plan1047818689.pdf
15. Authentication of Key Biological and/or Chemical Resources	Authentication_of_key_resources1047818692.pdf
Appendix	
16. Appendix	

SPECIFIC AIMS

In 2012, WHO estimated that over 350 million cases of *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV) occurred globally.[1] Sexually transmitted infections (STIs) 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.[2–13] STIs are common in pregnant women globally, but often go undiagnosed;[14–18] to address those concerns, we conducted a pilot study integrating molecular diagnostic testing for CT, NG and TV into **antenatal care (ANC)** services for HIV-infected pregnant women in South Africa. We found that diagnostic screening and **targeted treatment (TT)** during ANC was highly acceptable and feasible;[19] 97.8% of all eligible women agreed to be tested, and >93% with an STI received same-day treatment. We found a 41% STI prevalence, of which 65% of infections were asymptomatic.[19] Furthermore, our intervention decreased the prevalence of STIs at time-of-delivery by >50% compared to women receiving syndromic management (standard of care).

Though acceptable, feasible and effective, our current intervention design may have limitations. First, we found a 9.1% cumulative incidence of STIs between first ANC and delivery, suggesting a single point-in-time diagnostic screening + TT with **test of cure (ToC)** follow-up may not optimally decrease STIs at time of delivery. Consequently, *evaluating the impact and cost effectiveness of different diagnostic screening strategies that decrease the burden of STIs during pregnancy and at time-of-delivery is urgently needed.* Second, we found a 37% STI positivity at ToC. Participant interviews suggest that poor medication adherence and re-infection cannot explain the high post-treatment persistent positivity. Consequently, *biological factors that increase the risk for STI persistence and/or treatment failures must be further investigated.*

Research suggests the vaginal microbiome plays a critical role in STI acquisition, persistence, and treatment outcomes. Vaginal **community state types (CST)** with different concentrations of *Lactobacillus (L.)* spp. are associated with increased risk of acquiring STIs.[20–24] *In vitro* studies revealed that certain vaginal bacteria can inactivate metronidazole,[25–27] standard TV treatment, and bacterial vaginosis (CST-4) influenced TV treatment outcomes in HIV-infected women.[28] Vaginal microbiomes dominated by *L. crispatus*, *L. gasseri* and *L. vaginalis* may inhibit CT elementary bodies, while *L. iners may* increase the risk and duration of CT infection.[22,29,30]

In response to the need to 1) identify cost-effective screening strategies that optimally decrease the burden of STIs during pregnancy, and reduce adverse pregnancy and infant outcomes, 2) elucidate the role of the vaginal microbiome in treatment outcomes, and 3) inform STI screening and treatment guidelines in other low-middle income countries, we propose a novel, highly innovative study with the following three Specific Aims:

Aim 1: Evaluate different diagnostic screening interventions to decrease the burden of CT/NG/TV, and reduce adverse pregnancy and birth outcomes among pregnant women. Hypothesis 1 (H1): Compared to syndromic management, diagnostic screening with TT will significantly reduce adverse pregnancy/birth outcomes and decrease prevalent STIs at time of delivery. H2: Compared to single, point-in-time screening at 1st ANC with TT and ToC, periodic repeated diagnostic screening will decrease incident STIs at time of delivery. Approach: A hybrid type 1 effectiveness-implementation design three-arm randomized controlled trial will be conducted; Arm 1) diagnostic screening + TT at first ANC, with ToC follow-up; Arm 2) periodic diagnostic screening throughout ANC with TT, no ToC follow-up; Arm 3) syndromic management (standard of care). Prevalence and incidence of STIs at time of delivery, and frequency and type of adverse pregnancy/birth outcomes per intervention arm will be assessed.

Aim 2: Evaluate cost per pregnant woman diagnostically screened and treated, cost of adverse pregnancy and birth outcomes, and cost-effectiveness per STI and DALY averted. H1: Compared to syndromic management, diagnostic STI screening + TT will cost-effectively avert STIs at time of delivery, and reduce adverse pregnancy and birth outcomes. Approach: We will estimate the costs of alternative STI screening interventions relative to standard practice as well as the costs of managing adverse pregnancy/birth outcomes. Decision analytic modeling will estimate the cost-effectiveness per STI and DALY averted.

Aim 3. Investigate the relationship between the vaginal microbiome and CT treatment failure in pregnant women. H1: Chlamydia-infected pregnant women with BV-associated vaginal microbiota CSTs will be significantly more likely to have clinical treatment failure as identified at ToC. Approach: We will conduct a nested case-control (1:2) study using vaginal specimens collected from CT-infected women at first ANC, 1 and 2 weeks post-treatment and then at ToC (3 weeks post-treatment).

Our proposed 5-year study will enroll 1250 HIV-infected and 1250 HIV-uninfected pregnant women from three large ANC clinics in Tshwane District (ANC HIV positivity= 23.4%[31]), South Africa. 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.

SIGNIFICANCE

HIV and STIs among pregnant women in South Africa are a major problem. In 2013, the South African government estimated that 29.7% of women seeking antenatal care (ANC) were HIV-infected,[31] a prevalence that has remained relatively stable since 2007. That high HIV prevalence is compounded by high rates of STIs in women of reproductive age.[32–34] Our current study using molecular diagnostic tests found 40.5% of HIV-infected pregnant women presenting for their first ANC clinic visit were infected with CT, NG and/or TV; >60% were asymptomatic (Table 1).[19] Given that most STIs in women are asymptomatic and that the South African government currently only recommends symptomatic screening and syndromic management in line with WHOs global guidelines, the majority of STIs in HIV+ South African pregnant women go undiagnosed and untreated.

Table 1: Prevalence of *Chlamydia trachomatis (CT)*, *Neisseria gonorrhoeae (NG)* and *Trichomonas vaginalis (TV)* among HIV-Infected pregnant women in three healthcare facilities in Tshwane District, South Africa (N=430)

	n	%	95% CI	% Asymptomatic
Any STI (CT/NG/TV)	174	40.5%	36.1% - 45.5%	64.9%
Any CT infection	127	29.6%	25.4% - 34.2%	62.6%
Any NG infection	24	5.6%	3.9% - 8.5%	50.0%
Any TV infection	86	20.0%	16.7% - 24.5%	53.6%

STIs are associated with adverse birth outcomes and mother-to-child-transmission (MTCT) of HIV. Untreated CT, NG and TV infections during pregnancy are associated with intrauterine growth retardation, low birth weight (LBW), preterm delivery, and premature rapture of membranes.[35–45] Infants in South Africa routinely receive chloramphenicol eye ointment at birth to prevent neonatal bacterial conjunctivitis, most often caused by untreated maternal CT or NG infection.[46] Yet the risks to infants born to HIV-infected mothers are greater than conjunctivitis. A study of HIV-infected women in Tanzania found that NG co-infection increased intrauterine HIV transmission by >450%.[2] Our recent analysis in a NICHD HPTN 040 sub-study demonstrated that CT/NG infection increased HIV MTCT by 160% (RR=2.6, 1.1 – 5.8).[9] Prior research in non-pregnant women suggests that STIs in HIV-infected women may augment the risk of HIV transmission by increasing localized inflammatory responses and viral shedding; [47–56] subsequent treatment of those STIs reduced the risk of HIV transmission.[57,58] Our own study in South Africa has recorded 34.8% (of 607) with adverse birth outcomes including 17.8% with preterm delivery, 14.8% low birth weight and 4.8% stillbirth.

Current WHO STI screening recommendations, especially during pregnancy, leave a large burden of disease undetected and untreated. WHO recommends syndromic management of STIs in resource-limited settings due to its low cost and unavailability of appropriate laboratory infrastructure.[59,60] Syndromic management involves the provision of treatment for STIs based on an algorithm of common signs and symptoms. Given that most STIs are asymptomatic, as shown by our current research (Table 1) and that of others, the majority of STIs go untreated in settings where syndromic management is used.[19,61,62] Two major limitations of the syndromic approach is the non-determination of infectious etiologies and the limited specificity, especially during pregnancy, of the "symptoms" algorithm, both of which lead to inappropriate treatment or over-treatment.[62,63] Diagnosis of CT, NG, and TV has traditionally relied on culture and microscopy, and even when highly sensitive PCR assays became available, dedicated laboratory infrastructure and trained laboratory personnel were required.[64–66] However, with the advent of new PCR based 'near-patient' or **'point-of-care' (PoC)** technology for the diagnosis of STIs,[67,68] implementation of diagnostic screening in variety of clinical settings is now possible.[19,69–73] Despite this, optimal models for PoC testing, especially during pregnancy, have not been identified. This is highlighted by our recent work integrating PoC diagnostic screening for CT, NG and TV into ANC services for HIV-infected women in South Africa. Specifically, while single PoC diagnostic screening and targeted treatment with **Test of Cure (ToC)** follow-up decreased the prevalence of STIs at time of delivery by >50% compared to syndromic management, incident infections were not identified or treated, leaving many women with STIs at time of delivery.

South African and international decision-makers require data on the cost and cost-effectiveness of STI screening and treatment programs. The South African *National Strategic Plan for HIV, TB and STIs 2017-2022*[74] includes recommendations for the detection and treatment of STIs, including through PoC testing. However, to date, the South African government has not undertaken any efforts to identify any diagnostic platforms or testing algorithm. While some efforts are underway to plan for those interventions, to date, no South African study exists to inform those costing and budgeting efforts. Estimates from our proposed study can also inform policy decisions in other low-middle income countries, as well as WHO recommendations for the management of STIs during pregnancy. Ultimately, developing, evaluating and costing STI PoC testing algorithms, especially those implemented during antenatal care, is urgently needed.

Risk factors associated with STI treatment failure must be better understood. Given the increased risks of adverse outcomes from STIs during pregnancy, it is imperative that infections are cleared following treatment. This is especially important amongst HIV-infected pregnant women, where STIs may increase the risk of MTCT of HIV. As part of our recent STI study aimed at integrating molecular diagnostic screening for CT, NG and TV into ANC services, we performed repeat ToCs until a participant cleared their infection, or had a document birth outcome. At ToC1, we identified a 37% persistent positivity; a number of women required multiple rounds of ToC and treatment before clearing their infection (Table 2). Interviews with women at ToC visits suggest that behaviors associated with poor treatment adherence or re-exposure from untreated partners cannot explain the high persistent positivity with CT or TV. For those with a positive TV test following treatment, evidence is mounting that clinical treatment failure, rather than organism-specific metronidazole resistance or reinfection, is likely.[28,75,76] Gatski *et al.*[28] revealed that in HIV+/TV+ women, BV was significantly associated with metronidazole treatment failure, suggesting that a vaginal environment associated with BV decreased the efficacy of metronidazole. This hypothesis is supported by *in vitro* studies that have shown that metronidazole can be inactivated by bacteria present in the vaginal microbiome.[25–27] Repeat CT positivity following treatment are not well understood; organism-related resistance is infrequently documented.[77] Reports have suggested that heterotypic resistance associated with high organism loads may factor in treatment failures, however, no solid evidence has been reported.[77–80] Given that multiple rounds of ToC and treatment are not a financially viable intervention to identify treatment failures, especially in resource constrained settings, understanding the biological mechanisms that contribute to treatment failures is an urgent priority.

Table 2. High frequency of persistent STI positivity following standard treatment at Test-of-Cure (ToC)

	ToC 1	ToC 2	ToC 3
Any STI	31.2%	12%	7%
CT	26.5%	7.9%	2.4%
NG	6.3%	0%	--
TV	19.1%	5.8%	4.7%

Vaginal microbiota may play an important role in STI treatment outcomes. Epidemiological studies have demonstrated that BV is associated with an increased risk of acquiring and transmitting HIV and STIs.[81–89] Culture-independent studies of vaginal bacterial communities have revealed that BV is highly associated with vaginal community state types (CSTs) that are deficient in *Lactobacillus* spp., especially *Lactobacillus (L.) crispatus*,[20,90–92] and that these CSTs are associated with STIs such as CT and TV.[22,23,29] Furthermore, vaginal CSTs deficient in *Lactobacillus* spp. have been associated with increased risk of HIV acquisition,[21,24,93] while *L. crispatus*, specifically, is protective against HIV.[94] A recent study found that vaginal microbiota play an important role in modulating Tenofovir microbicide efficacy.[24] In that study, metabolism by *G. vaginalis* and other BV-associated bacteria led to Tenofovir depletion, decreasing the protection of pre-exposure prophylaxis (PrEP) and increasing the risk of acquiring HIV, regardless of medication adherence. Other work has shown Metronidazole treatment for TV to be inactivated by certain bacteria in the vaginal microbiome.[25–27] However, there are little data on the role of the vaginal microbiota on CT treatment outcomes in women.

Vaginal microbiota may play an important role in genital CT infections.[95–97] Women with CT are more likely to have vaginal microbiota dominated by *L. iners* or diverse anaerobic bacteria.[22] In addition, risk of genital CT increases during BV episodes.[98] Interferon-gamma (IFN-γ), a host pro-inflammatory cytokine known for its anti-chlamydial properties, is an important part of the host immune response to genital CT infection. IFN-γ activates indoleamine 2,3-dioxygenase in host epithelial cells, which then catabolizes L-tryptophan into N-formylkynurenine. When that happens, the host cell's pool of tryptophan is depleted, which may result in CT eradication by tryptophan starvation. *In vitro*, genital CT strains have been found to rescue themselves by producing tryptophan from indole using a tryptophan synthase gene when indole is present in the local environment.[96] Indole-producing bacteria (e.g., *Prevotella* spp,[96] *Fusobacterium nucleatum*, *Propionibacterium acnes, Porphyromonas gingivalis, Escherichia coli*, and *Enterococcus faecalis*) present in altered vaginal microbiota may contribute to genital CT survival by providing a source of indole. It is currently unknown if treatment for genital CT is inactivated by certain bacteria, or if the presence of indole producing bacteria in an altered vaginal microbiome increase the risk for poor treatment outcomes. Consequently, additional research on the role of the vaginal microbiome in genital CT treatment outcomes is urgently needed, particularly in pregnant women where the adverse effects of CT infection are substantial.

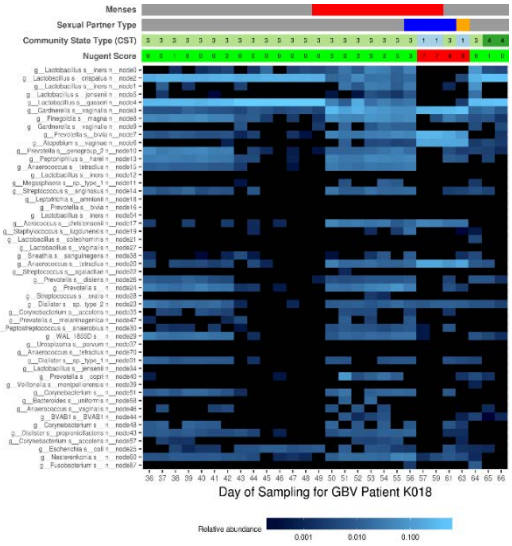
INNOVATION

1) Use of a hybrid type 1 effectiveness-implementation study design to decrease STIs and adverse birth outcomes at time of delivery: A major issue in health care is the relatively slow speed at which promising interventions, supported by rigorous research evidence, move into clinical practice. One way to 'speed up' the traditional step-wise progression from a clinical effectiveness trial to implementation science trial is to simultaneously combine the collection of effectiveness and implementation relevant data. Towards this end, we will conduct a hybrid type 1 effectiveness-implementation design study.[103] Our hybrid type 1 design allows for

the primary focus to be on collecting data on the effectiveness of our intervention, while also allowing us to incorporate process evaluation methods into our effectiveness randomized controlled trial. This will help us to explain our effectiveness results and efficiently inform future implementation efforts. Ultimately, should our intervention(s) effectively reduce the burden of STIs during pregnancy and adverse pregnancy and birth outcomes, we will be able to better inform the development of future intervention strategies.

2) Investigating clinical- and cost-effectiveness of routine CT/NG/TV testing of pregnant women: Our study will enhance knowledge of STIs during pregnancy, especially among high HIV prevalence populations, and the effectiveness of routinizing same-day PCR screening and treatment for these STIs in reducing adverse pregnancy and birth outcomes. Furthermore, until now there have been no studies in low and middle-income countries that have evaluated the costs and benefits of CT/NG/TV screening and treatment during pregnancy as it relates to pregnancy, neonatal and infant outcomes. Our cost/cost-effectiveness study has the potential to influence health policy in South Africa and globally, especially as it compares to syndromic management of STIs during pregnancy. If successful, this study would also provide reproducible cost-effectiveness analysis models for countries to better plan for and implement routine CT/NG screening and treatment in pregnancy.

Figure 1: Heatmap of incident BV case K018. Meta-data includes presence of menses (red), partner gender (gray=female, blue=male, orange= unknown), Nugent score, and CST.



3) Prospectively investigating associations between the vaginal microbiome and antibiotic treatment outcomes for STIs: CT and TV treatment failures not associated with poor medication adherence or drug resistance have been reported. [28,75,78,99–101] Studies have hinted at a role for the vagina microbiome in STI treatment failures, yet to our knowledge, none have investigated the vaginal microbiome and treatment failures in a prospective manner. As part of our study, we will longitudinally collect vaginal specimens from both HIV-infected and un-infected participants 1) before, during and after antibiotic treatment for STIs, and 2) from those with successfully treatment outcomes and treatment failures. These specimens will allow us to investigate the potential impact that the vaginal microbiome may play in STI persistence, with a focus on treatment failures.

4) Vaginal microbiome data analysis approach: We have developed methods to visualize changes in vaginal microbiota over time, including methods to display microbiome changes via heatmaps and analysis of changes in CSTs over time (manuscript in submission; Figure 1). Another innovative aspect of our analytic methods will be the use of the PECAN classifier, developed in Jacques Ravel's lab (U Maryland). PECAN uses a specialized vaginal microbiota database for accurate classification of vaginal microbiome components down to species level.[102] By using PECAN in tandem with the DADA2 processing pipeline, we are able to interrogate common bacteria sequence variants.

APPROACH

Study Setting: This study will take place in Tshwane District, South Africa. Study participant recruitment will be conducted in three large ANC clinics (Table 3; Figure 2 on next page). Clinics are located in the referral zone of two **maternal obstetric units (MOUs)**; Kalafong Hospital and Laudium Community Health Centre. Together, the three clinics see ~442 pregnant women each monthly attending a first ANC visit. Research staff embedded within the Kalafong and Laudium MOUs will collect birth outcomes. Study clinics are proximal to, and provide care for persons living in informal settlements and lower socio-economic status communities (Figure 2 pink shapes). Key ANC indicators for the three study clinics are shown in Table 3.

Facility Name	Annual ANC 1st visit headcount	Average Monthly 1st ANC Head Count	Annual ANC HIV Prevalence	HIV diagnosis at 1st ANC (Annual)
Laudium CHC	2853	238	23.3% (665)	403 (60.7%)
Olievenhout Clinic	1125	94	24.7% (278)	131 (47.1%)
Phomolong Clinic	1323	110	23.1% (306)	129 (42.2%)
Total	5301	442	23.6% (1249)	663 (53.1%)

Table 3: Key ANC indicators for selected study clinics in Tshwane District, South Africa extracted from the South African District Health Information Systems (July 2016 – June 2017)

Research Team: Details of the expert team may be found in the biosketches. Of note, Drs. Klausner and Medina-Marino have collaborated successfully on grants, publications, NIH-Fogarty training and infectious disease/ reproductive health projects since first meeting and working together at CDC-PEPFAR South Africa in 2010. Their current successful R21 (2015-2017) from NICHD directly informs this new proposal.

Preliminary Studies: The proposed study will build upon our study team's preliminary work and expertise.

1) Acceptability/Feasibility of STI testing among HIV-infected pregnant women, South Africa (Medina-Marino/Klausner, co-PIs; R21HD084274): We recently completed enrollment in a study of HIV-infected pregnant women attending their 1st ANC visit (N=845) and offered diagnostic testing for CT, NG and TV on self-collected vaginal swabs.[104] Of 442 eligible women approached in the screening arm, 430 accepted screening (Acceptability= 97.3%). All women had valid test results; >95% received test results within 90 min. Among the 174 women with a positive test result, 92% (n=159) received same-day test results and treatment. *Those results show that integrating diagnostic STI screening into ANC services is acceptable and feasible, and that our study team has the capacity and experience to conduct the proposed study*.

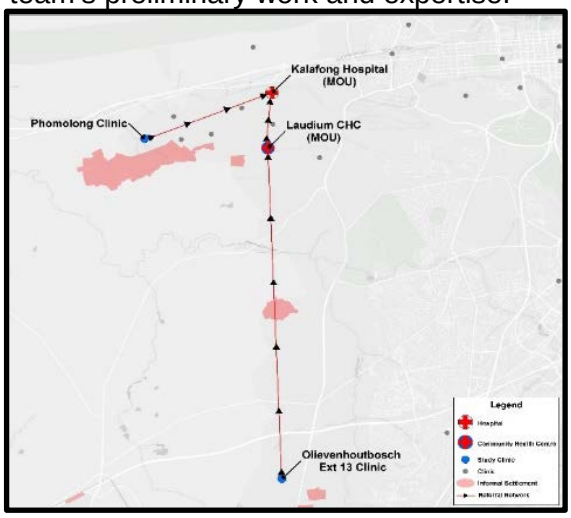


Figure 2. Study Clinics & Referral Network

2) Antenatal prevalence and behavioral risk factors of STIs (Medina-Marino/Klausner, co-PIs; R21HD084274): Our current work has identified an overall STI prevalence of 40.5% (CT= 29.5%; TV= 20.2%; NG= 5.6%) among HIV-infected pregnant women attending their first ANC visit.[105] Of those with STIs, 64.4% were asymptomatic. Factors associated with STIs at first ANC consultation were alcohol use during pregnancy (aOR=1.96, 95% CI=1.06-3.64) and having a non-cohabitating partner (aOR=1.42, 95% CI=0.97-2.03, p=0.07), controlling for maternal age and employment status.

3) Test of Cure (ToC) and treatment outcomes (Medina-Marino/Klausner, co-PIs; R21HD084274): Among 174 participants with a positive STI result at first ANC, 80% returned for a ToC 3 weeks later. Of these, 37% had any positive ToC results (CT= 26.5%; TV= 19.1%; NG= 6.3%).[106] ToC interviews revealed 91.2% of women disclosed their results to their partner(s), and 55.2% provided their partner(s) with a treatment packet. Interviews also suggested that behaviors associated with re-infection or poor medication adherence cannot account for the high persistent positivity after treatment. Those findings suggest that *a single point-in-time diagnostic screening with targeted treatment may not optimally decrease STIs at time of delivery*. Furthermore, *biological mechanisms that increase the risk for STI persistence and/or treatment failures must be further investigated.*

4) STI incidence during pregnancy and prevalence at time of delivery (Medina-Marino/Klausner, co-PIs; R21HD084274): Among 148 women negative for CT, NG, and TV at first ANC visit, we identified 11 incident infections immediately post-delivery. Moreover, in those women with a documented negative test result after treatment, an additional 10 had an incident infection immediately post-delivery, resulting in a 9.1% cumulative incidence of STIs between first ANC and delivery. Comparing the postnatal STI prevalence of intervention and control arm participants, we found that our diagnostic screening intervention decreased the prevalence of STIs by >50% compared to women receiving syndromic management (RR = 0.52; Intervention=11.1%, 95% CI: 7.9%–15.5%; Control=21.2%, 95% CI: 16.7%–26.6%).[106] Ultimately, *while diagnostic screening and targeted treatment significantly decreased the prevalence of STIs at time of delivery, a single point-in-time diagnostic test cannot identify incident infections, thus leaving women and neonates at risk of sequelae associated with STIs*.

5) Gestational age measurements (Medina-Marino/Klausner, co-PIs; R21HD084274): We assessed the reliability of last menstrual period (LMP) dating in estimating gestational age at first ANC with estimates obtained from vaginal ultrasound. Among 153 women, the median estimated gestational age was 19 weeks (IQR: 14 – 24 weeks) by LMP and 19 weeks (IQR: 15 – 24 weeks) by ultrasonography. Gestational age estimate obtained by LMP differed from the ultrasonography estimate by ≤2 weeks in 76.5% (n=117) of participants. The mean difference between gestational age estimated by last menstrual period vs. ultrasonography was 0.26 weeks (95% CI: -4.8 weeks to 5.3 weeks; manuscript in preparation).

6) Adverse birth outcomes (Medina-Marino/Klausner, co-PIs; R21HD084274): Among 607 women delivered to date, the median gestational age at delivery was 38 weeks. We have recorded 34.8% with adverse outcomes including preterm delivery 17.8% (4.9% <33 weeks), low birth weight 14.8% (1.3% very low or extremely) and miscarriage or stillbirth 4.8%. Two early neonatal deaths < 24 hours after birth have been recorded.

7) Vaginal microbiome of HIV-negative South African women (Meiring, PI; NRF RCA 13100150715/91478): We recently completed a study assessing the association between the vaginal microbiome and prevalent human papillomavirus (HPV) infection in 87 reproductive age HIV-uninfected Black South African women. A minority of the women (N=23, 26.4%) were found to have *Lactobacillus* spp. dominant vaginal microbiota; two (2.3%) were CST I, *L. crispatus* dominated; two (2.3%) were CST V, *L. jensenii* dominated; 19 (21.8%) were CST III, *L. iners* dominant; zero were *L. gasseri* dominant. The majority of women (n=64, 73.5%) had diverse vaginal microbiota

with low to no *Lactobacilli* spp. present and complex mixtures of BV-associated bacteria. *Gardnerella vaginalis*, *Atopobium vaginae* and *Sneathia* were identified as putative biomarkers for prevalent hrHPV (manuscript in preparation). *This work provides insight into the structure and composition of the vaginal microbiome of HIV-uninfected South African women, and can provide a useful comparison for our proposed study.*

8) Pathogenesis of BV in African American women who have sex with women (Muzny, PI; K23AI106957). Women with a baseline Nugent score of 0-3 were followed prospectively. Women with incident BV and controls were matched by age, race, and days of menstrual cycle; 16S rRNA sequencing targeting V4 was performed on specimens for 21 days prior to incident BV. DADA2 was used to process raw MiSeq reads. Species-level taxonomy was assigned to variants using PECAN[102] and merged with RDP assigned taxonomy using GreenGenes13_5. Longitudinal microbiome data for BV-candidate bacteria and lactobacilli of interest were analyzed using the phyloseq library. Of 31 participants that completed the study, 14 (45.2%) developed incident BV. Sequencing was performed on 448 specimens from 14 cases and 8 controls. Of controls, 75% were dominated by *L. crispatus* while 78.6% of cases were dominated by *L. iners* and/or *L. jensenii* and *L. gasseri* prior to incident BV. The relative abundance of *L. crispatus* became significantly lower in cases 14 days before incident BV. The relative abundance of *Gardnerella vaginalis, Prevotella bivia,* and *Atopobium vaginae* became significantly higher in cases 7-8 days before, 4 days before, and on the day of incident BV, respectively. There was no significant difference between cases and controls in the relative abundance of *Megasphaera* Type 1, *Sneathia sanguinegens*, BVAB1-BVAB3 or of *L. iners* leading up to incident BV (submitted *JID*). *Novel methodologies used in this study will be incorporated into Aim 3 of this proposal.*

9) Consequences of vaginal microbiota on IFNγ-mediated clearance of *Chlamydia trachomatis* (Taylor, MPI; 1R01AI118860-01A1). This study will assess the influence of vaginal microbiota on the incidence of CT clearance without treatment. Vaginal swabs from women with persistent or spontaneous CT clearance are subjected to 16S rRNA gene sequencing targeting the V4 region and processed through the DADA2 pipeline. Species-level taxonomy is assigned using the PECAN classifier and vaginal-specific database. Preliminary results have shown a prevalence of indole-producing microbiota in the vaginal microbiome of women who had persistent CT infection, and a lack of indole-producing microbiota in the vaginal microbiome of women who did clear this infection without treatment. *These results help elucidate the role of the vaginal microbiome in CT testing outcomes and further support our rationale for studying the vaginal microbiome in pregnant women with CT treatment failure.*

METHODOLOGY AND STUDY AIMS

Specific Aim 1: Evaluate different diagnostic screening interventions to decrease the burden of CT/NG/TV, and reduce adverse pregnancy and birth outcomes among pregnant women.

Methods and Procedures: To achieve Aim 1, we will conduct an effectiveness-implementation hybrid type 1 3-arm randomized controlled trial, with participants randomized from within each clinic (1:1:1) to one of the following arms: **Arm 1)** single point-in-time molecular diagnostic screening for CT, NG and TV with targeted treatment at first ANC visit and infection-specific ToC 3 weeks post-treatment. Women with a positive ToC will be re-treated and requested to return every 3 weeks for follow-up ToC visits until a negative ToC or birth outcome is documented. **Arm 2)** periodic molecular diagnostic screening for CT, NG and TV at first ANC visit and week 30–34 gestation with targeted treatment. No ToC will be conducted for women with positive test results. **Arm 3)** syndromic management (standard of care) at every ANC visit per South African National Guidelines.[128,129]

Through these methods we plan to achieve four main sub-aims: **1(a)**: compare the effectiveness of diagnostic screening (Arms 1/2) to syndromic management (Arm 3; standard of care) in reducing the prevalence of STIs during pregnancy and at time of delivery; **1(b)**: compare the effectiveness of (i) single point-in-time diagnostic screening and targeted treatment plus ToC follow-up (Arm 1) *versus* (ii) periodic diagnostic screening throughout ANC and targeted treatment without ToC follow-up (Arm 2) in reducing prevalent and incident STIs at time of delivery; **1(c)**: estimate the frequency of adverse pregnancy and birth outcomes (e.g., premature rupture of membranes, preterm labor or delivery, low birth weight/small for gestational age) and their association with screening interventions; **1(d):** collect process measures to inform future implementation and scale-up activities.

Recruitment and Eligibility: We will recruit 1250 HIV-infected and 1250 HIV-uninfected pregnant women presenting for their first ANC visit at one of our 3 study clinics in Tshwane District (Figure 2), South Africa. Eligibility criteria: 1) Age ≥18 years, 2) Currently pregnant, 3) Attending first ANC visit for their current pregnancy, 4) Willingness to self-collect up to four vulvo-vaginal swabs, 5) Residence in Tshwane District, and 6) Intent to stay in Tshwane District through delivery. Gestational age will NOT be used as an inclusion/exclusion criterion.

All pregnant women attending their first ANC visit will be screened for eligibility by study staff following standard HIV testing per South African National Guidelines for the prevention of MTCT of HIV.[130] Study staff will be trained in the study's methods, protocol, and human subjects research. Study staff will also receive training

on South Africa's syndromic management algorithms for STIs. Staff will read all eligible women a brief description of the study. Interested women will then be read aloud, in their preferred language, the study consent form which will provide specific information about CT, NG and TV infections, the consequences and treatment of those infections, and study risks and benefits, and then will be invited to participate in the study. Those providing informed consent will be enrolled and within each clinic randomized (1:1:1) into one of the 3 study arms using a simple random allocation list created in Microsoft Excel before the initiation of recruitment activities; each study arm will be composed of 50% HIV-infected (purposive enrichment) and 50% HIV-uninfected women.

Those providing informed consent will be asked to provide detailed contact information (e.g., phone numbers and "home address" for self, family, friend/neighbor) to ensure follow-up. Staff will record reason for ineligibility or refusal. Staff will collect basic de-identified information from clinic logs (i.e., age, cultural group, gestational age, HIV status) to use for descriptive analysis of the general ANC patient population.

Data Collection at Enrollment/First ANC: Trained study staff will administer an ACASI-based questionnaire to all participants. The ACASI questionnaire, adapted in part from measures used by Drs. Medina-Marino, Klausner and Pattinson in previous and current STI screening and maternal-child health studies, or documented in the literature, will include: 1) participant demographics and socio-economic status, 2) obstetric, gynecological and sexual health history, 3) sexual behaviors, risk factors and self-perception of risk for HIV and STI acquisition before and during pregnancy,[131] 3) partner characteristics and HIV status,[132,133] 4) knowledge and previous history of STIs, and 8) screenings for depression,[134,135] substance abuse,[136] interpersonal violence and social support. Staff will translate ACASI questionnaires into the major local languages (i.e., English, Sepedi, Setswana, Zulu, and Ndebele). Participants may select their preferred language in which to take the ACASI questionnaire, but will also be able to toggle between languages during the questionnaire to ensure linguistic comprehension of all questions. Staff will abstract from clinical records additional clinical history, including HIV status, date of diagnosis, and immunological characteristics associated with HIV infection (e.g., CD4 T-cell level, HIV viral load, antiretroviral therapy (ART) use and duration). Staff will verify self-reported and medical record-abstracted HIV-related information with data from the South African national HIV database, Tier.net, and the South African National Health Laboratory Service corporate data warehouse, both of which contain individual-level heath data.

Specimen Collection, Handling, Transport and Storage: Consenting participants will be instructed on how to self-collect a vulvo-vaginal swab specimen and asked to provide up to four swabs: 2x swabs for STI testing, 1x swab for microbiome analysis (Aim 3), and 1x swab for bio-banking (NOTE: pregnant women in our current study found it acceptable and feasible to collect up to four vaginal swabs at a visit). If a participant is not comfortable with self-collecting a vulvo-vaginal swab specimen they will be given the option to provide a urine specimen for testing and bio-banking (women that only provide urine specimens for testing will not be included in the cohort for microbiome analysis, Aim 3). Staff will handle specimens and label with a unique study barcode to link a participant's STI test results, medical chart and questionnaire data (see Data Collection section). For immediate GeneXpert testing, participants will use the GeneXpert Vaginal/ Endocervical Specimen Collection kit [Cepheid, Sunnyvale, CA] for vaginal swab specimen collection. For vaginal microbiome analysis, participants will use a Dacron swab [Qiagen, Digene] for self-collection, with subsequent storage in DNA AssayAssure® [Sierra Molecular, Incline Village, Nevada] at ambient, air-conditioned room temperature. For specimen bio-banking, participants will use a dry FLOQswab® [COPAN, Murrieta, CA] for specimen collection, with subsequent storage in a sterile tube. Collection of vaginal swabs for microbiome analysis and bio-banking (Aim 3) will occur before any STI treatment. Specimens will be securely stored at 2-8°C and transported to the Department of Medical Microbiology, University of Pretoria, on a bi-weekly basis according to Good Laboratory Practice. Specimens will then be flash frozen and stored at -80°C for long-term bio-banking. We will ship specimens for microbiome processing and analysis to the University of Cape Town on Dry Ice quarterly.

Diagnostic Testing: Vaginal specimens collected from participants will be PCR-tested for CT, NG and TV using the Xpert® CT/NG and Xpert® TV cartridges [Cepheid, Sunnyvale, CA]. Trained staff (STI Test Counselors and Research Nurses) will conduct the Point-of-care (POC) testing at each of the clinical sites. Once collected, research staff will follow test kit instructions for swab preparation and testing. Xpert® CT/NG provides 90-minute detection and differentiation of CT and NG, while Xpert® TV provides 60 min detection of TV; both test cartridges have high sensitivity and specificity[137] and function well in resource-constrained environments and clinical settings such as those proposed here. Each test includes a sample processing control (SPC) to ensure correct cell lysis/DNA extraction of the sample, a sample adequacy control (SAC) which ensures adequate human DNA in the specimen and a probe check control (PCC). The PCC monitors reagent rehydration, reaction-tube filling, probe integrity, and dye stability. If testing cannot be conducted due to power failures, errors, or testing delays, specimens will be stored at 2-4°C in a secure storage area for up to 24 hours until tested.

Reporting and Treatment: The GeneXpert systems consist of an instrument, computer, and preloaded software for running tests and displaying results as either positive or negative. STI Test Counselors will report all test results to the ANC Research Nurse embedded within each study clinic. Research nurses will be responsible for providing same-day test results notification and immediate treatment (and partner treatment) to all STI-infected study participants per the South African Department of Health's STI treatment protocols.[48,49]

Partner Treatment: All women testing positive for an STI will be asked to notify their partners, and given the option to either request their partner(s) to present to the clinic for treatment, or be given an infection-specific partner treatment packet of oral medication to take to their partner(s). Targeted treatment for partners will be provided according to the South African STI National Guidelines; however, in lieu of the recommended intramuscular injection of ceftriaxone for NG infections, which would require a male partner to present to a clinic, South African National Guidelines allow for oral cefixime 400mg tablet/ azithromycin 1 gm oral to be administered for NG infection.[128,129] Partner treatment will be placed inside a small yellow envelope labelled with the medication name, dosage, instructions, expiration date, and lot number. This manner of providing partner treatment was found to be highly acceptable and feasible in our current study.

Arm 1 Specific Activities: Per Table 4, at first ANC visit, participants randomized to Arm 1 will be asked to collect four vaginal swab specimens as described above (Specimen Collection section). Two specimens will be used for CT/NG and TV testing (as described in Diagnostic Testing section), while specimens for microbiome analysis (Aim 3) and bio-banking will be handled as described in the *Specimen Handling, Transport and Storage* section. Test result reporting and the provision of treatment for those with a positive test result will be conducted as described in the *Reporting and Treatment* section. Test of Cure (ToC): Arm 1 study participants that were treated for a diagnostically detected CT, NG and/or TV infection at first ANC visit will be requested to return to the clinic 3 weeks post-treatment for a targeted ToC (i.e., women will only be tested for the STI for which they were treated). At the ToC visit, women will be asked to self-collect vaginal specimens, as described above, for STI ToC as well as for microbiome analysis and bio-banking. Women with a positive ToC will again be provided treatment (and partner treatment) and asked to return 3 weeks later for another ToC; ToC will be repeated until a participant has a negative test result or a documented birth outcome.

Arm 2 Specific Activities: Per Table 4, at first ANC visit, and an ANC visit occurring between 30-34 weeks gestation, participants randomized to Arm 2 will be asked to collect four vaginal swab specimens as described (Specimen Collection section). Two specimens will be used for CT/NG and TV testing (as described in Diagnostic Testing section), while specimens for microbiome analysis and bio-banking will be handled as described in the Specimen Handling, Transport and Storage section. Test result reporting and the provision of treatment for those with a positive test result will be conducted as described in the Reporting and Treatment section. No ToC activities will be performed for Arm 2 participants.

Clinic Visit	Specimen Collection	CT, NG and TV PoC Testing	Syndromic Management
First ANC Visit	All Participants	Arms 1 and 2	Arm 3 Only
ToC 3-Weeks Post-treatment	Arm 1 Only	Arm 1 Only	-----
30 – 34 Weeks Gestation	Arm 2 Only	Arm 2 Only	As needed
First Postnatal Clinic Visit	All Maternal-Infant Pairs	All Maternal-Infant Pairs	-----

Table 4: Specimen Collection and STI Testing Schedule

Arm 3 Specific Activities: Per Table 4, at first ANC visit participants randomized to Arm 3 will be asked to collect four vaginal swab specimens as described (Specimen Collection section). All specimens will be immediately bio-banked as described in the Specimen Handling, Transport and Storage section. Arm 3 participants will be provided standard of care syndromic screening and management for STIs per South African National Guidelines.[128,129] Specimens collected from Arm 3 participants will be tested for CT, NG and TV infections after a birth outcome is documented; specimens will be tested using the GeneXpert systems as described in the Diagnostic Testing section.

Retention and Follow-up: To ensure retention, we will collect multiple forms of contact information for all participants. To develop and maintain a strong relationship with participants, study staff will conduct welcome phone calls within 3 days of enrollment, and check in with participants during regular ANC clinic visits, or during monthly ART pickup for those with HIV infections. To further support active follow up, participants will also be encouraged to enroll in the 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, and automatically generates alerts for clinic staff when appointments are missed. Clinic and study staff will contact participants who do not return for scheduled ANC or ART visits and encourage return for care. We will flag participant charts so that clinic staff will notify study staff on the date of delivery. Seven days post-delivery, study staff will contact participants that have not yet presented for their first postnatal clinic visit to schedule an outcomes interview. We will make up to 7 attempts to follow up with participants via text, phone call, and home visits.

Post-partum and Infant Testing: Per Table 4, ALL STUDY PARTICIPANTS will be asked to provide four vaginal swab specimens (as described in *Specimen Collection* section) during their first postnatal clinic visit; the first postnatal clinic visit is typically 3-6 days after discharge from the MOU or at the earliest time possible after they give birth. Two specimens will be used for CT/NG and TV testing (as described in *Diagnostic Testing section*), while specimens for microbiome analysis and bio-banking will be handled as described in the *Specimen Handling, Transport and Storage* section. Reporting of test results and provision of treatment for those with a positive test result will be conducted as described in the *Reporting and Treatment* section. Two **nasopharyngeal (NP)** swab specimens will be collected from all infants during the first postnatal visit. For any woman with a post-partum prevalent STI, staff will test the infant's NP swab at that visit for that same infection (CT, NG and/or TV) to exclude mother-to-child transmission. If no maternal infections are identified, both NP swabs will be bio-banked. Any neonate who has an NP specimen positive for CT, NG and/or TV will be treated according to the South African Medical Formulary recommendations and guidelines.[128]

Data Collection at Postnatal Clinic Visit: We will collect data on adverse pregnancy events in all study participants via abstraction of MOU discharge records and face-to-face interviews with participants during the first postnatal clinic visit. Staff will collect information on fetal loss, preterm labor, preterm birth, birth weight, the calculated small-for-gestational-age status, and infant mortality. Information on potential confounding variables such as maternal history of chronic illness (e.g., hypertension, diabetes), other infections during pregnancy (e.g., urinary tract infections, syphilis), antibiotic use during pregnancy, and pregnancy complications (e.g., premature rupture of membranes, maternal fever, chorioamnionitis, and pre-eclampsia) will also be collected. HIV PCR results from routine at-birth testing of HIV-exposed infants will be collected via clinical records, and verified using the South African National Health Laboratory Service (NHLS)'s database. At the routine 6-week immunization visit, we will access neonatal morbidities (i.e., respiratory distress, conjunctivitis, sepsis) via maternal interviews and patient medical records. A study supervisor will perform weekly reviews to ensure completeness and validity of the data collected; discrepancies will be resolved via interview with the birth attendant (midwife or physician).

Data Collection for Process Evaluation: We will use the **R**each-**E**ffectiveness-**A**doption-**I**mplementation-**M**aintenance (RE-AIM) model as our **conceptual framework**[138–140] to guide the collection of valuable information during our effectiveness trial. Per Table 5, a mixed methods approach will be used to collect process measures such as recruitment rates, refusal characteristics, perceived and experienced barriers and facilitators to optimal implementation, intervention costs, impact of intervention on patient outcomes, perceived health system readiness to implement our interventions, and to assess modifications that can be made to maximize future implementation success. We will extract quantitative measures from implementation tracking tools, recruitment/refusal logs, participant demographic data, and participant tracking/retention tools. Qualitative data will be collected during interviews with different stakeholders, including participants, research and clinic staff, facility managers, and the South Africa NHLS and National Department of Health (NDoH).

Element	Questions	Measures	Data Sources/Tools
Reach	1) What % of eligible patients consented to receive the intervention? 2) Do those that consent differ significantly from those that do not? 3) What aspects of the intervention do patient like/dislike?	1) Recruitment rates 2) Socio-demographics of all eligible participants stratified by consent/refused 3) Perception of participants	1) Enrollment tracking sheets 2) Enrollment tracking sheets 3) Post-intervention participant survey
Effectiveness	What is the effect of the intervention on patient outcomes?	Main study outcomes comparing interventions & Control	Study datasets
Adoption	1) What are the main barriers/facilitators to adopting the intervention? 2) What systems need to be in place for the health system to adopt intervention?	1) Perceptions of research/clinic staff, facility management, NHLS & NDoH	1) Staff observational logs and post-intervention interviews 2) Post-intervention interviews clinic and national stakeholders
Implementation	1) What does the intervention cost? 2) What support and tools are needed for consistent delivery of intervention?	1) Cost/Cost-effectiveness data 2) Perceptions of study and clinic staff, NHLS and NDoH	1) Study datasets 2) Post-intervention interviews w/ clinic & national stakeholders
Maintenance	1) What resources will be needed for the intervention to be sustainable? 2) What adaptions are needed to integrate intervention into current practices?	1) Perceptions of research staff, facility managers, NHLS and NDoH	1) Research staff observation logs, post-intervention interviews 2) Post-intervention interviews clinic and national stakeholders

Table 5: RE-AIM Conceptual Framework Guiding Process Evaluation (adapted from Hagedorn *et al.*[138])

Data Analysis: We will analyze data using R [R Foundation for Statistical Computing, Vienna, Austria]. Participant demographic and clinical characteristics will be described per study arm using proportions (categorical variables) and mean, median, and interquartile range (continuous variables). Statistical significance

will be assessed using chi-square and t-tests, or their non-parametric equivalents. Primary Outcomes, stratified by HIV status include: 1) change in STI prevalence between baseline (1st ANC) and delivery (1st postnatal clinic visit) per study arm, and 2) frequency of adverse pregnancy and birth outcomes per study arm. We will assess primary outcome measures based on intention-to-treat, modified intent-to-treat and a per-protocol analysis. Secondary Outcomes: 1) incident infections identified at time of delivery by study arm; 2) incidence and risk factors of CT, NG, and TV colonization in neonates, stratified by HIV status; 3) rates and risk factors for treatment failures, stratified by HIV status; 4) factors associated with STIs at first ANC and risk factors for incident STIs during pregnancy; and 5) process evaluation measures, as described in Table 5. Exploratory Outcomes: 1) type and frequency of adverse pregnancy/birth outcomes as a function of STI exposure time; 2) infant outcomes, including pneumonia and neonatal conjunctivitis, at 6-week immunization clinical visit. Significance level will be set at p-value <0.05 and all tests for significance will be two-tailed. We will calculate the change in CT, NG, and TV prevalence by subtracting the prevalence at delivery from the prevalence at baseline. We will use difference in differences analysis and average treatment effects estimation techniques to compare net changes in CT/NG/TV prevalence between baseline and delivery. We will assess differences in the frequency of adverse pregnancy and birth outcomes between study arms in both absolute and relative terms using risk (R) and relative risk (RR) estimates, respectively. We will use stratified analysis and multivariate multinomial logistic regression analysis to compute relative risks adjusted for potential effect modifiers, and confounding variables, such as exposure time to an STI. We will consider multiple imputation of missing data when missing values exceed 10% and not more than 30%, and satisfy the condition of "missing at random." We will conduct sensitivity analyses to determine how imputed data affect the study results. Analytic Plan for Process Evaluation Qualitative Data: We will employ aspects of deductive analysis that take into account the RE-AIM framework through the creation of initial *a priori* codes. Data coding and analysis will be iterative and interactive processes. We will first read all interview transcripts in order to increase familiarity with the data. Next, we will assign *a priori* codes and create emergent codes. Transcripts will then be re-read to create pattern codes that connect subsequent concepts under larger headings. Consistent patterns in meaning, concepts, and themes across all interviews will be identified, and data matrices created as visual representations of the findings.[141-143] We will also examine any differences based on stakeholder type (i.e., study staff, non-study clinic staff, NHLS and Health Department) to identify unique viewpoints. Coding and analytic activities will be discussed during qualitative data analysis meetings; discrepancies in coding and interpretation will be resolved through consensus.

Potential Challenges and Quality Assurance: Loss-to-follow up at ToC, postnatal specimen collection and interviews, and 6-week infant follow-up visits may be the dominant Aim 1 challenges. In our current R21 study, optimized retention strategies resulted in >85% retention. Strategies included enhanced participant tracking, welcome phone calls, employing a community-based roving nurse that visited women in their homes for follow-up visits, and telephonic interviews to collect self-reported outcomes data. We will also hire a midwife research assistant with full access to maternal-obstetric units to collect maternal and neonatal specimens, and abstract medical records and discharge summaries. Based on current experiences, we believe that we are well prepared to overcome typical retention challenges. Given that syndromic screening/management is performed at all ANC visits, we will abstract medical records of all participants to determine if syndromic management was conducted outside research study events. We will take such events into consideration when analyzing and interpreting our results. Finally, all research study personnel will meet weekly to review study enrollment, specimen collection, processing, test turn-around-time, data management, and treatment outcomes. Meetings will discuss descriptive study results to date, problems encountered and remedial actions to be taken.

Aim 2: Evaluate the cost per pregnant woman diagnostically screened, the costs of adverse pregnancy and birth outcomes, and the cost-effectiveness per STI and DALY averted.

Rationale: While Aim 1 will determine the efficacy of our screening interventions in improving birth outcomes for pregnant women, it is also crucial to determine whether the monetary costs of our interventions are cost-saving or cost-effective. This crucial analysis will take into account the costs of each intervention, costs averted and the overall cost-effectiveness using a societal (government provider and patient) perspective.

Data Collection: *The Provider Perspective*: We will assess the full economic costs of each study arm and the full economic costs of adverse pregnancy and birth outcomes. A full economic costing approach includes financial and opportunity costs, and is necessitated by the reality of severely constrained capacity within the South African and similar low/middle-income country health systems. Our approach to costing establishes the utilization of health services (e.g. diagnostic and treatment visits), diagnostic tests, and medication directly from trial data specific to each arm. Within a decision analytic modeling framework, those utilization estimates are multiplied by the full economic or unit cost of each service, diagnostic test or medicine. Unit costs are computed using a combined bottom-up and step-down approach, as appropriate. For example, for diagnostic visits, bottom-

up costing captures staff time for diagnosis (using time and motion tools), while step-down approaches are used to apportion shared costs within the facility such as managerial, clerical, cleaning and security staff, and utilities. For diagnostic tests, bottom-up costing is used to capture the costs of the test cartridges and GeneXpert machines (appropriately annuitized). Similarly, the costing of adverse pregnancy or birth outcomes entails the bottom-up costing of clinical staff, infrastructure and equipment within the facility where care is provided (e.g. neonatal ICU), together with a step-down allocation of shared costs such as overheads within the hospital. When valuing resources within the cost analysis that are paid from the research budget, we will use routine public sector 'prices' for staff and medication and will seek to cost GeneXpert machines and cartridges at a level commensurate with a potential public sector scale-up. Care will be taken to exclude any costs that are incurred only as part of research activities. ***The Patient Perspective*:** We will collect demographic, socio-economic, patient cost and household income data. Data will be collected at each interview unless the variable is expected to stay constant over the study period (e.g. educational status). Socio-economic status will be computed via a multiple correspondence analysis on household type, assets, and access to services following established methodology.[122,123] Patient costs will include transport costs, opportunity costs of travel, waiting and visit times, and other out-of-pocket payments, such as user fees (applicable for public inpatient care in South Africa but not for ANC). Productivity gains or losses will not be included, as the study population includes pregnant women and their babies. To increase response rates, questions about household income will include quantitative and categorical approaches.[122] The categorical income variable will be transformed into a quantitative variable using a regression methodology, where household income can be predicted as a function of demographic and socioeconomic status. Per capita household income will be computed as total household income divided by total number of household members, with appropriate adjustments for children. The opportunity cost of time can be valued using wages/salary earnings foregone.[144] In order to value these costs equitably, the mean per capita household income reported at the baseline interview will be used as a proxy of this opportunity cost. In contrast, time, travel and user fee costs will be compared to the mean per capita income of the respondent's own household in order to assess the share of per capita household income spent on these costs.

Decision Analytic Modeling: Upon estimating unit costs and utilization, we will build a decision analytic model to estimate the cost per pregnant woman diagnostically screened, screened positive, treated, and cured at time of delivery for each study arm and each perspective (provider/patient). Deterministic sensitivity analyses will assess the impact of key parameter uncertainty (e.g. the cost of GeneXpert machines within a scale-up scenario). Probabilistic sensitivity analysis will assess uncertainty around each utilization estimate from the trial.[145] If Arm 3 costs (hypothesized to include higher costs for adverse pregnancy and birth outcomes) are greater than Arm 1 or Arm 2 costs, the intervention(s) are cost-saving and no further analysis would be required. However, if we find that the costs of Arms 1 and/or 2 exceed the costs of Arm 3, we will compute incremental costs per STI and Disability-Adjusted Life Year (DALY) averted. DALYs associated with preterm births will come from common reliable sources such as the WHO and the Institute for Health Metrics and Evaluation.[146–148] DALYs will be modeled in two steps: 1) we will model the proportion of preterm infants dying within the first year. For that group of preterm infants, the lost DALYs are the estimated life expectancy for South African neonates surviving at age one. Second, we will model the 1) proportion of preterm infants surviving past the first year, 2) average life expectancy of these children, and 3) average degree of disability of these children. That will enable an estimation of DALYs and DALYs averted within each study arm. For the patient perspective, catastrophic expenditure will be computed by comparing patient costs to household expenditure using 10% and 20% thresholds per other South African and low and middle-income country studies.[122]

Potential Challenges: Assuming sample size, STI prevalence, and birth outcome data are sufficient, the main challenge of Aim 2 involves accurate data collection of newborn hospital care costs, particularly those costs incurred by any higher-level neonatal care. Building on previous experience of costing a variety of conditions within hospital settings, we plan to collect newborn cost data until discharge or death, whichever comes first, though this will likely be a few months of hospital care for babies born very pre-term.[109,149–152]

Specific Aim 3. Investigate the relationship between the vaginal microbiome and CT treatment failure in pregnant women.

Methods and Procedures: For Aim 3, we will conduct a nested case-control study (1:2) using selected bio-banked vaginal specimens collected from participants enrolled and randomized in Aim 1. We will accomplish two main sub-aims: 3(a): determine the impact of vaginal microbiota on CT treatment outcomes; 3(b): explore the natural history of the vaginal microbiome in the context of antibiotic treatment for CT infections.

Recruitment and follow-up visits: Participants randomized into Arm 1 of Aim 1, and who test positive for a CT mono-infection during their first ANC visit will be invited to participate in a weekly vaginal specimen collection

activity until a negative ToC result or a birth outcome is documented. Participants with multiple STIs will be excluded from this sub-study, as the presence of TV and NG may also alter vaginal microbiota.[153–155]

Specimen collection, handling and shipping: We will use the swab collected for bio-banking to smear a glass slide for Nugent score determination prior to its storage.[156] At week 1, 2 and 3 (i.e., ToC visit), vaginal specimen collection for microbiome analysis, glass slide smearing for Nugent scoring and specimen bio-banking will occur. At ToC, participants will be repeat CT-tested (Aim 1: Diagnostic Testing section). Those with positive CT test results at ToC will again be treated with azithromycin 1g, and asked to return for subsequent weekly specimen collection (weeks 4 and 5) and ToC2 (week 6). Specimens will be collected and stored as previously described. (Aim 1: Specimen Collection, Handling, Transport and Storage section).

Nugent scoring: Air-dried slide smears will be heat-fixed and Gram stained per standard procedure.[157] Nugent scores (0-3: normal, 4-6: intermediate and 7-10: BV flora[156]) will be recorded in a laboratory-based data system (REDCap) and linked to a participant's metadata via their unique study ID.

Selection of Stored Specimens for Nugent Scoring and Vaginal Microbiota Analysis: "Cases" will be defined as participants who test positive for CT by GeneXpert at first ANC visit (week 0) and at ToC visit (week 3; 'no clearance'). "Controls" will be participants who test positive for CT by GeneXpert at first ANC visit (week 0) but test negative at ToC (week 3; 'clearance'). The four stored vaginal swab specimens (weeks 0-3) from cases and controls will be selected for Nugent scoring and vaginal microbiota analysis. Additional weekly vaginal swab specimens from "cases" who remained persistently positive for CT by GeneXpert at first ToC will also be selected for vaginal microbiota analysis.

Molecular Methods/Interpretation of Sequence Data: Vaginal swabs will be subjected to sequencing of the V4 hypervariable region of the 16S rRNA gene using the well characterized 515F/805R primers; Illumina sequencing primers typically produces amplicons of ~290-292 base pairs. Paired end sequencing using an Illumina V2 sequencing kit 2x250bp produces reads with significant overlap, which will be processed through the DADA2 pipeline to assign high quality sequence variants. Taxonomic classification will be performed using the PECAN classifier (https://github.com/pgajer/MCclassifier) and vaginal_319_806_rc_MCo7p2 database for precise assignment of taxonomy. Phyloseq[158] and QIIME[159] analysis packages will be used to assess taxonomic composition, and alpha and beta diversity of vaginal microbiome communities. Vaginal CSTs will be formed using the Phyloseq package based on hierarchical clustering of samples using Bray-Curtis distance.[160]

Estimated effective sample size: Based on 834 pregnant women randomized to Arm 1 of Aim 1 (see Sample Size Calculations below), and a 30% CT prevalence among pregnant women (Table 1), approximately 246 CT infected women will be included in Aim 3. Considering 26.5% of CT-infected women had a positive ToC (Table 2), approximately 65 women will be "cases" and 130 women will be "controls" (1:2 match). Furthermore, given that 7.9% of CT-infected women may still positive for CT at ToC2 (week 6), 5 women will continue to collect weekly vaginal specimens. Given that each participant will have 4 stored specimens, ~800 vaginal specimens will be sequenced.

Data analysis and statistical considerations: We will analyze associations between Nugent scores, vaginal CSTs, CT treatment outcomes, and other clinical data. We intend to compare the relative abundance of microorganisms between cases and controls to determine which organisms are associated with CT treatment failure in pregnant women. Several statistical methods have been proposed to evaluate differential abundance in microbiome data (DESeq, DESeq2, and Voom).[161–163] We propose to use the DESeq2 method, which is based on the negative binomial Wald test, as it provides increased sensitivity and has several desirable characteristics compared to other competing methods.[164] Data will be analyzed at 4 time points, correlating to specimen collection (see above). We will perform preliminary analysis at each time point to account for individual effects of different microbiota at different study stages, and to understand any time/environmental-specific differences in microbiome composition over time. We will then perform longitudinal data analysis to account for longitudinal trends, random effects and fixed effects of different factors. We will use the generalized linear mixed model framework to remove the confounding effects of these factors on microbiome composition, and detail the effects of individual microorganisms on CT treatment. CSTs will be constructed using linkage clustering of microbiome species data. We will use generalized linear mixed models again to determine if different CSTs are associated with successful CT treatment. Other covariates affecting the microbiome (e.g. HIV status, CD4 count, ART exposure) will be included in the models to assess the effect of these factors on the treatment success rate. Primary Outcomes: Association of CT treatment outcomes and BV-associated CSTs. Findings from this sub-study could be clinically significant, as they may suggest that all pregnant women who are persistently positive for CT should be screened and treated for BV, even if they are asymptomatic. Current evidence is insufficient to recommend routine screening for BV in asymptomatic pregnant women for the prevention of preterm birth.[165] Secondary Outcomes: 1) prevalence of BV in cases vs. controls based on Nugent score of 7-10 at first ANC

visit, week 1 and 2, and ToC visit, and 2) Association of composition and structure of the vaginal microbiome over time at first ANC visit, week 1 and 2, and ToC in cases vs. controls at as a function of HIV viral load, CD4 count, and ART exposure. Exploratory Objectives: 1) Change in average relative abundance of indole-producing bacteria (i.e. *Prevotella* spp, *Fusobacterium nucleatum*, *Propionibacterium acnes, Porphyromonas gingivalis, Escherichia coli*, and *Enterococcus faecalis)* over time in cases vs. controls, and 2) association of BV-associated CSTs with symptomatic or asymptomatic CT infection in cases vs. controls at first ANC visit.

Potential Limitations: Changes in the structure and composition of the vaginal microbiome can occur rapidly, at times within days.[166] As such, our currently proposed weekly sampling frame may limit our resolution to detect important changes. However, a recent prospective microbiome study in pregnant women found that vaginal community taxonomic composition and diversity remained remarkably stable during pregnancy.[160] Another limitation is our inability to exclude re-infection as the cause for a positive test result at ToC. Consequently, we will exclude or adjust our analysis based on self-reported high-risk sexual behavior between first ANC and ToC visits. To assess for re-infection, study consultant Dr. Remco Peters will perform CT genotyping on paired specimens of persistently positive participants using other existing funds.

Sample Size Calculations: Aim 1 analyses will explore intervention effects on reducing probabilities for two primary outcomes: adverse pregnancy / birth events, and prevalent STIs. Based on a total sample size of approximately 2500 participants (834 participants in each study arm), calculations show that we will have at least 80% power to detect study arm differences of approximately 10% or larger at birth. We conducted two sets of calculations. 1) Calculations for the probability of an adverse pregnancy / birth event were conducted in PASS 2008 software (https://www.ncss.com/) for differences in proportions at a single timepoint (i.e., at birth). Calculations were run for a range of base rates ranging from 30% to 50%; this is in line with base rates from preliminary data (~40%). 2) We calculated changes in STI prevalence based on two timepoints (i.e., first ANC visit and birth) and conducted simulation studies in two steps. First, we simulated STI data from a binomial distribution with parameter values based on preliminary data. Preliminary results gave pregnancy STI rates around 40%; simulations used a range of pregnancy STI rates from 30% to 50%. Based on preliminary data, we anticipate that the intervention will reduce STI rates by 20% (absolute); simulations used a range of values from 10% to 20%. Second, we fit random effects logistic regressions to each simulated data set and recorded the number of significant intervention effects for a given sample size. We assumed an attrition rate of 15%.

A sample size of 2500 is a reasonable target based on data contained within the South African District Health Information System (Table 3). The annual total head count of women presenting for first ANC services at the three participating clinics is 5301. Given the combined estimated HIV prevalence rates at the three study clinics (Table 3), we expect a total of 663 HIV-infected pregnant women to seek services each year. The number of HIV-infected pregnant women will support a 50:50 ratio of HIV-infected to HIV-uninfected pregnant women in each study arm. Based on our recent study, and the rate at which we identified eligible participants that provided consent, we expect to meet our proposed sample size within 27 months from the start of enrollment.

Timeline: This study encompasses four major phases, as color highlighted in Table 6.

- Phase 1 (yellow): Protocol development, IRB submission; Develop and pilot clinical and costing data collection tools; Develop participant, specimen and implementation tracking tools; Staff hiring and training
- Phase 2 (green): Participant recruitment, testing, treatment, ToC and follow-up; Microbiome specimen collection; Clinical and costing data collection; Postnatal follow-up, testing and outcomes data collection
- Phase 3 (blue): Specimen selection for Nugent scoring and vaginal microbiota analysis; Microbiome specimen processing and sequencing
- Phase 4 (brown): Data analysis, dissemination of findings, and preparation for future research.

Table 6: Study Timeline	Year 1				Year 2				Year 3				Year 4				Year 5			
Aim 1. Evaluation of Screening Interventions and Outcomes																				
Preparations, Tool Piloting, Training																				
Implement Intervention																				
Post-delivery Follow-up, Pregnancy and Birth Outcomes																				
Data Analysis and Dissemination																				
Aim 2. Cost/ Cost-effectiveness																				
Tool Development and Piloting																				
Data Collection																				
Data Analysis and Dissemination																				
Aim 3. Microbiome Analysis																				
Specimen Collection																				
Specimen Processing																				
Data Analysis and Dissemination																				

PROTECTION OF HUMAN SUBJECTS

Involvement of Human Subjects and Their Characteristics

Proposed involvement of human subjects: Study participant recruitment will be conducted in 3 large antenatal care (ANC) clinics. Clinics are located in the referral zone of two maternal obstetric units (MOUs); Kalafong Hospital and Laudium Community Health Centre. Together, the 3 clinics see ~442 pregnant women each month attending a first ANC visit.

For Aim 1, All pregnant women attending their first ANC visit at one of the participating clinics will be screened for eligibility by study staff following standard HIV testing per South African National Guidelines for the prevention of mother-to-child transmission of HIV. Those providing informed consent will be enrolled and within each clinic randomized (1:1:1) into one of the 3 study arms using a simple random allocation list created in Microsoft Excel before the initiation of recruitment activities; each study arm will be composed of 50% HIV-infected (purposive enrichment) and 50% HIV-uninfected women. **Arm 1)** single point-in-time molecular diagnostic screening for CT, NG and TV with targeted treatment at first ANC visit and infection-specific ToC 3 weeks post-treatment. Women with a positive ToC will be re-treated and requested to return every 3 weeks for follow-up ToC visits until a negative ToC or birth outcome is documented. **Arm 2)** periodic molecular diagnostic screening for CT, NG and TV at first ANC visit and week 30–34 gestation with targeted treatment. No ToC will be conducted for women with positive test results. **Arm 3)** syndromic management (standard of care) at every ANC visit per South African National Guidelines.

Consenting participants will be instructed on how to self-collect a vulvo-vaginal swab specimen and asked to provide up to four swabs: 2x swabs for STI testing, 1x swab for microbiome analysis, 1x swab for bio-banking (NOTE: our recent study has demonstrated that pregnant women found it acceptable and feasible to collect up to four vaginal swabs at a visit). If a participant is not comfortable with self-collecting a vulvo-vaginal swab specimen they will be given the option to provide a urine specimen for testing and bio-banking. Vaginal specimens collected from participants will be PCR-tested for CT, NG and TV using the Xpert® CT/NG and Xpert® TV cartridges [Cepheid, Sunnyvale, CA]. Study nurses will be responsible for providing same-day test results notification and immediate treatment (and partner treatment) to all STI-infected study participants per the South African Department of Health's STI treatment protocols.

Regardless of the Arm to which they are randomized, all study participants will also be asked to provide four vaginal swab specimens during their first postnatal clinic visit (typically 3-6 days after discharge) or at the earliest time possible after they give birth. Reporting of test results and provision of treatment for those with a positive test result will be conducted as described above. Two nasopharyngeal (NP) swab specimens will also be collected from all infants during the first postnatal visit. For any woman with a post-partum prevalent STI, staff will test the infant's nasopharyngeal swab at that visit for that same infection (CT, NG and/or TV) to exclude mother-to-child transmission. If no maternal infections are identified, both nasopharyngeal swabs will be bio-banked. Any neonate who has an NP specimen positive for CT, NG and/or TV will be treated according to treatment recommended in the South African Medical Formulary.

For Aim 2, no human subjects will be involved.

For Aim 3, participants randomized to Arm 1 in Aim 1 and who test positive for a CT mono-infection during their first ANC clinic visit will be invited to participate in the Aim 3 CT sub-study: a weekly vaginal specimen collection activity until a negative ToC result or a birth outcome is documented. At week 1, week 2 and the Test of Cure (ToC) visit (week 3), participants will be asked to collect vaginal swabs as described in Aim 1. At ToC (week 3), participants will be repeat CT-tested. Those with a positive CT test result at ToC will again be treated with azithromycin 1 gm by directly observed therapy, and asked to return for subsequent weekly specimen collection (weeks 4 and 5) and ToC2 (week 6), to be collected as previously described.

Characteristics of the subject population, including their anticipated number, age range, and health status: All participants enrolled in the study (2500 total) will be pregnant women over age 18, receiving antenatal care at one of three participating clinics in Tshwane District, Pretoria, South Africa.

Inclusion and exclusion criteria:

Inclusion Criteria:

1. Age: 18 years or older
2. Currently pregnant
3. Attending first ANC visit for their current pregnancy
4. Willing to self-collect up to three vulvo-vaginal swabs
5. Residence in Tshwane District
6. Intention to stay in Tshwane District through delivery

Exclusion Criteria:

1. Unable to give informed consent

Collaborating sites where human subjects research will be performed. Specimen collection and STI testing using the Gene Xpert will be performed on-site at each of the participating ANC clinics in Tshwane district. Specimens will be transported to the Department of Medical Microbiology, University of Pretoria, on a bi-weekly basis, where they will then be flash frozen and stored for long-term bio-banking. Specimens will be processed at the University of Cape Town for microbiome analysis.

Sources of Material. In additional to vaginal specimens collected as described above, trained study staff will administer an ACASI-based questionnaire to all participants. The ACASI questionnaire will include: 1) participant demographics and socio-economic status, 2) obstetric, gynecological and sexual health history, 3) sexual behaviors, risk factors and self-perception of risk for HIV and STI acquisition before and during pregnancy, 3) partner characteristics and HIV status, 4) knowledge and previous history of STIs, and 8) screenings for depression, substance abuse, interpersonal violence and social support. Staff will translate ACASI questionnaires into the major local languages (i.e., English, Sepedi, Setswana, Zulu, and Ndebele). Participants may select their preferred language in which to take the ACASI questionnaire, but will also be able to toggle between languages during the questionnaire to ensure linguistic comprehension of all questions. Staff will abstract from clinical records additional clinical history, including HIV status, date of diagnosis, and immunological characteristics associated with HIV infection (e.g., CD4 T-cell level, HIV viral load, antiretroviral therapy (ART) use and duration). Staff will verify self-reported and medical record-abstracted HIV-related information with data from the South African national HIV database, Tier.net, and the South African National Health Laboratory Service corporate data warehouse, both of which contain individual heath data.

Linkages to subjects and access to subject identities. All study participants will be assigned a unique participant ID that does not include personally identifying information such as initials or date of birth. All identifiable contact information will only be accessible by study staff who need it in the course of their work, and will be kept in a locked cabinet, unlinked and in a separate location from all participant IDs at all times, with the linking key only available to one key staff member of the team to protect confidentiality.

Risks to Participants. The primary potential risks to participants due to study participation are psychological and social in nature. Physical risks from vaginal swab collection (i.e., mild discomfort) are negligible.

A. Psychological: Participants could experience psychological distress such as anxiety when discussing issues related to personal experiences, sexual health, or pregnancy. However, we do not expect any serious events to occur based on our experience across multiple previous studies, including our pilot study with this same population in South Africa. Participants may experience some stress related to the knowledge of STI or HIV status. Participants will be given information and education about the nature and consequences of all infections and treatment, and those testing positive (including newborns) will be provided treatment as per standard treatment protocols. The likely harmful consequences of learning one's STI status are low.

B. Social: Participation in this study may cause social harm (e.g., discrimination, false assumptions, rumors) if the participation of the participant becomes known to others. One of the more significant risks is notification of sexual partners about positive results of CT, NG, or TV testing, which is an important step to protect the health of the partners and their future contacts. It is possible that notifying partners about a positive CT, NG, or TV

test could put the participant at risk for intimate partner violence (IPV). Given this, we will provide IPV prevention counseling and will take steps to mitigate and monitor such outcomes, providing intensive participant support as needed.

Alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research. Participants from the target population invited to participate will be able to decline participation, with no consequence to them.

Plans for the recruitment of subjects and the process for obtaining informed consent. All recruitment will occur in one of three ANC clinics in Tshwane District South Africa. Study staff will be trained in the study's methods, protocol, and human subjects research. Staff will read all eligible women a brief description of the study. Interested women will then be read aloud the study consent form in their preferred language, which will provide specific information about CT, NG and TV infections, the consequences and treatment of those infections, and study risks and benefits, and then will be invited to participate in the study. Those providing informed consent will be asked to provide detailed contact information (e.g., phone numbers and "home address" for self, family, friend/neighbor) to ensure follow-up. Staff will record reason for ineligibility or refusal. Staff will collect basic de-identified information from clinic logs (i.e., age, cultural group, gestational age, HIV status) to use for descriptive analysis of the general ANC patient population.

Protection Against Risk. The risk of loss of privacy will be controlled using standard data collection protocols, trained staff with regular supervision and unique participant ID numbers on all data (including specimens) rather than participant names. Research staff will take an oath of confidentiality. Psychological stress will be reduced for STI testing through information and education and the use of trained staff, who will have experience in mitigating IPV. Participants who wish to disclose their test results to key individuals in their life will be offered help and counseling to do so, including an information sheet for significant others which has been developed by FPD for their current PrEP R01 study, and will be adapted for this study. For women reporting IPV upon disclosure to their partners, appropriate counseling, care and referral will be offered. Furthermore, a toll-free telephone/text hotline will be set up for all participants that encounter such social harms to receive support and/or advice.

Potential Benefits to Participants. The potential benefits to subjects include receiving basic information about STIs and HIV, as well as learning their CT, NG, and TV status and receiving treatment when indicated, which could have positive effect on their health and the health of their baby.

Importance of the Knowledge Being Obtained. Findings from this study have the potential to substantially affect STI screening and treatment guidelines for pregnant women in low and middle-income countries, to decrease the burden of STIs during pregnant and reduce adverse pregnancy and infant outcomes as a result of undiagnosed STIs.

IRB Review Procedures to Protect Human Participants. This protocol will be subject to review and approval by institutional review boards at UCLA and FPD. This will include approval prior to the initiation of research, ongoing adverse event monitoring, periodic review, and final study reporting.

Adverse Event Reporting. Although none anticipated, all adverse events will be reported to each IRB.

Data and Safety Monitoring Board (DSMB). A DSMB is not planned for this study, as described in the attached Data Safety Monitoring Protocol.

DATA AND SAFETY MONITORING PLAN

OVERSIGHT RESPONSIBILITIES

Oversight of the trial is provided by the Principal Investigators (PIs), Dr. Klausner and Dr. Medina-Marino, throughout. A detailed Data and Safety Monitoring Plan will be submitted to the UCLA IRB and approved by the NIH prior to the accrual of human subjects.

MONITORING PROCEDURES

Dr. Medina-Marino will ensure that informed consent is obtained prior to performing any research procedures, that all subjects meet eligibility criteria, and that the study is conducted according to the IRB-approved research plan.

Study data are accessible at all times for Drs. Klausner and Medina-Marino to review. The PIs will review study conduct (including enrollment, drop-outs or loss to follow-up, and protocol deviations) on a monthly basis. The PIs, Co-Investigators and an external monitoring board convened for the purpose of this study, will review, in real-time and in aggregate on a monthly basis, any Adverse Events (AEs) that occur. Due to the low-risk nature of this intervention trial, however, we expect few to no AEs to occur. The PIs will work closely with the monitoring board to review serious adverse events (SAEs) in real-time should they occur, though again no SAEs are reasonably expected during this trial. The PIs will ensure all protocol deviations, AEs, and SAEs are reported to the NIH and UCT IRB according to the applicable regulatory requirements.

COLLECTION AND REPORTING OF SAEs AND AEs

For this study, the following standard AE definitions will be used:

Adverse event: Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure.

Serious Adverse Event: Any AE that results in any of the following outcomes:

- Death
- Life-threatening
- Event requiring inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity

AEs will be graded according to the following scale:

Mild: An experience that is transient, and requires no special treatment or intervention. The experience does not generally interfere with usual daily activities. This includes transient laboratory test alterations.

Moderate: An experience that is alleviated with simple therapeutic treatments. The experience impacts usual daily activities. Includes laboratory test alterations indicating injury, but without long-term risk.

Severe: An experience that requires therapeutic intervention. The experience interrupts usual daily activities. If hospitalization (or prolongation of hospitalization) is required for treatment it becomes an SAE.

The study will use the following AE attribution scale:

Not related: The AE is clearly not related to the study procedures (i.e., another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event).

Possibly related: An event that follows a reasonable temporal sequence from the initiation of study procedures, but that could readily have been produced by a number of other factors.

Related: The AE is clearly related to the study procedures.

AEs will be identified through participant self-report, by clinician or project staff report, or during follow-up survey periods as described in the study methods.

SAEs and specific procedure-associated AEs will be reported, in writing and with a follow-up phone call by Dr. Klausner to the NIH and UCLA IRB within 24 hours after an AE or SAE is identified. In addition, all AEs are reported according to the UCLA IRB's AE reporting guidelines.

PLAN FOR ASSURING DATA ACCURACY AND PROTOCOL COMPLIANCE

Compliance of regulatory documents and study data accuracy and completeness will be maintained through an internal study team quality assurance process, which includes monthly review of collected data by the UCLA Research Assistant, and quarterly review of collected data by the PIs.

INCLUSION OF WOMEN AND MINORITIES

100% of participants in this study will be pregnant South African women, which is appropriate given the study focus and aims. Therefore all participants will be women, and all will be minorities (Black Africans).

INCLUSION OF CHILDREN

No children under the age of 18 will be included in this study, the age of consent in South Africa. Only adults of legal consent (18 years of age or older per South African Law) and able to give informed consent will be included in the study population.

MULTIPLE PI LEADERSHIP PLAN

PI Klausner and PI Medina-Marino have collaborated together on infectious disease epidemiology and multiple intervention-based projects since 2010, when both were working together at CDC South Africa. They will share in the oversight of the entire project and the development, implementation and monitoring of all policies, procedures and processes. In these roles, PI Klausner and PI Medina-Marino will be responsible for the implementation of the scientific agenda and the specific aims, and ensure that systems are in place to guarantee institutional compliance with US and South African laws, DHHS and NIH policies including biosafety, human research activities, data collection and storage and facilities. Specifically, PI Klausner will oversee study design, methods, and clinical treatment protocols throughout the project, as well as oversight of US subcontracting partners as needed. PI Medina-Marino will be responsible for ensuring timely on-site implementation in South Africa, handling logistics, laboratory performance and ensuring community collaboration and communication with the study sites, government and non-government partners throughout the project. PI Klausner and PI Medina-Marino will jointly handle human subjects concerns and will jointly interpret and disseminate all study findings. All key decisions will be made by consensus whenever possible.

PI Klausner will serve as the contact PI and will assume fiscal and administrative management including maintaining communication among PIs and key personnel through regular weekly teleconference calls, e-mail communications, telephone calls, and an in-person site visit to South Africa in each year of the project. He will be responsible for communication with NIH and submission of annual reports. Publication authorship will be based on the relative scientific contributions of the PIs and key personnel.

Conflict Resolution

If a potential conflict develops, the PIs shall meet via telephone and attempt to resolve the dispute. If they fail to resolve the dispute, the disagreement shall be referred to an arbitration committee consisting of one impartial senior executive from each PI’s institution and a third impartial senior executive mutually agreed upon by both PIs. No members of the arbitration committee will be directly involved in the research grant or the disagreement.

CONSORTIUM/CONTRACTUAL AGREEMENTS

Subaward Institution: FPD, a foreign institution

Subaward PI: Andrew Medina-Marino, PhD

Project Period Dates of Sub: Years 1 - 5

Total Cost for Each Year:

Year 1: $424,359
Year 2: $458,462
Year 3: $467,871
Year 4: $334,941
Year 5: $327,167

SCOPE OF WORK

PI Klausner will provide support for this study, led by PI Medina-Marino at the Foundation for Professional Development, from within the University of California, Los Angeles (UCLA).

FPD will house PI Medina-Marino, who will work with UCLA PI Klausner to oversee study design, methods, data analysis and dissemination efforts. Under Dr. Medina-Marino's leadership, the research team at FPD will oversee all field work and data collection, including contracts with laboratories at the University of Pretoria and University of Cape Town, which will manage microbiome processing and analysis in Aim 3.

UCLA will house Dr. Klausner. Under his leadership, UCLA will be responsible for completing all NIH and UCLA administrative and IRB-related requirements, supporting the implementation and analysis of the study in coordination with Dr. Medina-Marino.

While Dr. Medina-Marino and FPD have an important role in this project and represent a substantial portion of the total project budget as a result of field and laboratory costs, it is appropriate for UCLA to be the main grantee. Dr. Klausner and UCLA have extensive experience with NIH research projects and other major research grants of this nature, including their existing partnerships with other subcontracting partners in this project. The consortium agreement is appropriate, as Dr. Medina-Marino will support Dr. Klausner's ultimate oversight of the conceptualization, design, and analysis of the study in-country.

The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the agency's consortium agreement policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy.

CONSORTIUM/CONTRACTUAL AGREEMENTS

Subaward Institution: University of Alabama at Birmingham, a domestic institution

Subaward PI: Christina Muzny, MD

Project Period Dates of Sub: Years 1 - 5

Total Cost for Each Year:

Year 1: $32,140
Year 2: $16,552
Year 3: $17,049
Year 4: $70,239
Year 5: $72,346

SCOPE OF WORK

Dr. Muzny will provide vaginal microbiome expertise for this study, led by PI Klausner at UCLA and Medina-Marino at the Foundation for Professional Development, from within the University of Alabama at Birmingham (UAB).

While Dr. Muzny and UAB have an important role in this project, it is appropriate for UCLA to be the main grantee. UCLA has extensive experience with NIH research projects and other major research grants of this nature, including their existing partnerships with other subcontracting partners in this project. The consortium agreement is appropriate, as Dr. Muzny will provide guidance and support for the microbiome-related activities conducted in other laboratories, while PI Klausner will oversee and coordinate the entire study along with PI Medina-Marino, including planning, implementation, analysis, and dissemination.

The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the agency's consortium agreement policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy.

CONSORTIUM/CONTRACTUAL AGREEMENTS

Subaward Institution: Louisiana State University, a domestic institution

Subaward PI: Christopher Taylor, PhD

Project Period Dates of Sub: Years 1 - 5

Total Cost for Each Year:

Year 1: $14,381
Year 2: $14,381
Year 3: $14,381
Year 4: $43,140
Year 5: $43,140

SCOPE OF WORK

Dr. Taylor will provide vaginal microbiome expertise for this study, led by PI Klausner at UCLA and Medina-Marino at the Foundation for Professional Development, from within the Louisiana State University (LSU).

While Dr. Taylor and LSU have an important role in this project, it is appropriate for UCLA to be the main grantee. UCLA has extensive experience with NIH research projects and other major research grants of this nature, including their existing partnerships with other subcontracting partners in this project. The consortium agreement is appropriate, as Dr. Taylor will collaborate with UCLA on the analysis and visualization of the vaginal microbiome during years 4 and 5, and will provide consultation during years 1,2, and 3 on data collection and processing for the vaginal microbiome aim. During years 4 and 5, Dr. Taylor will utilize his computational resources, open source microbiome analysis software, and custom scripts and software developed in the Taylor lab for processing and analysis of the vaginal microbiome data. He will work with other investigators on data visualization and preparation of the manuscripts; meanwhile, PI Klausner will oversee and coordinate the entire study along with PI Medina-Marino, including planning, implementation, analysis, and dissemination.

The appropriate programmatic and administrative personnel of each organization involved in this grant application are aware of the agency's consortium agreement policy and are prepared to establish the necessary inter-organizational agreement(s) consistent with that policy.

December 1, 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development (FPD)

Re: Letter of Commitment for FOA PA-18-345 (R01)

Dear Drs. Klausner and Medina-Marino:

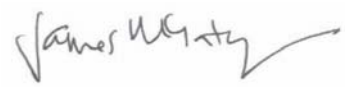
It is my pleasure to write this letter of commitment to serve as a scientific and clinical consultant for your proposed study ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy***, to be funded by the NIH. I have thoroughly enjoyed, both personally and professionally, our collaboration over the past two years on your current NIH R21 study, *Pilot Study of STI Screening and Treatment for PMTCT*. It is always scientifically rewarding to see R21 funded exploratory work produce the type of exciting results that warrant submission of an R01. Yours has proven to be such a project.

I have spent more than 30 years as an OB-GYN physician-scientist, and working to eliminate mother-to-child transmission of HIV and improve the health of women and children worldwide. In my current role as executive director of the Anova Health Institute, my staff and I conduct research and provide technical assistance to national and local health departments in South Africa, Botswana, Malawi and Mozambique in order to improve health systems and delivery for people infected with or affected by HIV, STIs, and TB. I believe that your proposal to evaluate the impact and cost-effectiveness of different screening strategies to mitigate the burdens of untreated STIs on health outcomes of pregnant women and their babies is innovative and critically important. Your work may not only decrease the burden of STIs in your participants, their unborn children and communities but may also directly inform the outdated WHO guidelines relating to STI screening, especially during pregnancy. Furthermore, your aim to investigate the role of the vaginal microbiome in STI treatment failures and persistent infections is highly novel and innovative. Leveraging your intervention platform to also answer such cutting edge research questions will further the impact of your work.

For this study, I will provide support and advice as an OB-GYN and an expert in STIs, HIV, and Prevention-of-Mother-to-Child-Transmission of HIV. I will leverage my extensive experience conducting implementation science and public health research on the scale of that proposed here to ensure that your research study is a success. From my home in Johannesburg and my work throughout South Africa, I am in a strong position to lend critical thinking and logistical support to the implementation of this study and interpretation and contextualization of study findings. I will also continue to be a member of your Clinical Advisory Committee. I am able to commit an average of five hours of consultation per month, at the rate of $75 an hour, for a total of $4500.00 per year.

I am excited to continue collaborating with you both, and look forward to another fruitful scientific endeavor.

Sincerely,



Prof. James McIntyre, MBChB, FRCOG
Executive Director, Anova Health Institute
Honorary Professor, School of Public Health & Family Medicine, University of Cape Town

UMMC
Department of Data Science

2500 North State Street - Jackson, Mississippi 39216
Phone: 601-984-2696 – datascience@umc.edu

December 12, 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development (FPD)

Re: Letter of Commitment

Dear Drs. Klausner and Medina-Marino:

I am pleased to write this letter of commitment to serve as a consultant with you and your team at UCLA, the Foundation for Professional Development (FPD), and the University of Alabama at Birmingham (UAB), for your proposed NIH R01 "The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy." I have worked closely with Dr. Christina Muzny at UAB, and welcome the opportunity to do so again, especially on such a significant and innovative proposal. Your work is the first to prospectively investigate associations between the vaginal microbiome and antibiotic treatment outcomes for STIs among HIV-positive pregnant women. This proposal has the potential to have far-reaching effects on STI prevention and control recommendations for pregnant women living with HIV, in South Africa and internationally.

For this project, I will be pleased to provide expert oversight of statistical data analyses in years 4 and 5. I have a strong computational background, with experience in parallel computation and big data analyses. I am a strong proponent of reproducible research, which will not only help with the analyses for your work in particular, but will also help to advance the field in this area, ensuring that others can learn directly from your methods and procedures.

I am able to commit to providing the above for a total compensation of $9,568 USD in year 1 and $19,136 in years 4 and 5.

I look forward to working with you as a partner in this exciting proposal.

Sincerely,

Rajesh Talluri

Rajesh Talluri, Ph.D.
Assistant Professor, Department of Data Science
The University of Mississippi Medical Center

904 Caribbean Drive
Sunnyvale, CA 94089
Telephone: (408) 541 4191
Facsimile: (408) 541 4192

December 11, 2017

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development
Pretoria, South Africa

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Public Health
University of California, Los Angeles
United States

Dear Drs. Medina-Marino and Klausner:

I enthusiastically write this letter of support for your study, "**The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy**," to examine the impact of different screening and treatment strategies on decreasing the burden of STIs among HIV-infected and uninfected pregnant women in South Africa.

Cepheid is dedicated to improving health and preventing the spread of STIs. Our GeneXpert® diagnostic platform is a rapid, PCR-based, point-of-care system that allows for the reliable and highly accurate detection of STIs in decentralized, community settings. Cepheid is happy to lend the required number of Xpert machines for the duration of your study at no cost. Finally, we will include training and technical support to your staff as needed, so they are able to use the equipment comfortably.

We thank you for the opportunity to continue to collaborate with you in this important work. We are confident this will be a fruitful partnership. Good luck with your proposal.

Sincerely,

David H. Persing, MD, PhD
Executive Vice President
Chief Medical and Technology Officer

School of Public Health and Family Medicine
Head of Department and Director: Professor Landon Myer

Division of Health Economics
Head: Associate Professor Edina Sinanovic

Private Bag X3, Rondebosch, 7701, South Africa
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December 1, 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development (FPD)

Re: Letter of Commitment for FOA PA-18-345 (R01)

Dear Drs. Klausner and Medina-Marino:

It is with great enthusiasm that I write this letter in support of your proposed study, ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy***. I am an Associate Professor in the Health Economics Unit and Division at the School of Public Health and Family Medicine, University of Cape Town. I have significant experience and expertise as a health economist and health systems researcher, with particular interest in the costs and cost-effectiveness of interventions to decrease the burden of HIV and STIs. Undiagnosed and untreated STIs among pregnant women in South Africa, like in other countries, is a significant problem, as your current study of STIs in HIV-infected pregnant women shows. Consequently, your study to evaluate the cost and cost effectiveness of different diagnostic testing algorithms to decrease the burden of STIs during pregnancy and their impact on pregnancy and birth outcomes is of great potential benefit to public health and may inform future WHO recommendations.

As Co-Investigator, I will oversee all aspects related to the cost and cost-effectiveness component (Aim 2) of this grant proposal. In year 1 I will contribute 10% LOE, during which time I will develop all data-collection tools and oversee database development for the cost/cost-effectiveness components of the project. During years 2 and 3 (implementation phase), I will support and advise on data collection activities for Aim 2, and will contribute 5% LOE. Finally, in years 4 and 5, I will perform all data analysis and oversee all results dissemination emanating from Aim 2. This will require I contribute 45% and 55% LOEs in years 4 and 5, respectively.

Given the excellent resources available at UCT and the history of partnership between UCT and FPD, I believe our team will produce a well-executed study with critical impact on the field. I look forward to hearing the results of the Study Section's review.

Sincerely,

Susan Cleary, PhD
Health Economics Division
University of Cape Town

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

DEPARTMENT OF MEDICAL MICROBIOLOGY
NELSON R. MANDELA SCHOOL OF MEDICINE /
NATIONAL HEALTH LABORATORY SERVICE
LEVEL 4, Laboratory Building,
Inkosi Albert Luthuli Central Hospital
800 Bellair Road, Mayville, 4058

NATIONAL HEALTH LABORATORY SERVICE

December 1, 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development (FPD)

Re: Letter of Commitment for FOA PA-18-345 (R01)

Dear Drs. Klausner and Medina-Marino:

It is my pleasure to submit this letter of support to demonstrate my commitment as a co-Investigators for your proposed NIH R01 grant entitled ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy***. I have thoroughly enjoyed collaborating with Dr Medina-Marino since his time at CDC-South Africa, and look forward to collaborating with you both on this extremely important, timely and innovative research project.

I have spent more than 30 years as a medical microbiologist and was actively involved in HIV Pathogenesis and Prevention research since 2003. I am currently Associate Professor and Head of the Department of Medical Microbiology at the University of KwaZulu-Natal (UKZN)/ South African National Health Laboratory Services (NHLS). In this capacity, I oversee all aspects relating to the KZN provincial microbiology services for NHLS and provide expert consultation to the South African National Department of Health (NDoH) relating to the clinic-lab interface, implementation of new diagnostic platforms as well as any other issues relating to infectious diseases. Our laboratory performs all the TB culture for the KZN province and provides supervisory support to all the GeneXpert laboratories in the province. Our laboratory has recently established an STI diagnostic molecular platform and currently provides this service to research institutions like Centre for the Programme of AIDS Research in SA (CAPRISA) and another research unit at UCT.

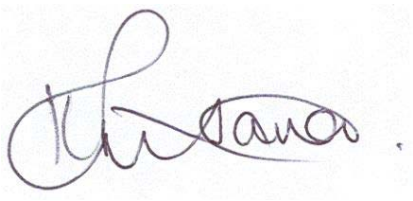
I was the previous Head of HIV Pathogenesis and Vaccine research at CAPRISA, as well as a co-investigator and Project Director of the CAPRISA 004 tenofovir gel trial. I have extensive expertise in STIs and HIV; my PhD thesis was entitled "The Impact of Sexually Transmitted Infections (STI) and Genital Tract Inflammation on HIV-1 Acquisition and Rate of Disease Progression in Subtype C Infected Women." I therefore am highly familiar with the context of STIs in South Africa and was previously involved in the establishment of the STI syndromic management guidelines for the country in the mid-90s. Based on my experiences and insights, I can say that this study is very important to the field, innovative, and well-designed.

For this project, I will serve as the co-Investigator providing expert support and oversight for 1) the implementation and operations of the GeneXpert diagnostic platform in all study clinics, 2) ensure access to and facilitate access to all laboratory test results from NHLS's laboratory information system, 3) facilitate process evaluations and costing data collection from key stakeholders within NHLS and NDoH. For this project, I will devote 10% level of effort (LOE). However, my salary is fully covered by

UKZN and NHLS, as such I do not require any salary support for this project. In exchange for my time and LOE, I kindly request budget support for a fully-funded trip (i.e., conference registration, transport, accommodations and per diem) in years 1, 4 and 5 of the grant to attend relevant HIV/AIDS and STI conferences to assist in the dissemination of findings.

FPD frequently works closely with NHLS, and I know that your robust relationship with Cepheid and experience using the Gene Xpert in the field will make this a strong partnership. Furthermore, I am well acquainted with the results of your current STI research project and believe that your proposal is an excellent example of building an R01 submission from solid pilot work funded through an R21 mechanism. Ultimately, I look forward to working closely with you both on this project, and look forward to hearing the results of NIH review.

Sincerely,



Koleka Mlisana, MBChB, MMedPath(Micro)
Associate Professor, Department of Medical Microbiology
University of Kwa-Zulu Natal
National Health Laboratory Services
Inkosi Albert Luthuli Central Hospital; Academic Complex
Durban, South Africa

Dr Tracy L. Meiring
Division of Medical Virology
Institute of Infectious Diseases & Molecular Medicine
Faculty of Health Sciences
Rm S3.01 Wernher Beit South
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December 12, 2017

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development
Pretoria, South Africa

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Public Health
University of California, Los Angeles
United States

Re: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Dear Drs. Medina-Marino and Klausner:

I am pleased to provide this letter of support for your research proposal ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy***, submitted as an NIH R01. As you are aware, I have served as a laboratory technical advisor on your recent NIH-funded STI project, during which we successfully built a very unique biorepository of self-collected vaginal specimens from a cohort of HIV-infected pregnant women for the analysis of the vaginal microbiome. We have also developed a strong collaboration and research infrastructure for the proposed research. The project will provide extremely important information on the vaginal microbiome and associations with STI treatment outcomes in pregnant women and future opportunities for research into the complex interplay between the vaginal microbiome, HIV and STIs during pregnancy and their potential impact on birth outcomes.

The Division of Medical Virology of the University of Cape Town (UCT) contributes to the diagnosis, treatment, prevention and eradication of viral diseases in South Africa through a diagnostic laboratory service together with a dynamic research and teaching programme. It is affiliated with and supported by the South African National Health Laboratory Service (NHLS). As an Early Research Career Fellow in the Division of Medical Virology and the Institute of Infectious Disease and Molecular Medicine at UCT, I look forward to providing my expertise toward this study as a Co-Investigator at 0.1 FTE in year 1 and 0.25 FTE in years 4 and 5.

I was among the first to use next generation sequencing to characterize human papillomaviruses (HPVs) in clinical specimens and I am currently carrying out a project examining the genital microbiome of South African women and men and associations of the microbiome with HPV infection. I was awarded a South African National Research Foundation Research Career Award in 2014 to begin establishing myself as an independent researcher and have set up the necessary resources and skills for the generation and analysis of microbiome data. For this project, I will be responsible for the laboratory components of the bacterial community profiling in the self-collected vaginal specimens, and overseeing all microbiome related research activities on behalf of UCT. I will also be working very closely with Drs. Muzny and Taylor in the analysis and interpretation of the microbiome data.

Given the excellent research environment and resources at UCT, together with your history of collaboration with me and others at UCT, I am confident that the proposed research will be carried out successfully. I look forward to working with you and the other members on this critical and innovative proposal. There have, to date, been no studies of the vaginal microbiome in South African pregnant women or HIV-infected pregnant women.

Sincerely,

Tracy Meiring, PhD
University of Cape Town

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences

SAMRC-UP MATERNAL AND INFANT HEALTH CARE STRATEGIES RESEARCH UNIT

Tel: 012-373 1082
Fax: 086-623 7121
Robert.pattinson@up.ac.za

Director: Prof RC Pattinson

University of Pretoria
Klinikala Building
Private Bag X323
Arcadia, 0007

December 1, 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development (FPD)

Re: Letter of Commitment, R01

Dear Drs. Klausner and Medina-Marino:

It is my pleasure to submit this letter of support to demonstrate my commitment to your proposed NIH R01 grant proposal entitled The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy. As Professor and Clinical Head of the Department Obstetrics and Gynaecology, University of Pretoria, Chief Specialist at Kalafong Hospital, and Director of the South Africa Medical Research Council's (SA-MRC) Maternal and Infant Health Care Strategies Research Unit, I have more than 30 years of extensive expertise in maternal-infant health. Given this, I can say without hesitation, that this project is extremely important, timely and innovative. Over the past 7 years, I have worked closely with FPD on a number of projects, including our current collaboration to strengthen South Africa's public sector obstetric emergency medical services systems. I have enjoyed all of our collaborations, and look forward to working with you both on this currently proposed research project.

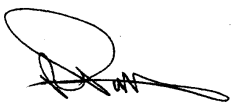
For this project, I will serve as the Co-Investigator overseeing 1) the collection of specimens from mother-infant pairs admitted to hospital during and after delivery, and 2) the abstraction of medical records and discharge summaries for birth and pregnancy outcomes. Given that Kalafong Hospital

is the main maternal-obstetric facility to which your study participants would be referred, I will ensure that vaginal specimens from the mothers and nasopharyngeal specimens from the neonates will be collected, and that all birth outcomes are properly recorded and reported. Additionally, as Director SA-MRC Maternal and Infant Health Care Strategies Research Unit, I have local and national networks of collaborators. I will leverage these networks and relationships, especially at Laudium Community Health Centre (the other local facility with a maternal-obstetric unit to which your study participants would give birth at) to ensure that they will provide the same type of access and support that I will provide at Kalafong Hospital. Our unit has had extensive experience with monitoring and following up pregnant women and their offspring. In one study we recruited 215 HIV infected women and followed these women throughout their pregnancies and the women and their babies for 3 years.

For this project, I will devote 10% level of effort (LOE). However, my salary is fully covered by the University of Pretoria, as such I do not require any salary support for this project. In exchange for my time and LOE, I kindly request budget support for a fully-funded trip (i.e., conference registration, transport, accommodations and per diem) in years 1, 4, and 5 of the grant to attend local AIDS, STI and maternal-infant health conferences to assist in the dissemination of findings. I also appreciate that you will provide 1) 100% LOE for a mid-wife research assistant in my unit starting in Q4 Year 1 through end of Year 3, and 2) 30% LOE for an administrative assistant for Y1 through Y3. The mid-wife research assistant will directly oversee all the post-delivery, in-hospital specimen collection and birth outcomes data collection for the project. The administrative assistant will provide programmatic support for any and all project specific activities occurring within my unit at Kalafong Hospital.

You have assembled an outstanding research team and I very much look forward to the important work that I will conduct with you on this project. I eagerly await the NIH review.

Sincerely,



Robert Pattinson, MBBCh, MMed, FCOG, MCCOG, MD
Director, Maternal and Infant Health Care Strategies Research Unit
South African Medical Research Council

ANOVA HEALTH INSTITUTE

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit
Foundation for Professional Development (FPD)

Re: Letter of Commitment for FOA PA-18-345 (R01)

Dear Drs. Klausner and Medina-Marino:

It is my pleasure to write this letter of commitment to serve as a scientific and clinical consultant for your proposed study ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy***, to be funded by the NIH. I have thoroughly enjoyed, both personally and professionally, our collaboration over the past two years on your current NIH R21 study, *Pilot Study of STI Screening and Treatment for PMTCT*. It is always scientifically rewarding to see pilot studies produce the type of exciting results that warrant submission of an R01. Yours has proven to be such a project.

As you know, I am a Clinical Programme Specialist at Anova Health Institute, and an extraordinary professor in medical microbiology at the University of Pretoria. In these capacities, I oversee both clinical work and laboratory work. In my recent collaboration with you, I was part of your Clinical Advisory Clinic, provided support and oversight for the collection of vaginal swab specimens to be bio-banked for future analysis, and shipping of specimens to collaborating laboratories at University of Cape Town. Furthermore, I also developed and oversaw proficiency testing of vaginal swab specimens, from which we co-authored a publication.

For this study, I will provide support and oversight of the laboratory work in the Department of Medical Microbiology at the University of Pretoria. I will leverage my laboratory infrastructure to conduct all Nugent scoring of vaginal specimens, specimen bio-banking, proficiency testing for study sights, and general support relating to specimen collection. Furthermore, I will also continue to be a member of your Clinical Advisory Committee, and will happily collaborate on data analysis and dissemination. For this work, I will only ask compensation for five hours of consultation per month, at the rate of $75 an hour, for a total of $4500.00 per year.

Given the strong history of collaboration between the Foundation for Professional Development, UCLA, and Anova Health Institute, I am certain that our research team will bring success to this proposed project. I look forward to again working with you and the other members of our team.

Sincerely,

Remco Peters, MD, PhD, DLSHTM, Dip HIV Man (SA)
Anova Health Institute

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

Enquiries: Prof Ute Feucht
Tshwane District Clinical Specialist Team
Tshwane District Health Offices
The Fields Building, 427 Hilda Street, Hatfield, Pretoria 0028
Tel: +27 724280465
ute.feucht@up.ac.za
7 December 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit, Foundation for Professional Development (FPD)

Re: Letter of Commitment for FOA PA-18-345 (R01)

Dear Drs. Klausner and Medina-Marino

I am very excited to learn about your latest proposal to the NIH, ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome during Pregnancy***. I am well aware that your previous work, *Pilot Study of STI Screening and Treatment for PMTCT in South Africa,* was also done in Tshwane District with our support and collaboration. Your findings have been well received, and your professionalism much appreciated. I am thankful for your continuous feedback sessions with district stakeholders, and for your respectful collaboration with your three study clinics; KT Motubatse clinic, Soshanguve CHC and Stanza Bopape CHC. It is my understanding that you adhered to all policies and requests made by facility managers, and that your staff integrated and worked well with facility staff. All this leads me to my willingness to continue supporting your research endeavours in collaboration with the district and our clinics.

Regarding your current proposed project, your effort to determine optimal diagnostic screening strategies to decrease the burden of STIs during pregnancy and on adverse birth outcomes is extremely important. Results showing that your interventions have impact will be necessary to reconsider health department guidelines and policy. However, your inclusion of a cost/cost-effectiveness component will be absolutely key to our ability to act on any recommendations. If proven to be impactful and cost effective, your work in Tshwane District may well have national, and perhaps international, consequences. We will be proud to say that your work was done in support of and in collaboration with Tshwane District Health Services.

I am fully aware that you both have substantial expertise as leaders in HIV and STD prevention and control research and program implementation, here in South Africa and internationally. Furthermore, the Foundation for Professional Development is one of our main partners supporting health-systems strengthening, thus you are known well within the district health system. As such, given this and our previous collaborations, I fully support the submission of your proposal and will happily work with you to continue this important work in Tshwane. This said, please note that this letter does not provide approval to conduct your research in Tshwane. Should you be awarded this grant, you will still be required to go through all appropriate process and procedures, including institutional review board approval from University of Pretoria, and district research committee approval before initiating your study.

I look forward to the sharing of study findings thereof. Best of luck on your application. If there's anything else I can do to support this work, please do not hesitate to contact me.

Sincerely,

Dr. Ute Feucht
Paediatrician, Tshwane District Clinical Specialist Team

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Enquiry: Prof Ute Feucht
Paediatrician, Head of Clinical Unit
ute.feucht@up.ac.za

Faculty of Health Sciences
Department of Paediatrics
Kalafong Hospital

P/Bag X396, Pretoria, 0001, RSA
☏ +27 12 - 373-1038/1009
🖷 +27 12 - 373-7977

Date: 7 December 2017

Jeffrey D. Klausner, MD, MPH
Professor of Medicine and Global Health
Division of Infectious Diseases and Program in Global Health
David Geffen School of Medicine and Fielding School of Public Health
University of California Los Angeles

Andrew Medina-Marino, PhD
Head, Research Unit, Foundation for Professional Development (FPD)

Re: Letter of Support for FOA PA-18-345 (R01)

Dear Drs. Klausner and Medina-Marino

As the Clinical Specialist Team Paediatrician for the Tshwane District Health Services and the University of Pretoria, it is my pleasure to write this letter of commitment to serve as a clinical consultant for your proposed study ***The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome during Pregnancy***, to be funded by the NIH. I have thoroughly enjoyed, both personally and professionally, our collaboration over the past two years on your current NIH R21 study, *Pilot Study of STI Screening and Treatment for PMTCT*. Given our collaboration, my expertise in maternal-child health, I know first-hand that your study to evaluate the impact of different screening and treatment strategies on decreasing the burden of STIs during pregnancy is a vital one, with the potential for huge impacts on our health district.

For this project, I will serve as a consultant Senior Technical Advisor. As you know I am a neonatal and infant health specialist, and an adjunct professor in the Department of Paediatrics and Child Health at the University of Pretoria. As I already do for your current R21 project, I will continue to serve on your study's Clinical Advisory Committee. From an implementation point of view, I will support and facilitate access to the antenatal care clinics in Tshwane District, where participant recruitment and STI testing will occur, and to maternal obstetric and paediatric units at local hospitals. From a research point of view, I will support data analysis and interpretation related to birth and neonate outcomes, and ensure ongoing support and dissemination of your findings within the leadership of Tshwane District Health Services.

For my time, I kindly request 5% level of effort salary support in years 1, 4 and 5, to be paid into a dedicated research fund at the Department of Paediatrics, Kalafong Hospital, University of Pretoria. Furthermore, I kindly request budget support for a fully-funded trip (i.e., conference registration, transport, accommodations and per diem) in years 2 and 3 of the grant to attend local HIV/AIDS, STI or maternal-child health conferences to assist in the dissemination of findings.

I am excited to continue collaborating with you both, and look forward to another fruitful scientific endeavor with a stellar research team.

Sincerely,

Dr. Ute Feucht
Adjunct Professor, Paediatrician, Head of Clinical Unit

RESOURCE SHARING PLAN

Data Sharing

In order to support the free flow of information and ideas to improve scientific research, the project team is solidly committed to regular sharing of data collected through this study. All study data will be kept in electronic databases, with access provided to all key staff. Programming codes will be available to any investigators who request such data directly from the Project PIs. All data will be provided on CD and will be completely de-identified. A data sharing agreement must be completed and signed by the requesting investigator and representatives of UCLA, FPD, the University of Alabama at Birmingham, Louisiana State University, and/or the University of Cape Town (as applicable) before this transfer of data can be made. Datasets will be available outside the core study team at a minimum once the data have been accepted for peer-reviewed publication, and earlier if the data are deemed by the PIs to be clean and the sharing of data is not expected to inhibit future opportunities for publication.

AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

All key biological and chemical resources used in this project will be standard laboratory reagents, not expected to vary.

PHS Assignment Request Form

Funding Opportunity Number: PA-16-160

Funding Opportunity Title: NIH Research Project Grant (Parent R01)

Awarding Component Assignment Request *(optional)*

If you have a preference for an Awarding Component (e.g., NIH Institute/Center) assignment, please use the link below to identify the most appropriate assignment then enter the short abbreviation (e.g., NCI or National Cancer Institute) in "Assign to/Do Not Assign To Awarding Component" sections below. Your first choice should be in column 1. All requests will be considered; however, locus of review is predetermined for some applications and assignment requests cannot always be honored.

Information about Awarding Components can be found here:
https://grants.nih.gov/grants/phs_assignment_information.htm#AwardingComponents

	1	**2**	**3**
Assign to Awarding Component:	NIAID	NICHD	
Do Not Assign to Awarding Component:			

Study Section Assignment Request *(optional)*

If you have a preference for a study section assignment, please use the link below to identify the most appropriate study section then enter the short abbreviation for that study section in the "Assign to/Do not Assign to Study Section" sections below. Your first choice should be in column 1. All request will be considered; however, locus of review is predetermined for some applications and assignment request cannot always be honored.

For example, you would enter "CAMP" if you wish to request assignment to the Cancer Molecular Pathobiology study section or enter "ZRG1 HDM-R" if you wish to request assignment to the Healthcare Delivery and Methodologies SBIR/STTR panel for informatics. Be careful to accurately capture all formatting (e.g., spaces, hyphens) when you type in the request.

Information about Study Sections can be found here:
https://grants.nih.gov/grants/phs_assignment_information.htm#StudySection

	1	2	3
Assign to Study Section: *(only 20 characters allowed)*			
Do Not Assign to Study Section: *(only 20 characters allowed)*			

PHS Assignment Request Form

List individuals who should not review your application and why *(optional)* *Only 1000 characters allowed*

Identify Scientific areas of expertise needed to review your applications *(optional)*

Note: *Please do not provide names of individuals*

	1	2	3	4	5
Expertise: *Only 40 characters allowed*	STI	Microbiology	Cost-effectiveness analysis	HIV	Maternal-Fetal Medicine

PHS Inclusion Enrollment Report

Study Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

*** Delayed Onset Study?**	❍ **Yes**	● **No**
If study is not delayed onset, the following selections are required:		
Enrollment Type	● **Planned**	❍ **Cumulative (Actual)**
Using an Existing Dataset or Resource	❍ **Yes**	● **No**
Enrollment Location	❍ **Domestic**	● **Foreign**
Clinical Trial	❍ **Yes**	● **No**
NIH-Defined Phase III Clinical Trial	❍ **Yes**	● **No**

Comments:

Racial Categories	**Ethnic Categories**									
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			**Total**
	Female	**Male**	**Unknown/ Not Reported**	**Female**	**Male**	**Unknown/ Not Reported**	**Female**	**Male**	**Unknown/ Not Reported**	
American Indian/ Alaska Native	0	0		0	0					0
Asian	0	0		0	0					0
Native Hawaiian or Other Pacific Islander	0	0		0	0					0
Black or African American	2500	0		0	0					2500
White	0	0		0	0					0
More than One Race	0	0		0	0					0
Unknown or Not Reported										
Total	2500	0		0	0					2500

Proposal Summary

Proposal Number: **Proposal Status:**
Sponsor Deadline: 01/07/2018 **Submission Method:**
Submission Type: Application

INVESTIGATOR DATA

PROJECT DIRECTOR / PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix:	First Name:	Middle Name:	Last Name:	Suffix:
Dr.	Jeffrey		Klausner	MD

Position/Title:	Professor	**Organization:**	UCLA David Geffen School of Medicine
Department:	Medicine	**Division:**	Infectious Diseases
Street1:	9911 West Pico Blvd	**Street2:**	Suite 955
City:	Los Angeles	**County:**	Los Angeles County
State:	CA	**Zip Code:**	90035-2738
Country:	USA	**Employee ID:**	
Phone:	310-557-3044	**Fax:**	310-557-3679
Email:	JDKlausner@mednet.ucla.edu		

First Budget Period Effort: **Calendar:** 1.20 **Academic:** **Summer:**

Status of PI:
Status Waiver Required?
Signed Intellectual Property Waiver Attached?
Signed Conflict of Interest Disclosure Attached?
Agency Certification Documentation Attached?
Cost Sharing Authorization Form Attached?

SPONSOR DATA

Agency: National Institutes of Health
Proposal Type
Sponsor Mechanism: NIH Research Project Grant (Parent R01)
Sponsor Type:
Sponsor Code:
Sponsor Name:
SubDivision 1:
SubDivision 2:

PROJECT DATA

Title of Project: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy
Is This a Subcontract?
If Yes, who is prime?
Type of Proposal:
Type of Agency:
Kind of Application: New
Previous Grant # or Federal Identifier:
Change in grantee institution?
Type of Project:

PROJECT ADMINISTRATION

Who is responsible for this research?

Departmental Identification Number:	**Primary:**	**Secondary:**
Departmental Name:	**Primary:**	**Secondary:**
Primary Dept. Contact Info:		
Account Classification:	**Primary:**	**Secondary:**

Other Institutional Code:
NAICS Code:

COMPLIANCE DATA

Are animal subjects used? No
Is IACUC review pending?
IACUC Protocol #
IACUC Approval Date:
Are human subjects used? Yes
Is IRB review pending? Yes
IRB Protocol #
IRB Approval Date:
Does this project involve use of any of the following? Radioactive Material(s), Radiation Producing Devices(s), Recombinant DNA, Biohazardous Chemical(s), Class IIIb or IV Lasers, Other certifications of health, safety and/or environmental compliance.

BUDGET DATA

Performance Dates	Begin Date	End Date
First Budget Period:	07/01/2018	06/30/2019
Cumulative Budget Period:	07/01/2018	06/30/2023

Cost Sharing Information	Mandatory	Voluntary
Committed:		
Amount:		
Source:		

Budget Period	Direct Cost	Indirect Cost	Total Cost
Period 1:	545,615	77,586	623,201
Period 2:	544,353	31,121	575,474
Period 3:	544,761	25,238	569,999
Period 4:	561,536	61,501	623,037
Period 5:	561,621	64,307	625,928
Total:	2,757,886	259,753	3,017,639

AWARD DATA

Award #: **Contract #:** **Date:**

Budget Period	Direct Cost	Indirect Cost	Total Cost
Period 1:			
Period 2:			
Period 3:			
Period 4:			
Period 5:			
Total:			

EXPORT CONTROL

1. Will the project involve participation, collaboration or access to information by foreign nationals, defined as: individuals with foreign citizenship, foreign governments, foreign associations and corporations, or foreign political parties? Note: Foreign nationals granted US citizenship, or permanent residence "green card" or granted status as a "protected individual", e.g., political refugees and political asylum holders are "EXEMPT" from deemed export rule.
2. Will the project involve the shipment of equipment, technology, software, materials data or other information?
3. Will the project involve a foreign subcontract or other foreign contractual agreement?

COMMENTS AND EXPLANATIONS

PLEASE INDICATE ANY SPECIAL INSTRUCTIONS BELOW:

UCLA

UCLA RESEARCH
EXTRAMURAL PROPOSAL APPROVAL AND SUBMISSION SUMMARY
"EPASS"

Print

Reset

1. Principal Investigator(s)/Co-PIs (Not Co-Investigators)

	First Name	M.I.	Last Name	Employee ID	Email Address	Extension
PI:	JEFFREY	DAVID	KLAUSNER	604207032	jdklausner@mednet.ucla.edu	3108257225
Other PI/Co-PI:						
Other PI/Co-PI:						
Fellow *(if Individual Fellowship)*:						

Named individuals must sign certification below. Attach additional pages if needed.

2. Department or Organized Research Unit (ORU)

Administering Department Name: MEDICINE-INFECTIOUS DISEASE FS Code (Dept. Code): 1560

Account #: 441344 Cost Center: JK Recharge ID: mz77

Dept. Contact Name: YAVARI, ROYA A Extension: 3108257225 Email Address: ryavari@mednet.ucla.edu

If your department/unit has a single e-mail address for all proposal/award related correspondence, enter it here:

Have the services of any campus Center or ORU been used in the development of this proposal?

If yes, select: Not Applicable

If "Other Center/Institute" is selected above, please specify name, or if multiple Center(s)/Institute(s) please add additional selection(s) here:

3. Proposal Identification

Proposal Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Project Begin Date: 7/1/2018 Project End Date: 6/30/2023

4. Award/Proposal/Program Type

Award Type: Grant Proposal Type: New

Program Type: Applied Org Research Special Program Type: Not Applicable

If this EPASS relates to an existing Award or Master Agreement, select an Action Type:

Current Sponsor Award/ ID#:

5. Sponsor Information (Entity which will provide funding directly to UCLA)

Sponsor Name: NIH-NIAID NATIONAL INSTITUTE OF ALLER

Sponsor Due Date: 1/7/2018 Time (Pacific): 5:00pm

Deadline Type: Electronic

Sponsor Guidelines and/or FOA/RFA/RFP:

☑ Yes ☐ No

Attached: ☐ URL (Section 9) ☐ Name/No. # PA-16-160

Contact (*if known*):

Email Address:

Phone #:

Prime Sponsor Information (Complete this section when UCLA is a subrecipient)

Prime Sponsor Name:

Prime Sponsor Due Date: Time (Pacific):

Prime Sponsor Guidelines and/or FOA/RFA/RFP:

☐ Yes ☑ No

Attached: ☐ URL (Section 9) ☐ Name/No. #

Contact (*if known*):

Email Address:

Phone #:

6. Proposal Checklist - *Carefully Review and Answer All Questions*

Yes	No	
☑	☐	PI Exception Required? (Check Requirements and Look up Eligibility). If yes, attach approval form (Sample Approval Form)
☑	☐	On Campus Space? Indicate location: Building: Center for Health Science Room: 52-254
☐	☑	Off Campus Space? Indicate location:
☑	☐	Outgoing Agreements? If yes, provide entity names in Section 9, Remarks, and attach Sub-recipient Commitment Form(s) or FDP Expanded Clearinghouse Subrecipient Letters(s) of Intent for each entity. PI signature below indicates review and approval of cost reasonableness. (See Outgoing Subawards Overview)
☑	☐	Does this project involve activities outside the U.S. or partnership with International Collaborators?
☐	☑	**Is any Cost Sharing/Matching proposed in this application? (Cash, unfunded effort, or in-kind contributions - do not include salary cap differential.) If Yes, required by sponsor?** ☐ Yes (mandatory committed) ☐ No (voluntary committed) Cost Share Amount: Source/FAU#:
☐	☑	**Is any unfunded effort proposed in this application? In accordance with UC Policy**, "unfunded effort", must be reported in ERS.(**Do not include salary cap differential here**) Source/FAU#:
☐	☑	Do you anticipate program income? If yes, specify:

☐	☑	**Does this proposal involve the use of significant IT resources (beyond basic academic infrastructure); the generation of datasets or digital assets; or a budget with over $10,000 in IT-related hardware, software, or staff expenditures?** (Check additional requirements)
☑	☐	**Human Subjects?** If yes, indicate "Pending", IRB # or Exemption #: Pending Delayed Onset ☐
☑	☐	**NIH-funded Clinical Trial?** If yes, investigators and staff involved in the conduct, oversight, or management of clinical trials should be trained in Good Clinical Practice. Training is available through CITI Program. Provide names on the next page.
☐	☑	**Will the clinical research study utilize UCLA Health System resources, including but not limited to, any patient care costs? If yes, then a Policy 915 Coverage Analysis is required (contact coverageanalysis@mednet.ucla.edu).**
☐	☑	**Animal Subjects?** If yes, indicate "Pending" or ARC#: Delayed Onset ☐
☐	☑	**Human Embryonic Stem Cell Research?** If yes, refer to the Stem Cell Policy and Procedures.
☐	☑	**Non-UCLA materials/equipment to be used?** If yes, indicate type: Source:
☐	☑	**Human or primate cells, tissue, or fluids; recombinant or synthetic nucleic acids; potentially infectious materials; exotic plants or plant pathogens; select agents or toxins?** For more information, see IBC website.
☐	☑	**Use of UC IP?** If yes, specify case number:

Yes	No	**Export Control (see RPC Website) – Does the project involve the following:**
☐	☑	**Shipping or carrying any tangible object or item to a foreign country?** If yes, specify:
☑	☐	**Conducting research or other activities in, taking money to or planning to have money transferred to a foreign country?** If yes, specify: Subaward to FDP, South Africa
☐	☑	**Training foreign persons in using equipment, technology, or technical data?** If yes, specify:
☐	☑	**Traveling to or doing research in a country currently under a US Trade or Economic Embargo (See OFAC Website)?** If yes, specify:

7. Additional Forms Required

Yes	No	**COI (Disclosure Requirements)**
☑	☐	**Sponsor/Prime Sponsor is Federal Public Health Service (PHS) or agency that has adopted the PHS regulations? If yes, provide names of other investigators on page 3 (See UCLA Policy 926).**
☐	☑	**Sponsor/Prime Sponsor is Federal (other than PHS), CIRM or special research programs managed by the UC Research Grants Program Office (RGPO)?** If yes, attach COI Form 740 & Supplement to Form 740 (if applicable). **See UCLA Procedure 925.3.**
☐	☑	**Non-Government Sponsor/Prime Sponsor?** If yes and project is ***Research***, attach Form 700-U, 700-U Addendum and 700-U Supplement, as applicable, unless sponsor is exempt. **See UCLA Procedure 925.2**

Yes	No	**Industry Sponsored Research**
☐	☑	**Industry Sponsored Non-Clinical Proposal?** If yes, attach Industry Sponsored Research Checklist.
☐	☑	**Industry Sponsored Clinical Trial?** If yes, view the Clinical Trials Contracts & Strategic Relations Checklist to determine additional required attachments.

8. Funds Requested

1st Budget Period

Direct Costs ($): 545,615 Excluded Direct Costs ($): 407,069 F&A Costs ($): 77,586 Total Costs ($): 622,631

All Project Periods (*complete only when multiple budget periods are involved*)

Direct Costs ($): 2,757,886 Excluded Direct Costs ($): 2,294,041 F&A Costs ($): 259,753 Total Costs ($): 3,017,639

F&A: F&A Rate (%): 56 F&A Base Type: MTDC If Other, specify:

9. Remarks

3 outgoing subawards, FDP, UAB, LSU.

10. Accepts Responsibility

Approvals: Includes Certifications

The Investigator(s) certifies to the following: (1) that the information submitted within this application is true, complete and accurate to the best of their knowledge; (2) that any false, fictitious, or fraudulent statements or claims may subject the Investigator(s) to criminal, civil or administrative penalties; (3) agrees to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of the application; and (4) that you are not currently debarred, suspended or ineligible to receive federal or non-federal funds; (5) all Clinical Trials based upon FDAAA 801, will be registered in ClinicalTrials.gov. When multiple Investigators are proposed in an application this assurance must be obtained by all named Investigators.

Approved Electronically by JEFFREY DAVID KLAUSNER	12/18/2017	Approved Electronically by JUDITH SILVERSTEIN CURRIER	12/18/2017
Principal Investigator (Required)	Date	Chair/ORU Director/Dean/Medical Center Director (Required)	Date
Approved Electronically by RAELLEN GARIFE MAN	12/19/2017		
DRA	Date		Date
	Date		Date

For proposal submissions funded by Federal Public Health Service (PHS) or an agency that has adopted the PHS regulations, provide, below, the name and email address for all project personnel responsible for the design, conduct, or reporting of research. All named individuals must have a current disclosure in eDGE, which is accessed at coi.research.ucla.edu.

☐ **No other project personnel responsible for the design, conduct, or reporting of research.**

Click here to copy Investigatorsinformationfrom section 1

First Name	M.I.	Last Name	Email Address	eDGE Disclosure Date
Jeffrey	D	Klausner	jdklausner@mednet.ucla.edu	10/20/17
Warren	S	Comulada	wcomulada@mednet.ucla.edu	11/10/17

For NIH-funded clinical trials, provide names of all investigators and staff involved in the conduct, oversight, or management of the project. Recipients of GCP training are expected to retain documentation of their training.

First Name	M.I.	Last Name	Email Address	GCP Training Completion Date
Jeffrey	D	Klausner	jdklausner@mednet.ucla.edu	

Request for Exception to UCLA Policy 900.1 / Principal Investigator Status

Please process an exception to UCLA Policy 900.1 on behalf of:

Name: Jeffrey D. Klausner Current Academic Title: HS Clinical Professor

Department: Infectious Disease Email Address: jdklausner@mednet.ucla.edu

Campus Address: 37-121 CHS

Campus Phone: x70409 Campus Fax: x53632

Please allow this individual to serve as ■ Principal Investigator ☐ Co-Principal Investigator

This exception applies to the project listed below.

Specific Project: R01

Proposal Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the

Agency: NIH - NIAID

Other Investigators/Co-PIs (if any): _____

Project Number (if available): PA-16-160 Date Proposal Submitted/Due: 1/7/18

Dr. Jeffrey D. Klausner has an appointment of 100 % time.

Please justify the request for exception (attach an addition sheet if necessary):

Dr. Jeffrey D. Klausner has an appointment of 100 % time. Based on their record and skills, we feel it appropriate for them to serve as Principal Investigator on this project. The grant will provide support for them and enable them to continue their research programs. The Department of Infectious Disease will provide the necessary space and facilities for Dr. Jeffrey D. Klausner to conduct their research during the duration of this project.

Requested by:

Chair: Judith Currier	Judith S. Currier Digitally signed by Currier DN: cn=Currier, o, ou, email=soeunkim@mednet.ucla.edu, c=US Date: 2017.12.20 15:50:40 -08'00'	jscurrier@mednet.ucla.edu
Name	Signature	E-mail

Approved by Vice Dean for Research:

Stephen Smale, Ph.D.	Dr Stephen Smale Digitally signed by Dr Stephen Smale Date: 2017.12.22 17:42:29 -05'00'	Smale@mednet.ucla.edu
Name	Signature	E-mail

Other:		
Name	Signature	E-mail

University of California, Los Angeles | Office of Contract and Grant Administration

Subrecipient vs. Contractor Determination Checklist

The following checklist must be analyzed and filled out per OCGA process and the Uniform Guidance 200.330 in order to determine whether the agreement between UCLA and the third party receiving funds constitutes a Subrecipient or a Contractor (Vendor). Submit completed form to the UCLA Office of Contract and Grant Administration (OCGA/Department Research Administrator (DRA) at the proposal stage (before submission of proposal). NOTE: This form is not required for Multi-Campus Awards

UCLA PI: Jeffrey Klausner PATS Number (if available): _____

Third Party Name: Foundation for Professional Development

Third Party PI: Andrew Medina-Marino

Project Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Prime Sponsored by (e.g. federal agency, non-profit organizations etc.): NIH

SUBRECIPIENT: A subaward is for the purpose of a third party to carry out a portion of an award and creates an assistance relationship between UCLA and the third party. Characteristics which support the classification of the third party entity as a subrecipient include when the third party (check all that apply):

- ☒ Performance represents an intellectually significant portion of the overall programmatic effort and is measured against the objectives of the program;
- ☒ There is an identified principal investigator for the subrecipient who has responsibility for making programmatic decisions;
- ☐ Work could result in the development of intellectual property;
- ☒ Is expected to author or co-author publications on the results of program/project work;
- ☒ Will need animal and/or human subject approval for its work;
- ☐ Provides cost sharing or matching funds;
- ☒ Will use the funds to carry out a program for a public purpose, as opposed providing goods or services for the benefit of the pass-through entity (i.e. UCLA).

Entities that include these characteristics are responsible for adherence to applicable program requirements specified in the Award

CONTRACTOR (VENDOR): A contract is for the purpose of obtaining goods and services for UCLA's own use and creates a procurement relationship between UCLA and the third party contractor. Characteristics indicative of a procurement relationship between UCLA and a contractor are when the third party receiving the funds (check all that apply):

- ☐ Provides the goods and services within normal business operations;
- ☐ Provides similar goods or services to many different purchasers;
- ☐ Performs a series of repetitive tests or activities requiring little or no discretionary judgment;
- ☐ Normally operates in a competitive environment;
- ☐ Provides goods or services that are ancillary to the operation of the program; and

Entities that include these characteristics are NOT subject to compliance requirements of the program as a result of the agreement, though similar requirements may apply for other reasons.

Description: *All of the characteristics listed above may not be present in all cases. Therefore, judgment must be used in classifying the agreement as either a subaward or a procurement contract. In determining whether an agreement constitutes a subaward or a procurement contract, the substance of the relationship is more important than the form of the agreement.*

Based on your analysis of the above checklist results, the organization is determined to be a

☒ **SUBRECIPIENT *** ☐ **CONTRACTOR (VENDOR)**

Digitally signed by Jeffrey D. Klausner
DN: cn=Jeffrey D. Klausner, o=UCLA, ou=UCLA David Geffen School of Medicine and Fielding School of Public Health, email=JDKlausner@mednet.ucla.edu, c=US

12/15/17

UCLA Principal Investigator Signature **Date**

***Submit this form along with Subrecipient Commitment Form as part of the proposal package for the minimum requirements**

ORA/DRA REVIEW:

☐ AGREE ☐ DISAGREE, RETURN TO DEPT COMMENTS _____

Name of Authorized Institution Official (e.g. DRA, OCGA) _____

Signature of Above Authorized Institution Official _____ Date _____

University of California, Los Angeles

Office of Contract and Grant Administration

SUBRECIPIENT COMMITMENT FORM

All Subrecipients must complete this form when submitting a proposal to UCLA. It provides a checklist of documents and certifications required by sponsors and it must be endorsed by the authorized institutional representative prior to proposal submission.

Subrecipient's Legal Name: Foundation for Professional Development

Subrecipient's Principal Investigator: Dr Andrew Medina-Marino

UCLA's Principal Investigator: Jeffrey D. Klausner Prime Sponsor: National Institute of Health

UCLA's Proposal Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Subrecipient Total Funds Requested: $2,031,327 Performance Period Begin Date: July 1 2018 End Date: June 30, 2023

Section A: Proposal Documents – ALSO SEE SECTION E (pg.5); Answer the questions and if categorized as a Subrecipient continue to fill out the rest of the form.

The following documents are included in our subaward proposal submission and covered by the certifications below:

☒ STATEMENT OF WORK (Required)

☒ BUDGET AND BUDGET JUSTIFICATION (Required)

☒ SUBRECIPIENT COMMITMENT FORM (This form)

Section B: Certifications

1. **Facilities & Administrative Rates** included in this proposal have been calculated based on the following:
   - ☐ Our federally recognized negotiated F&A rates for this type of work. If this box is checked, a copy of your F&A rate agreement *must* be furnished to UCLA Office of Contract & Grant Administration (OCGA).
   - ☒ A reduced F&A rate dictated by the prime sponsor that we hereby agree to accept. Rate: 8% Base Type: Foreign entity
   - ☐ Not applicable (No indirect costs are requested by Subrecipient).

2. **Fringe Benefit Rates** included in this proposal have been calculated based on the following:
   - ☐ Rates are consistent with our Federally negotiated rates. If this box is checked, a copy of your Federal fringe benefit rate agreement *must* be furnished to UCLA OCGA.
   - ☒ Other rates as specified in Section F: Comments (please specify the basis on which the rate has been calculated)

3. **Human Subjects** **YES** ☒ **NO** ☐

   If **YES** copies of the following documentation must be provided before any subaward can be issued:
   1) IRB approval certification
   2) IRB approved project protocol
   3) Approved "Informed Consent" form
   4) Verification of IRB training
   5) Verification of FWA number and Expiration date

   Please forward these documents to UCLA's Principal Investigator as soon as they become available.

   If **YES** and NIH funding is involved:
   - Have all key personnel completed human subjects training at the subrecipient's institution? **YES** ☒ **NO** ☐
   - Please attach a list of key personnel who are on this project on a separate sheet.

4. **Animal Subjects** **YES** ☐ **NO** ☒

   If **YES**, a copy of the IACUC approval must be provided before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available.

   If **YES** and NIH funding is involved:

   Please provide your institution's PHS Assurance number. PHS Assurance No.: _____ Expiration Date: _____

   If you do not have one on file, you will need to apply for one and provide it to us before any subaward will be issued.

5. **Stem Cells** **YES** ☐ **NO** ☒

   If **YES**, a copy of the Stem Cell approval must be provided before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available.

6. **Dual Use Research of Concern (DURC)** (Applicable to projects funded by PHS/NIH)

☒ Not applicable.

Will this project use one or more of the following agents or toxins (Check all that apply)?

☐ Marburg virus	☐ Reconstructed 1918 Influenza virus	☐ Avian influenza virus (highly pathogenic)
☐ Variola minor virus	☐ Variola major virus	☐ Toxin-producing strains of Clostridium botulinum
☐ Rinderpest virus	☐ Yersinia pestis	☐ Bacillus anthracis
☐ Botulinum neurotoxin	☐ Francisella tularensis	☐ Foot-and-mouth disease virus
☐ Burkholderia mallei	☐ Burkholderia pseudomallei	☐ Ebola virus

If at least one box is checked, a copy of your Institution's Review Entity determination as to whether the research qualifies as DURC must be provided. Once we receive it, and it is determined by PHS/NIH that the research is in fact DURC; a copy of the mitigation plan must be provided to UCLA before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available. For more information, please see NIH Guide notice NOT-OD-15-017.

7. **Genomic Data Sharing Policy** (Applicable to projects funded by PHS/NIH, see announcement NOT-OD-14-124) **YES** ☐ **NO** ☒

If **YES**, a copy of the Institutional Certification for large-scale human genomic data must be provided before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available. Additionally, investigators are expected to make all large scale data (human and non-human) publicly available through a data repository (e.g. dbGaP, GEO, SRA).

8. **Cost Sharing** **YES** ☐ if **YES**, $_____ **NO** ☒

If **YES**, explanation of Cost Sharing sources *must* be included in the subrecipient's budget. Please note that an annual verification of cost share commitment will be required.

9. **National Science Foundation (NSF) Conflict of Interest**

Applicable to NSF, including NSF flow-through or any other program *except PHS/NIH* requiring Federal Financial disclosure.

☒ Not applicable because this project is not being funded by NSF or any other program requiring Federal Financial disclosure.

☐ Subrecipient organization/institution hereby certifies that it has an active and enforced policy on conflict of interest consistent with the provision of NSF Award & Administration Guide Chapter IV.A.

10. **Public Health Service (PHS) Financial Conflict of Interest**

Applicable to projects funded by PHS/NIH, or any other program requiring DHHS Financial Conflict of Interest (FCOI) disclosure.

☐ Not applicable because this project is not being funded by PHS/NIH or any other program requiring DHHS FCOI.

☒ Subrecipient organization/institution hereby certifies that it has an active and enforced policy on conflict of interest consistent with the provision of 42 CFR Part 50 Subpart F.

☐ My organization **DOES NOT HAVE** a PHS compliant policy in place but will have one at the time of award.
(A sample FDP FCOI policy can be found at http://sites.nationalacademies.org/PGA/fdp/PGA_061001).
List the names of individuals working on this project that is responsible for the design, conduct, or reporting of the research.
Each individual listed MUST fill out and attach the PHS Financial Disclosure form.

11. **National Science Foundation (NSF) Ethics in Research Training**

Applicable to projects funded by NSF or any other programs requiring Ethics in Research Training.

☒ Not applicable because this project is not being funded by NSF or any other programs requiring Ethics in Research Training.

☐ Subrecipient organization/institution hereby certifies that it will ensure that all undergraduates, graduate students, and postdoctoral researchers who will be supported by this NSF proposal will be trained on the oversight in the responsible and ethical conduct of research.

12. **Public Health Service (PHS) Research Misconduct**

Applicable to projects funded by PHS/NIH

☐ Not applicable because this project is not being funded by PHS/NIH.

☒ Subrecipient organization/institution hereby certifies that it has completed and submitted the "Assurance of Compliance by Sub-Award Recipients available at: http://ori.hhs.gov/sites/default/files/PHS-6315.pdf

13. **Certification of Debarment, Suspension, Proposed Debarment**
Is the Subrecipient Entity, Subrecipient PI, or any other employee or student participating in this project, debarred, suspended or otherwise excluded from or ineligible for participation in federal assistance programs or activities? **YES** ☐ **NO** ☒
If **YES**, please explain in Section F: Comments.
Subawards to any entity or individual include in the Federal Excluded Parties are prohibited.

If **NO**, the Organization Certifies they: (answer all questions below)

☐ are ☒ are not presently debarred, suspended, proposed for debarment, or declared ineligible for award of federal contracts
☐ are ☒ are not presently indicted for, or otherwise criminally or civilly charged by a government agency.
☐ have ☒ have not within three (3) years preceding this offer, been convicted of or had a civil judgment rendered against them for commission of fraud or criminal offense in connection with obtaining , attempting to obtain, or performing a public (federal, state, or local) contract or subcontract; violation of Federal or State antitrust statutes relating to the submission of offers, or commissions of contract or subcontract; violation of Federal or State antitrust statutes relating to the submission of offers, or commission of embezzlement, theft, forgery, bribery, falsification, or destruction of records, making false statements or receiving stolen property.
☐ have ☒ have not within 3 years preceding this offer, had one or more contracts terminated for default by any federal agency.

14. Subrecipient is what type of entity? Non-domestic (non-US) Entity
Is the Subrecipient a for-profit entity? **YES** ☒ **NO** ☐
If **YES**, UCLA PI should complete the Fair and Reasonable Cost Analysis and attach it to this form.

Section C: Audit Status

1. Does the subrecipient receive an annual audit in accordance with OMB Circular A-133/Uniform Guidance? **YES** ☒ **NO** ☐
If **YES**,
   a) A complete copy of subrecipient's most recent audit report, or the Internet URL link to a complete copy, must be furnished to UCLA OCGA before a subaward will be issued.
   b) Has the audit been completed for the most recent fiscal year? **YES** ☒ **NO** ☐
   c) Were there any audit findings reported? **YES** ☐ **NO** ☒

   If **YES**, UCLA requires that the entity complete the Certificate of Compliance

If **NO**, UCLA requires that the entity complete a Financial Audit Management Questionnaire and may require a limited-scope audit before a subaward can be issued.

Section D: Subrecipient Institutional Information

1. Location of Subrecipient
   Address: 173 Mary Road
   City, State, Zip: The Willows, Pretoria, South Africa Congressional District: N/A
   Primary Place of Performance *(If primary place of performance is different than Location of Subrecipient)*
   Address: _____
   City, State, Zip: _____ Congressional District: _____
2. Subrecipient DUNS Number: 568904572
3. Subrecipient EIN Number: 1900217648A1
4. Subrecipient NAICS Code: 611430
5. Is Subrecipient owned or controlled by a parent entity? **YES** ☐ **NO** ☒ If **YES**, provide information for the parent entity below:
   Address: _____
   City, State, Zip: _____ Congressional District: _____
   Parent DUNS Number: _____
   Parent EIN Number: _____

6. Is subrecipient currently registered in System for Award Management (SAM)? (www.sam.gov) **YES** ☒ **NO** ☐
If **NO**, organizations that have not registered with SAM will need to obtain a DUNS number first and then access the online registration through the SAM (System for Award Management) home page at https://www.sam.gov (U.S. organizations will also need to provide an Employer Identification Number from the Internal Revenue Service that may take an additional 2-5 weeks to become active). Completing and submitting the registration takes approximately one hour to complete and your SAM registration will take 3-5 business days to process. **Subrecipient *must have* a current SAM registration and maintain their current information in SAM prior to issuance of a Subaward.**

7. Is the Subrecipient's Principal Investigator and/or any other Investigator (key personnel) on the proposed subaward a UCLA student (undergraduate or graduate), postdoctoral scholar, or other trainee, or a faculty or staff employee? **YES** ☐ **NO** ☒
If **YES,** please describe the relationship in Section F: Comments and notify the OCGA Subaward Team at ocgasubawards@em.ucla.edu.

8. Federal Funding and Accountability Transparency Act (FFATA)
Provide the names and total compensation of the five (5) most highly compensated officers of the subrecipient entity if:
   a. The recipient in its preceding fiscal year received:
      i. 80 percent or more of its annual gross revenues in Federal awards; **AND**
      ii. $25,000,000 or more in annual revenues from the Federal awards; **AND**
   b. The public does NOT have access to information about the compensation of the senior executives of the entity through periodic reports filed under section 13(a) or 15(d) of the Securities and Exchange Act of 1934 (15 U.S. C. 78m(a), 78o(d) or section 6104 of the Internal Revenue Service Code of 1986 [26 USC 6104]

If **YES** to a and b: Attach List
If **NO** to a and/or b: Check this box ☐
Note: "Total compensation" means the cash and noncash dollar value earned by the executive during the subrecipient's past fiscal year of the following (for more information see 17 CFR 229.402 (c)(2)).

1) Salary and Bonus
2) Award of stock, stock options, and stock appreciation rights. Use the dollar amount recognized for financial statement reporting purposes with respect to the fiscal year in accordance with FAS 123R
3) Earnings for services under non-equity incentive plans. Does not include group life, health, hospitalization, or medical reimbursement plans that do not discriminate in favor of executives, and are available generally to all salaried employees.
4) Change in pension value. This is the change in present value of defined benefit and actuarial pension plans.
5) Above-market earning of deferred compensation which are not tax-qualified
6) Other compensation. For Example, severance, termination payments, value of life insurance paid on behalf of the employee, perquisites or property if the values for the executive exceed $10,000

Project Description: In compliance with FFATA reporting obligations, please provide a succinct description of the overall purpose and expected outcomes. This information will be displayed on the https://www.USAspending.gov website and will be available to the general public.

STIs are common in pregnant women but often go undiagnosed; we recently 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 cost effective screening strategies that optimally decrease the burden of STIs during pregnancy, and reduce adverse pregnancy and infant outcomes, 2) elucidate the role of the vaginal microbiome in treatment outcomes, and 3) inform STI screening and treatment guidelines in other low-middle income countries, we propose a the following three Aims: Aim 1: Evaluate different diagnostic screening interventions to decrease the burden of CT/NG/TV, and reduce adverse pregnancy and birth outcomes among pregnant women. Aim 2: Evaluate the cost per pregnant women diagnostically screened, and the cost-effectiveness per STI averted at time of delivery and adverse birth outcome Aim 3: Investigate the relationship between the vaginal microbiome and STI treatment outcomes.

Section E: Subrecipient Requirements and Responsibilities

Before submitting a subaward proposal, the subrecipient must verify that it fits the characteristics of a subrecipient, rather than those of a contractor. The following chart outlines the differences. Please check all that apply.

Subrecipient	Contractor
☒ Performance represents an intellectually significant portion of the overall programmatic effort and is measured against the objectives of the Federal program	☐ Provides goods or services that are ancillary to the operation of the Federal program
☒ Will use the Federal funds to carry out a program for a public purpose, as opposed to providing goods or services for the benefit of UCLA	☐ Provides the goods or services purchased with the Federal funds within normal business operations
☒ Is responsible for adhering to applicable Federal program requirements specified in the Federal award	☐ Provides similar goods or services to many different purchasers
☒ There is an identified principal investigator for the subrecipient who has responsibility for making programmatic decisions	☐ Is not subject to the compliance requirements of the Federal program as a result of the agreement with UCLA
	☐ Normally operates in a competitive environment

☒ **YES** ☐ **NO** My organization is properly categorized as a subrecipient as described above.

If "No," please contact the UCLA PI about procuring your organization's products and services as a contractor.

Section F: Comments (please attach additional pages if necessary)

FPD's fringe benefits rates are based on internal policies, and are specified in the detailed budget.

Approved for Subrecipient

The information, certifications, and representations above have been read, signed, and made by an authorized institutional representative of the Subrecipient named herein. The appropriate programmatic and administrative personnel involved in this application are aware of agency policies in regard to subawards and are prepared to establish the necessary inter-institutional agreements consistent with those policies. Any work begun and/or expenses incurred prior to execution of a subaward agreement are at the Subrecipient's own risk.

Signature of Subrecipient's Authorized Institutional Representative	173 Mary Road, The Willows Street Address
Henk Reeder Typed Name of Subrecipient's Authorized Institutional Representative	Pretoria, Gauteng, South Africa City, State, Zip
Mr Title of Subrecipient's Authorized Institutional Representative	+27128169000 Phone +27 86 567 0253 Fax
2017/12/15 Date	henkr@foundation.co.za Email Address

University of California, Los Angeles | Office of Contract and Grant Administration

Subrecipient vs. Contractor Determination Checklist

The following checklist must be analyzed and filled out per OCGA process and the Uniform Guidance 200.330 in order to determine whether the agreement between UCLA and the third party receiving funds constitutes a Subrecipient or a Contractor (Vendor). Submit completed form to the UCLA Office of Contract and Grant Administration (OCGA/Department Research Administrator (DRA) at the proposal stage (before submission of proposal). NOTE: This form is not required for Multi-Campus Awards

UCLA PI: Jeffrey Klausner PATS Number (if available): _____

Third Party Name: Foundation for Professional Development

Third Party PI: Andrew Medina-Marino

Project Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Prime Sponsored by (e.g. federal agency, non-profit organizations etc.): NIH

SUBRECIPIENT: A subaward is for the purpose of a third party to carry out a portion of an award and creates an assistance relationship between UCLA and the third party. Characteristics which support the classification of the third party entity as a subrecipient include when the third party (check all that apply):

- ☒ Performance represents an intellectually significant portion of the overall programmatic effort and is measured against the objectives of the program;
- ☒ There is an identified principal investigator for the subrecipient who has responsibility for making programmatic decisions;
- ☐ Work could result in the development of intellectual property;
- ☒ Is expected to author or co-author publications on the results of program/project work;
- ☒ Will need animal and/or human subject approval for its work;
- ☐ Provides cost sharing or matching funds;
- ☒ Will use the funds to carry out a program for a public purpose, as opposed providing goods or services for the benefit of the pass-through entity (i.e. UCLA).

Entities that include these characteristics are responsible for adherence to applicable program requirements specified in the Award

CONTRACTOR (VENDOR): A contract is for the purpose of obtaining goods and services for UCLA's own use and creates a procurement relationship between UCLA and the third party contractor. Characteristics indicative of a procurement relationship between UCLA and a contractor are when the third party receiving the funds (check all that apply):

- ☐ Provides the goods and services within normal business operations;
- ☐ Provides similar goods or services to many different purchasers;
- ☐ Performs a series of repetitive tests or activities requiring little or no discretionary judgment;
- ☐ Normally operates in a competitive environment;
- ☐ Provides goods or services that are ancillary to the operation of the program; and

Entities that include these characteristics are NOT subject to compliance requirements of the program as a result of the agreement, though similar requirements may apply for other reasons.

Description: *All of the characteristics listed above may not be present in all cases. Therefore, judgment must be used in classifying the agreement as either a subaward or a procurement contract. In determining whether an agreement constitutes a subaward or a procurement contract, the substance of the relationship is more important than the form of the agreement.*

Based on your analysis of the above checklist results, the organization is determined to be a

☒ **SUBRECIPIENT *** ☐ **CONTRACTOR (VENDOR)**

Digitally signed by Jeffrey D. Klausner
DN: cn=Jeffrey D. Klausner, o=UCLA, ou=UCLA David Geffen School of Medicine and Fielding School of Public Health, email=JDKlausner@mednet.ucla.edu, c=US

12/15/17

UCLA Principal Investigator Signature **Date**

***Submit this form along with Subrecipient Commitment Form as part of the proposal package for the minimum requirements**

ORA/DRA REVIEW:

☐ AGREE ☐ DISAGREE, RETURN TO DEPT COMMENTS _____

Name of Authorized Institution Official (e.g. DRA, OCGA) _____

Signature of Above Authorized Institution Official _____ Date _____

Form Approved Through 10/31/2018 OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Do not exceed character length restrictions indicated.

LEAVE BLANK—FOR PHS USE ONLY.		
Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT *(Do not exceed 81 characters, including spaces and punctuation.)*
The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☐ NO ☒ YES
(If "Yes," state number and title)
Number: PA-18-345 Title: NIH Research Project Grant (Parent R01 Clinical Trial Required)

3. PROGRAM DIRECTOR/PRINCIPAL INVESTIGATOR

3a. NAME (Last, first, middle)	3b. DEGREE(S)	3h. eRA Commons User Name
Taylor, Christopher	PhD	CTay15

3c. POSITION TITLE
Associate Professor

3d. MAILING ADDRESS *(Street, city, state, zip code)*
533 Bolivar Street, 6th Floor
New Orleans, LA 70112-1393

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Microbiology, Immunology, and Parasitology

3f. MAJOR SUBDIVISION
Medicine

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: 504-568-4065 FAX: 504-568-2918

E-MAIL ADDRESS:
CTay15@lsuhsc.edu

4. HUMAN SUBJECTS RESEARCH	4a. Research Exempt	If "Yes," Exemption No.
☒ No ☐ Yes	☐ No ☐ Yes	

4b. Federal-Wide Assurance No.	4c. Clinical Trial	4d. NIH-defined Phase III Clinical Trial
	☐ No ☐ Yes	☐ No ☐ Yes

5. VERTEBRATE ANIMALS ☒ No ☐ Yes — 5a. Animal Welfare Assurance No.

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
07/01/2018	06/30/2023	$9,850	$14,381	$88,646	$129,423

9. APPLICANT ORGANIZATION
Name: Louisiana State University Health Sciences Ctr. – NO
Address: 433 Bolivar Street
New Orleans, LA 70112

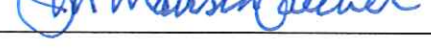
10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☒ State ☐ Local
Private: → ☐ Private Nonprofit
For-profit: → ☐ General ☐ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
1-726087770-A2
DUNS NO. 782627814 Cong. District LA-002

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name: Ella Lee
Title: Assistant Director, Sponsored Projects
Address: 433 Bolivar Street, 6th Floor
New Orleans, LA 70112-2256
Tel: 504-568-3674 FAX: 504-568-6376
E-Mail: Spon_Proj@lsuhsc.edu

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name: Joseph M. Moerschbaecher, III, PhD
Title: Vice Chancellor, Acad. Affairs
Address: 433 Bolivar Street, Suite 824
New Orleans, LA 70112-2256
Tel: 504-568-4804 FAX: 504-568-5588
E-Mail: ERA_SO_ACCT@lsuhsc.edu

14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 13. *(In ink. "Per" signature not acceptable.)*


DATE 12/11/17

LSU Health
NEW ORLEANS

School of Medicine
Department of Microbiology, Immunology and Parasitology

Date: December 6, 2017

Application Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome during Pregnancy

Proposed Project Period: July 1, 2018 – June 30, 2023
Proposed Budget: Year 1 Budget Request: $14,381; Project Budget Request: $129,423

On behalf of Louisiana State University Health Sciences Center - New Orleans (LSUHSC-NO) and the University of California, Los Angeles (UCLA), the undersigned are pleased to endorse the above referenced proposal.

This letter certifies that neither LSUHSC-NO nor UCLA is delinquent on any federal debt, nor is either institution presently debarred, proposed for debarment, declared ineligible or voluntarily excluded from covered transactions by a Federal department or agency.

This letter further certifies that both LSUHSC-NO and UCLA have valid Dun & Bradstreet (D&B) Universal Numbering System (DUNS) numbers.

Both LSUHSC-NO and UCLA certify that they are in compliance with 42 CFR Part 50.604 and currently maintain up-to-date, written, enforced policies on financial conflicts of interest (FCOIs). Each agrees to follow said policies throughout the life of any award. It is further certified that all study personnel have completed, or will complete prior to the expenditure of Public Health Service (PHS) funds (if applicable) the appropriate disclosures in accordance with their respective FCOI policies. Identified FCOIs will be made available to the grantee institution upon request.

The appropriate programmatic and administrative personnel of each institution involved in this grant application are aware of the pertinent Federal regulations and policies and are prepared to negotiate written inter-organizational agreements that will ensure compliance with all such policies.

Louisiana State University Health Sciences Center - New Orleans
(Consortium Institution)

(Signature) 12/06/17 (Date)
Christopher Taylor, PhD
Associate Professor
Dept. of Microbiology & Immunology

(Signature) 12/11/17 (Date)
Joseph M. Moerschbaecher, III, PhD
Vice Chancellor, Academic Affairs

University of California, Los Angeles
(Grantee Institution)

(Signature) (Date)
Jeffrey D. Klausner, MD, MPH
Professor of Medicine
School of Public Health

(Signature) (Date)
Ms. Raellen Man
Director of Research Administration

University of California, Los Angeles — Office of Contract and Grant Administration

SUBRECIPIENT COMMITMENT FORM

All Subrecipients must complete this form when submitting a proposal to UCLA. It provides a checklist of documents and certifications required by sponsors and it must be endorsed by the authorized institutional representative prior to proposal submission.

Subrecipient's Legal Name: The Board of Supervisors of LSU and A&M College, herein represented by Louisiana State University Health Sciences Center – N.O.

Subrecipient's Principal Investigator: Christopher Taylor, PhD

UCLA's Principal Investigator: Drs. Klausner & Medine-Marino Prime Sponsor: NIH-NIDCR

UCLA's Proposal Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Subrecipient Total Funds Requested: $129,423 Performance Period Begin Date: 07/01/2018 End Date: 06/30/2023

Section A: Proposal Documents – ALSO SEE SECTION E (pg.5); Answer the questions and if categorized as a Subrecipient continue to fill out the rest of the form.

The following documents are included in our subaward proposal submission and covered by the certifications below:

☒ STATEMENT OF WORK (Required)
☒ BUDGET AND BUDGET JUSTIFICATION (Required)
☒ SUBRECIPIENT COMMITMENT FORM (This form)

Section B: Certifications

1. **Facilities & Administrative Rates** included in this proposal have been calculated based on the following:
   - ☒ Our federally recognized negotiated F&A rates for this type of work. If this box is checked, a copy of your F&A rate agreement *must* be furnished to UCLA Office of Contract & Grant Administration (OCGA).
   - ☐ A reduced F&A rate dictated by the prime sponsor that we hereby agree to accept. Rate:_____ Base Type:_____
   - ☐ Not applicable (No indirect costs are requested by Subrecipient).

2. **Fringe Benefit Rates** included in this proposal have been calculated based on the following:
   - ☒ Rates are consistent with our Federally negotiated rates. If this box is checked, a copy of your Federal fringe benefit rate agreement *must* be furnished to UCLA OCGA.
   - ☐ Other rates as specified in Section F: Comments (please specify the basis on which the rate has been calculated)

3. **Human Subjects** YES ☐ NO ☒
   If **YES** copies of the following documentation must be provided before any subaward can be issued:
   1) IRB approval certification
   2) IRB approved project protocol
   3) Approved "Informed Consent" form
   4) Verification of IRB training
   5) Verification of FWA number and Expiration date

   Please forward these documents to UCLA's Principal Investigator as soon as they become available.
   If **YES** and NIH funding is involved:
   - Have all key personnel completed human subjects training at the subrecipient's institution? **YES** ☐ **NO** ☐
   - Please attach a list of key personnel who are on this project on a separate sheet.

4. **Animal Subjects** YES ☐ NO ☒
   If **YES**, a copy of the IACUC approval must be provided before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available.
   If **YES** and NIH funding is involved:
   Please provide your institution's PHS Assurance number. PHS Assurance No.: _____ Expiration Date: _____
   If you do not have one on file, you will need to apply for one and provide it to us before any subaward will be issued.

5. **Stem Cells** YES ☐ NO ☒
   If **YES**, a copy of the Stem Cell approval must be provided before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available.

6. **Dual Use Research of Concern (DURC)** (Applicable to projects funded by PHS/NIH)

☐ Not applicable.

Will this project use one or more of the following agents or toxins (Check all that apply)?

☐ Marburg virus	☐ Reconstructed 1918 Influenza virus	☐ Avian influenza virus (highly pathogenic)
☐ Variola minor virus	☐ Variola major virus	☐ Toxin-producing strains of Clostridium botulinum
☐ Rinderpest virus	☐ Yersinia pestis	☐ Bacillus anthracis
☐ Botulinum neurotoxin	☐ Francisella tularensis	☐ Foot-and-mouth disease virus
☐ Burkholderia mallei	☐ Burkholderia pseudomallei	☐ Ebola virus

If at least one box is checked, a copy of your Institution's Review Entity determination as to whether the research qualifies as DURC must be provided. Once we receive it, and it is determined by PHS/NIH that the research is in fact DURC; a copy of the mitigation plan must be provided to UCLA before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available. For more information, please see NIH Guide notice NOT-OD-15-017.

7. **Genomic Data Sharing Policy** (Applicable to projects funded by PHS/NIH, see announcement NOT-OD-14-124) **YES** ☐ **NO** ☒

If **YES**, a copy of the Institutional Certification for large-scale human genomic data must be provided before any subaward will be issued. Please forward these documents to UCLA's Principal Investigator as soon as they become available. Additionally, investigators are expected to make all large scale data (human and non-human) publicly available through a data repository (e.g. dbGaP, GEO, SRA).

8. **Cost Sharing** **YES** ☐ if **YES**, $_____ **NO** ☒

If **YES**, explanation of Cost Sharing sources *must* be included in the subrecipient's budget. Please note that an annual verification of cost share commitment will be required.

9. **National Science Foundation (NSF) Conflict of Interest**

Applicable to NSF, including NSF flow-through or any other program *except PHS/NIH* requiring Federal Financial disclosure.

☒ Not applicable because this project is not being funded by NSF or any other program requiring Federal Financial disclosure.

☐ Subrecipient organization/institution hereby certifies that it has an active and enforced policy on conflict of interest consistent with the provision of NSF Award & Administration Guide Chapter IV.A.

10. **Public Health Service (PHS) Financial Conflict of Interest**

Applicable to projects funded by PHS/NIH, or any other program requiring DHHS Financial Conflict of Interest (FCOI) disclosure.

☐ Not applicable because this project is not being funded by PHS/NIH or any other program requiring DHHS FCOI.

☒ Subrecipient organization/institution hereby certifies that it has an active and enforced policy on conflict of interest consistent with the provision of 42 CFR Part 50 Subpart F.

☐ My organization **DOES NOT HAVE** a PHS compliant policy in place but will have one at the time of award.
(A sample FDP FCOI policy can be found at http://sites.nationalacademies.org/PGA/fdp/PGA_061001).
List the names of individuals working on this project that is responsible for the design, conduct, or reporting of the research.
Each individual listed MUST fill out and attach the PHS Financial Disclosure form.

11. **National Science Foundation (NSF) Ethics in Research Training**

Applicable to projects funded by NSF or any other programs requiring Ethics in Research Training.

☒ Not applicable because this project is not being funded by NSF or any other programs requiring Ethics in Research Training.

☐ Subrecipient organization/institution hereby certifies that it will ensure that all undergraduates, graduate students, and postdoctoral researchers who will be supported by this NSF proposal will be trained on the oversight in the responsible and ethical conduct of research.

12. **Public Health Service (PHS) Research Misconduct**

Applicable to projects funded by PHS/NIH

☐ Not applicable because this project is not being funded by PHS/NIH.

☒ Subrecipient organization/institution hereby certifies that it has completed and submitted the "Assurance of Compliance by Sub-Award Recipients available at: http://ori.hhs.gov/sites/default/files/PHS-6315.pdf

13. **Certification of Debarment, Suspension, Proposed Debarment**

Is the Subrecipient Entity, Subrecipient PI, or any other employee or student participating in this project, debarred, suspended or otherwise excluded from or ineligible for participation in federal assistance programs or activities? **YES** ☐ **NO** ☒

If **YES**, please explain in Section F: Comments.

Subawards to any entity or individual include in the Federal Excluded Parties are prohibited.

If **NO**, the Organization Certifies they: (answer all questions below)

☐ are ☒ are not presently debarred, suspended, proposed for debarment, or declared ineligible for award of federal contracts

☐ are ☒ are not presently indicted for, or otherwise criminally or civilly charged by a government agency.

☐ have ☒ have not within three (3) years preceding this offer, been convicted of or had a civil judgment rendered against them for commission of fraud or criminal offense in connection with obtaining , attempting to obtain, or performing a public (federal, state, or local) contract or subcontract; violation of Federal or State antitrust statutes relating to the submission of offers, or commissions of contract or subcontract; violation of Federal or State antitrust statutes relating to the submission of offers, or commission of embezzlement, theft, forgery, bribery, falsification, or destruction of records, making false statements or receiving stolen property.

☐ have ☒ have not within 3 years preceding this offer, had one or more contracts terminated for default by any federal agency.

14. Subrecipient is what type of entity? Public/State Controlled Institution of Higher Education

Is the Subrecipient a for-profit entity? **YES** ☐ **NO** ☒

If **YES**, UCLA PI should complete the Fair and Reasonable Cost Analysis and attach it to this form.

Section C: Audit Status

1. Does the subrecipient receive an annual audit in accordance with OMB Circular A-133/Uniform Guidance? **YES** ☒ **NO** ☐

If **YES**,

a) A complete copy of subrecipient's most recent audit report, or the Internet URL link to a complete copy, must be furnished to UCLA OCGA before a subaward will be issued.

b) Has the audit been completed for the most recent fiscal year? **YES** ☐ **NO** ☒

c) Were there any audit findings reported? **YES** ☐ **NO** ☒

If **YES**, UCLA requires that the entity complete the Certificate of Compliance

If **NO**, UCLA requires that the entity complete a Financial Audit Management Questionnaire and may require a limited-scope audit before a subaward can be issued.

Section D: Subrecipient Institutional Information

1. Location of Subrecipient

Address: 433 Bolivar Street

City, State, Zip: New Orleans, LA 70112-2256 Congressional District: LA-002

Primary Place of Performance *(If primary place of performance is different than Location of Subrecipient)*

Address: 533 Bolivar Street, 6th Floor

City, State, Zip: New Orleans, LA 70112-1349 Congressional District: LA-002

2. Subrecipient DUNS Number: 782627814

3. Subrecipient EIN Number: 1-726087770-A2

4. Subrecipient NAICS Code: 611310 - Colleges, Universities, and Professional Schools

5. Is Subrecipient owned or controlled by a parent entity? **YES** ☐ **NO** ☒ If **YES**, provide information for the parent entity below:

Address: _____

City, State, Zip: _____ Congressional District: _____

Parent DUNS Number: _____

Parent EIN Number: _____

6. Is subrecipient currently registered in System for Award Management (SAM)? (www.sam.gov) **YES** ☒ **NO** ☐
If **NO**, organizations that have not registered with SAM will need to obtain a DUNS number first and then access the online registration through the SAM (System for Award Management) home page at https://www.sam.gov (U.S. organizations will also need to provide an Employer Identification Number from the Internal Revenue Service that may take an additional 2-5 weeks to become active). Completing and submitting the registration takes approximately one hour to complete and your SAM registration will take 3-5 business days to process. **Subrecipient *must have* a current SAM registration and maintain their current information in SAM prior to issuance of a Subaward.**

7. Is the Subrecipient's Principal Investigator and/or any other Investigator (key personnel) on the proposed subaward a UCLA student (undergraduate or graduate), postdoctoral scholar, or other trainee, or a faculty or staff employee? **YES** ☐ **NO** ☒
If **YES,** please describe the relationship in Section F: Comments and notify the OCGA Subaward Team at ocgasubawards@em.ucla.edu.

8. Federal Funding and Accountability Transparency Act (FFATA)
Provide the names and total compensation of the five (5) most highly compensated officers of the subrecipient entity if:
   a. The recipient in its preceding fiscal year received:
      i. 80 percent or more of its annual gross revenues in Federal awards; **AND**
      ii. $25,000,000 or more in annual revenues from the Federal awards; **AND**
   b. The public does NOT have access to information about the compensation of the senior executives of the entity through periodic reports filed under section 13(a) or 15(d) of the Securities and Exchange Act of 1934 (15 U.S. C. 78m(a), 78o(d) or section 6104 of the Internal Revenue Service Code of 1986 [26 USC 6104]

If **YES** to a and b: Attach List
If **NO** to a and/or b: Check this box ☒
Note: "Total compensation" means the cash and noncash dollar value earned by the executive during the subrecipient's past fiscal year of the following (for more information see 17 CFR 229.402 (c)(2)).

1) Salary and Bonus
2) Award of stock, stock options, and stock appreciation rights. Use the dollar amount recognized for financial statement reporting purposes with respect to the fiscal year in accordance with FAS 123R
3) Earnings for services under non-equity incentive plans. Does not include group life, health, hospitalization, or medical reimbursement plans that do not discriminate in favor of executives, and are available generally to all salaried employees.
4) Change in pension value. This is the change in present value of defined benefit and actuarial pension plans.
5) Above-market earning of deferred compensation which are not tax-qualified
6) Other compensation. For Example, severance, termination payments, value of life insurance paid on behalf of the employee, perquisites or property if the values for the executive exceed $10,000

Project Description: In compliance with FFATA reporting obligations, please provide a succinct description of the overall purpose and expected outcomes. This information will be displayed on the https://www.USAspending.gov website and will be available to the general public.

Dr. Christopher Taylor, Associate Professor at Louisiana State University Health Sciences Center - NO, is an expert in the field of microbiome visualization and analysis and has a specific research focus on the vaginal microbiome with relation to studies of STIs and chlamydia treatment. LSUHSC will collaborate with UCLA on the analysis and visualization of the vaginal microbiome data during years 4 and 5, and will provide consultation during years 1, 2, and 3 on data collection and processing for the vaginal microbiome aim. During years 4 and 5, Dr. Taylor will utilize his computational resources, open source microbiome analysis software, and custom scripts and software developed in the Taylor lab for processing and analysis of the vaginal microbiome data. He will work with the other investigators on data visualization and preparation of manuscripts.

Section E: Subrecipient Requirements and Responsibilities

Before submitting a subaward proposal, the subrecipient must verify that it fits the characteristics of a subrecipient, rather than those of a contractor. The following chart outlines the differences. Please check all that apply.

Subrecipient	Contractor
☒ Performance represents an intellectually significant portion of the overall programmatic effort and is measured against the objectives of the Federal program	☐ Provides goods or services that are ancillary to the operation of the Federal program
☒ Will use the Federal funds to carry out a program for a public purpose, as opposed to providing goods or services for the benefit of UCLA	☐ Provides the goods or services purchased with the Federal funds within normal business operations
☒ Is responsible for adhering to applicable Federal program requirements specified in the Federal award	☐ Provides similar goods or services to many different purchasers
☒ There is an identified principal investigator for the subrecipient who has responsibility for making programmatic decisions	☐ Is not subject to the compliance requirements of the Federal program as a result of the agreement with UCLA
	☐ Normally operates in a competitive environment

☒ YES ☐ NO My organization is properly categorized as a subrecipient as described above.

If "No," please contact the UCLA PI about procuring your organization's products and services as a contractor.

Section F: Comments (please attach additional pages if necessary)

Approved for Subrecipient

The information, certifications, and representations above have been read, signed, and made by an authorized institutional representative of the Subrecipient named herein. The appropriate programmatic and administrative personnel involved in this application are aware of agency policies in regard to subawards and are prepared to establish the necessary inter-institutional agreements consistent with those policies. Any work begun and/or expenses incurred prior to execution of a subaward agreement are at the Subrecipient's own risk.

Signature of Subrecipient's Authorized Institutional Representative

Joseph M. Moerschbaecher, III, PhD
Typed Name of Subrecipient's Authorized Institutional Representative

Vice Chancellor, Acad. Affairs
Title of Subrecipient's Authorized Institutional Representative

12/11/17
Date

433 Bolivar Street, Suite 824
Street Address

New Orleans, LA 70112
City, State, Zip

504-568-4804
Phone

504-568-5588
Fax

ERA_SO_ACCT@lsuhsc.edu
Email Address

COLLEGES AND UNIVERSITIES RATE AGREEMENT

EIN: 1726087770A2

ORGANIZATION:

LSU Health Sciences Center, New Orleans
433 Bolivar Street
Suite 811
New Orleans, LA 70112-2223

DATE: 05/25/2017

FILING REF.: The preceding agreement was dated 05/04/2016

The rates approved in this agreement are for use on grants, contracts and other agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

	EFFECTIVE PERIOD				
TYPE	FROM	TO	RATE(%)	LOCATION	APPLICABLE TO
PRED.	07/01/2013	06/30/2014	45.50	On Campus	Organized Research
PRED.	07/01/2014	06/30/2017	46.00	On Campus	Organized Research
PRED.	07/01/2013	06/30/2017	46.00	On Campus	Instruction
PRED.	07/01/2013	06/30/2017	45.00	On Campus	Other Sponsored Activities
PRED.	07/01/2013	06/30/2017	26.00	Off Campus	All Programs
PROV.	07/01/2017	Until Amended		"Use same rates and conditions as those cited for FYE June 30, 2017."	

*BASE

Modified total direct costs, consisting of all direct salaries and wages, applicable fringe benefits, materials and supplies, services, travel and up to the first $25,000 of each subaward (regardless of the period of performance of the subawards under the award). Modified total direct costs shall exclude equipment, capital expenditures, charges for patient care, rental costs, tuition remission, scholarships and fellowships, participant support costs and the portion of each subaward in excess of $25,000. Other items may only be excluded when necessary to avoid a serious inequity in the distribution of indirect costs, and with the approval of the cognizant agency for indirect costs.

ORGANIZATION: LSU Health Sciences Center, New Orleans
AGREEMENT DATE: 5/25/2017

SECTION I: FRINGE BENEFIT RATES**

TYPE	FROM	TO	RATE(%)	LOCATION	APPLICABLE TO
FIXED	7/1/2016	6/30/2017	46.00	All	F/T Faculty & Staff
FIXED	7/1/2017	6/30/2018	45.00	All	F/T Faculty & Staff
PROV.	7/1/2018	6/30/2020			Use same rates and conditions as those cited for fiscal year ending June 30, 2018.

** DESCRIPTION OF FRINGE BENEFITS RATE BASE:
Salaries and wages.

SECTION II: SPECIAL REMARKS

TREATMENT OF FRINGE BENEFITS:

The fringe benefits are charged using the rate(s) listed in the Fringe Benefits Section of this Agreement. The fringe benefits included in the rate(s) are listed below.

TREATMENT OF PAID ABSENCES

Vacation, holiday, sick leave pay and other paid absences are included in salaries and wages and are claimed on grants, contracts and other agreements as part of the normal cost for salaries and wages. Separate claims are not made for the cost of these paid absences.

OFF-CAMPUS DEFINITION: For all activities performed in facilities not owned by the institution and to which rent is directly allocated to the project(s) the off-campus rate will apply. Grants or contracts will not be subject to more than one F&A cost rate. If more than 50% of a project is performed off-campus, the off-campus rate will apply to the entire project.

Equipment Definition -
Equipment means an article of nonexpendable, tangible personal property having a useful life of more than two years and an acquisition cost of $5,000 or more per unit.

FRINGE BENEFITS:

Retirement
Unemployment Insurance
Health Insurance
Terminal Leave
Sabbatical Leave
Unfunded Retirement
Worker's Compensation
FICA
Life Insurance
Stipends

Your next fringe benefit proposal based on actual costs for the fiscal year ending 06/30/17 is due in our office by 12/31/17.

Your next F&A proposal based on actual costs for the fiscal year ending 06/30/16 is under review.

SECTION III: GENERAL

A. LIMITATIONS:

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions: (1) Only costs incurred by the organization were included in its facilities and administrative cost pools as finally accepted: such costs are legal obligations of the organization and are allowable under the governing cost principles; (2) The same costs that have been treated as facilities and administrative costs are not claimed as direct costs; (3) Similar types of costs have been accorded consistent accounting treatment; and (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

B. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from facilities and administrative to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the authority in Title 2 of the Code of Federal Regulations, Part 200 (2 CFR 200), and should be applied to grants, contracts and other agreements covered by 2 CFR 200, subject to any limitations in A above. The organization may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing facilities and administrative costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of facilities and administrative costs allocable to these programs.

BY THE INSTITUTION:

LSU Health Sciences Center, New Orleans

(INSTITUTION)

(SIGNATURE)

Ronald L. Rodriguez

(NAME)

Director of Accounting Services

(TITLE)

6/5/17

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

(AGENCY)

Arif M. Karim -A

Digitally signed by Arif M. Karim -A
DN: c=US, o=U.S. Government, ou=HHS, ou=PSC, ou=People, cn=Arif M. Karim -A, 0.9.2342.19200300.100.1.1=2000212895
Date: 2017.06.02 13:16:00 -05'00'

(SIGNATURE)

Arif Karim

(NAME)

Director, Cost Allocation Services

(TITLE)

5/25/2017

(DATE) 0024

HHS REPRESENTATIVE: Theodore Foster

Telephone: (214) 767-3261

DEPARTMENT OF HEALTH & HUMAN SERVICES

Program Support Center
Financial Management Portfolio
Cost Allocation Services

1301 Young Street, Room 732
Dallas, TX 75202
PHONE: (214) 767-3261
FAX: (214) 767-3264
EMAIL: CAS-Dallas@psc.hhs.gov

May 25, 2017

Mr. Ronnie Rodriguez, CPA
Director of Accounting Services
Louisiana State University Health Sciences Center – New Orleans
433 Bolivar Street
New Orleans, LA 70112-2223

Dear Mr. Rodriguez:

A copy of a facilities and administrative (F&A) cost and fringe benefit (FB) Rate Agreement are being sent to you for your signature. This Agreement reflects an understanding reached between your organization and a member of my staff concerning F&A and FB rates that may be used to support your claim for these indirect costs on grants and contracts with the Federal Government.

Please have the Agreement signed by an authorized representative of your organization and return it to me by email, retaining the copy for your files. Our email address is CAS-Dallas@psc.hhs.gov. We will reproduce and distribute the Agreement to the appropriate awarding organizations of the Federal Government for their use.

During our review of your proposal, it was disclosed that the Institution's actuarially determined pension contributions exceeded the Governmental Accounting Standards Board (GASB) Statement No. 68 calculated pension expense. However, 2 CFR 200.431(g)(3) only allows pension plan costs determined in accordance with GAAP (i.e., GASB 68). The Office of Management and Budget (OMB) is aware of this issue and is currently considering revising the regulations. Therefore, we reserve the right to revise this Agreement to disallow the pension contributions in excess of the GASB 68 calculated pension expense, if OMB does not revise the regulation or issue an exception.

In addition, your FB cost rate(s) for the fiscal year ending June 30, 2017 based on actual costs for the fiscal year ended June 30, 2015 and FB cost rates for the fiscal year ending June 30, 2018 based on actual costs for the fiscal year ended June 30, 2016 under-recovered (-) or over-recovered (+) amounts are listed below:

	2015/2017	2016/2018
F/T Faculty & Staff:	($6,199,407)	($4,012,571)

The fixed rate(s) for the fiscal years ended June 30, 2015 and June 30, 2016 are considered final.

A Fringe Benefit cost proposal, together with supporting information and the certified audit financial statement, is required each year. Thus, your next Fringe Benefit cost proposal based on actual costs for the fiscal year ending June 30, 2017 is due in our office by December 31, 2017. Your next Facilities and Administrative cost rate proposal based on actual costs for the fiscal year ending June 30, 2016 is currently under review.

Since this is an integral part of the negotiation agreement, please note your acceptance by signing in the space provided below of this letter.

Thank you for your cooperation.

Sincerely,

Arif M. Karim -A

Digitally signed by Arif M. Karim -A
DN: c=US, o=U.S. Government, ou=HHS, ou=PSC, ou=People, cn=Arif M. Karim -A, 0.9.2342.19200300.100.1.1=2000212895
Date: 2017.06.02 13:16:48 -05'00'

Arif Karim
Director
Cost Allocation Services

Enclosures

ACCEPTANCE

LSU HSC – New Orleans
Institution

Signature

Ronald L. Rodriguez
Name

Director of Accounting Services
Title

6/5/17
Date

Institutional Assurances and Certifications

Status

The Office of Research and Integrity Certification Status is: **Assurance OK**

This certification expires on: **04/30/2018**

Assurances and Certifications

This institution complies with all laws, policies and regulations prohibiting discrimination based on:

02/28/2007	Age Discrimination Assurance
02/28/2007	Civil Rights Assurance
02/28/2007	Handicapped Individuals Assurance
02/28/2007	Inclusion of Children Policy
02/28/2007	Sex Discrimination Assurance
02/28/2007	Women and Minority Inclusion Policy

This institution complies with all laws and regulations regarding:

08/11/2008	ClinicalTrials.gov Requirement
02/28/2007	Conflict of Interest Assurance
02/28/2007	Delinquent Debt Assurance
02/28/2007	Drugfree Workplace Assurance
08/11/2008	Impact of Grant Activities on the Environment and Historic Properties
02/28/2007	Institutional Debarment Assurance
02/28/2007	Lobbying Assurance
10/27/2009	Smoke-Free Workplace

Research at this institution meets all requirements for:

10/27/2009	Graduate Student Training for Doctoral Degrees (D43, TU2, T15, T32, T37, T90, U2R, U90, and U54/TL1 only)
02/28/2007	Human Subjects
05/08/2007	PI Assurance
05/08/2007	Prohibited Research
02/28/2007	Recombinant DNA and Human Gene Transfer
02/28/2007	Research Misconduct
02/28/2007	Research With Human Embryonic Stem Cells
05/08/2007	Select Agent Research
02/28/2007	Transplantation of Human Fetal Tissue
02/28/2007	Vertebrate Animals

Institutional Certification of Compliance with PHS FCOI Regulations as of 8/24/12

The institution below has certified on the FDP Clearinghouse that they are or will be compliant with PHS FCOI Regulations as of 8/24/12.

Institution Name	Louisiana State University Health Sciences Center - New Orleans
Authorized Representative	Joseph Moerschbaecher
Authorized Representative Title	Vice Chancellor, Academic Affairs
Authorized Representative Email Address	ERA_SO_ACCT@lsuhsc.edu
Primary DUNS Number Optional	782627814

Please consider the environment before printing this page.

Back to complete list
FCOI Homepage

University of California, Los Angeles | Office of Contract and Grant Administration

Subrecipient vs. Contractor Determination Checklist

The following checklist must be analyzed and filled out per OCGA process and the Uniform Guidance 200.330 in order to determine whether the agreement between UCLA and the third party receiving funds constitutes a Subrecipient or a Contractor (Vendor). Submit completed form to the UCLA Office of Contract and Grant Administration (OCGA/Department Research Administrator (DRA) at the proposal stage (before submission of proposal). NOTE: This form is not required for Multi-Campus Awards

UCLA PI: Jeffrey Klausner PATS Number (if available): _____

Third Party Name: University of Alabama at Birmingham

Third Party PI: Christina Muzny

Project Title: The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of the Microbiome During Pregnancy

Prime Sponsored by (e.g. federal agency, non-profit organizations etc.): NIH

SUBRECIPIENT: A subaward is for the purpose of a third party to carry out a portion of an award and creates an assistance relationship between UCLA and the third party. Characteristics which support the classification of the third party entity as a subrecipient include when the third party (check all that apply):

- ☒ Performance represents an intellectually significant portion of the overall programmatic effort and is measured against the objectives of the program;
- ☒ There is an identified principal investigator for the subrecipient who has responsibility for making programmatic decisions;
- ☐ Work could result in the development of intellectual property;
- ☒ Is expected to author or co-author publications on the results of program/project work;
- ☐ Will need animal and/or human subject approval for its work;
- ☐ Provides cost sharing or matching funds;
- ☒ Will use the funds to carry out a program for a public purpose, as opposed providing goods or services for the benefit of the pass-through entity (i.e. UCLA).

Entities that include these characteristics are responsible for adherence to applicable program requirements specified in the Award

CONTRACTOR (VENDOR): A contract is for the purpose of obtaining goods and services for UCLA's own use and creates a procurement relationship between UCLA and the third party contractor. Characteristics indicative of a procurement relationship between UCLA and a contractor are when the third party receiving the funds (check all that apply):

- ☐ Provides the goods and services within normal business operations;
- ☐ Provides similar goods or services to many different purchasers;
- ☐ Performs a series of repetitive tests or activities requiring little or no discretionary judgment;
- ☐ Normally operates in a competitive environment;
- ☐ Provides goods or services that are ancillary to the operation of the program; and

Entities that include these characteristics are NOT subject to compliance requirements of the program as a result of the agreement, though similar requirements may apply for other reasons.

Description: *All of the characteristics listed above may not be present in all cases. Therefore, judgment must be used in classifying the agreement as either a subaward or a procurement contract. In determining whether an agreement constitutes a subaward or a procurement contract, the substance of the relationship is more important than the form of the agreement.*

Based on your analysis of the above checklist results, the organization is determined to be a

☒ **SUBRECIPIENT *** ☐ **CONTRACTOR (VENDOR)**

Digitally signed by Jeffrey D. Klausner
DN: cn=Jeffrey D. Klausner, o=UCLA, ou=UCLA David Geffen School of Medicine and Fielding School of Public Health, email=JDKlausner@mednet.ucla.edu, c=US

12/15/17

UCLA Principal Investigator Signature **Date**

***Submit this form along with Subrecipient Commitment Form as part of the proposal package for the minimum requirements**

ORA/DRA REVIEW:

☐ AGREE ☐ DISAGREE, RETURN TO DEPT COMMENTS _____

Name of Authorized Institution Official (e.g. DRA, OCGA) _____

Signature of Above Authorized Institution Official _____ Date _____

UCLA OCGA Office of Contract and Grant Administration

FDP EXPANDED CLEARINGHOUSE PILOT SUBRECIPIENT LETTER OF INTENT

This can ONLY be used in lieu of the UCLA OCGA Subrecipient Commitment Form by Institutions who are listed as part of the FDP Expanded Clearinghouse Pilot at: *https://fdpclearinghouse.org/organizations*

Subrecipient (Sub) Legal Name:	University of Alabama at Birmingham	Pass-Through Entity (PTE) Legal Name:	The Regents of the University of California, Los Angeles
Sub DUNS:	063690705	PTE DUNS:	092530369

Information above must match FDP Expanded Clearinghouse Pilot Entity Profile

Sub Principal Investigator:	Christina Muzny	PTE Principal Investigator:	Jeffrey Klausner
Sub Internal Project Identifier *(optional)*:	000519252	PTE Internal Project Identifier *(ex. PATS #)*:	

Project Title:	The Rea Phela 003 Health Study: Evaluating STI Screening Interventions and the Role of The Microbiome During Pregnancy		
Prime Awarding Agency:	NIH	Complete Project Period:	*Start:* 7/1/2018 *End:* 6/30/2023
Total Proposed Amount for Complete Project Period:	$ 208,328	Cost Sharing Amount for Complete Project Period:	$ 0

If Cost Sharing, a separate cost share budget and justification should be attached

***Project Facilities & Administrative Rates** (check one):*

☐ Federally negotiated F&A rate that matches our FDP Expanded Clearinghouse Pilot Entity Profile
☐ A reduced F&A rate dictated by the prime awarding agency. Rate:_____ Base Type:_____
☐ Not applicable (no indirect costs are requested by Sub)

Project Use Information:

Human Subjects ☐ Yes ☒ No	Animal Subjects ☐ Yes ☒ No	Stem Cells ☐ Yes ☒ No	Genomic Data Sharing ☐ Yes ☒ No

If Yes, please forward approval(s) to PTE PI as soon as available as approval(s) must be provided before any subaward can be issued

Institutional Authorized Official Information:

Sub Name/Title:		PTE Name/Title:	Raellen Garife
Sub Phone:		PTE Phone:	310-825-8112
Sub Email:		PTE Email:	domdra@mednet.ucla.edu
Sub Email for Awards (if different from above):	osp@uab.edu		
Sub *Place of Performance* the same as FDP Expanded Clearinghouse Pilot Entity Profile's: ☐ Yes ☐ No (for FFATA reporting purposes)			

This proposal has been reviewed and approved by the appropriate official(s) of Subrecipient, and certified to its accuracy and completeness. The appropriate programmatic and administrative personnel of Subrecipient involved in this application are aware of the prime awarding agency's policies, agree to accept the obligation to comply with award terms, conditions and certifications, and are prepared to establish the necessary inter-institutional agreement consistent with that policy.

The following documents are attached to this Statement of Intent:

☒ Sub Statement of Work (required)	☒ Sub Budget Justification (required)
☒ Sub Detailed Line Item Budget (required)	☐ Other: _____

Melinda T. Cotten for 12/12/17

Signature of Subrecipient's Authorized Official — Date

Assistant Vice President, Sponsored Programs

Name and Title of Authorized Official

COLLEGES AND UNIVERSITIES RATE AGREEMENT

EIN: 1636005396A6

ORGANIZATION:
University of Alabama at Birmingham
921 Administration Building 701 20th Street South
Birmingham, AL 35294-0109

DATE:09/13/2017

FILING REF.: The preceding agreement was dated 09/01/2016

The rates approved in this agreement are for use on grants, contracts and other agreements with the Federal Government, subject to the conditions in Section III.

SECTION I: INDIRECT COST RATES

RATE TYPES: FIXED FINAL PROV. (PROVISIONAL) PRED. (PREDETERMINED)

	EFFECTIVE PERIOD				
TYPE	**FROM**	**TO**	**RATE(%)**	**LOCATION**	**APPLICABLE TO**
PRED.	10/01/2015	09/30/2016	47.00	On-Campus	Organized Research
PRED.	10/01/2016	09/30/2019	48.50	On-Campus	Organized Research
PRED.	10/01/2015	09/30/2019	45.00	On-Campus	Instruction
PRED.	10/01/2015	09/30/2019	36.00	On-Campus	Other Sponsored Activities
PRED.	10/01/2016	09/30/2019	5.40	On-Campus	(1) IPA
PRED.	10/01/2015	09/30/2019	26.00	Off-Campus	All Programs
PROV.	10/01/2019	Until Amended			Use same rates and conditions as those cited for fiscal year ending September 30, 2019.

*BASE

Modified total direct costs, consisting of all direct salaries and wages, applicable fringe benefits, materials and supplies, services, travel and up to the first $25,000 of each subaward (regardless of the period of performance of the subawards under the award). Modified total direct costs shall exclude equipment, capital expenditures, charges for patient care, rental costs, tuition remission, scholarships and fellowships, participant support costs and the portion of each subaward in excess of $25,000. Other items may only be excluded when necessary to avoid a serious inequity in the distribution of indirect costs, and with the approval of the cognizant agency for indirect costs.

SECTION I: FRINGE BENEFIT RATES**

TYPE	FROM	TO	RATE(%)	LOCATION	APPLICABLE TO
FIXED	10/1/2017	9/30/2018	30.20	University	Faculty
FIXED	10/1/2017	9/30/2018	9.80	University	Part-time, Temporary & Irregular
FIXED	10/1/2017	9/30/2018	16.10	University	Post Docs
FIXED	10/1/2017	9/30/2018	35.40	University	All Others
FIXED	10/1/2017	9/30/2018	15.40	Hospital	Part-time, Temporary & Irregular
FIXED	10/1/2017	9/30/2018	18.40	Hospital	Residents, Fellows & Post Docs
FIXED	10/1/2017	9/30/2018	34.60	Hospital	All Others
PROV.	10/1/2018	Until amended			Use same rates and conditions as those cited for fiscal year ending September 30, 2018.

** DESCRIPTION OF FRINGE BENEFITS RATE BASE:

Salaries and Wages

Part-time Temporary/Irregular are not being combined with Students. The University has elected to waive any recovery for the Students.

SECTION II: SPECIAL REMARKS

TREATMENT OF FRINGE BENEFITS:

The fringe benefits are charged using the rate(s) listed in the Fringe Benefits Section of this Agreement. The fringe benefits included in the rate(s) are listed below.

TREATMENT OF PAID ABSENCES

Vacation, holiday, sick leave pay and other paid absences are included in salaries and wages and are claimed on grants, contracts and other agreements as part of the normal cost for salaries and wages. Separate claims are not made for the cost of these paid absences.

OFF-CAMPUS DEFINITION: For all activities performed in facilities not owned by the institution and to which rent is directly allocated to the project(s) the off-campus rate will apply. Grants or contracts will not be subject to more than one F&A cost rate. If more than 50% of a project is performed off-campus, the off-campus rate will apply to the entire project.

Equipment means article of nonexpendable, tangible personal property having a useful life of more than one year(s) and an acquisition cost of $5,000 or more per unit.

Fringe Benefits Include: FICA, Health & Life Insurance, Workers' Compensation, Salary Continuation, State Unemployment, Disability Insurance, Educational Assistance, Employee Training, EAP, Terminal Vacation Pay, Teacher's Retirement and TIAA/CREF, New Employee Orientation, Parental Leave, Benefit Focus, and Health EFX.

This agreement updates the Fringe Benefits Rates only.

The next Fringe Benefit rate proposal based on FYE 09/30/17 is due in our office by 03/31/18. The next Facilities and Administration rate proposal based on actual cost for FYE 09/30/2018 is due in our office by 03/31/2019.

SECTION III: GENERAL

A. LIMITATIONS:

The rates in this Agreement are subject to any statutory or administrative limitations and apply to a given grant, contract or other agreement only to the extent that funds are available. Acceptance of the rates is subject to the following conditions: (1) Only costs incurred by the organization were included in its facilities and administrative cost pools as finally accepted: such costs are legal obligations of the organization and are allowable under the governing cost principles; (2) The same costs that have been treated as facilities and administrative costs are not claimed as direct costs; (3) Similar types of costs have been accorded consistent accounting treatment; and (4) The information provided by the organization which was used to establish the rates is not later found to be materially incomplete or inaccurate by the Federal Government. In such situations the rate(s) would be subject to renegotiation at the discretion of the Federal Government.

B. ACCOUNTING CHANGES:

This Agreement is based on the accounting system purported by the organization to be in effect during the Agreement period. Changes to the method of accounting for costs which affect the amount of reimbursement resulting from the use of this Agreement require prior approval of the authorized representative of the cognizant agency. Such changes include, but are not limited to, changes in the charging of a particular type of cost from facilities and administrative to direct. Failure to obtain approval may result in cost disallowances.

C. FIXED RATES:

If a fixed rate is in this Agreement, it is based on an estimate of the costs for the period covered by the rate. When the actual costs for this period are determined, an adjustment will be made to a rate of a future year(s) to compensate for the difference between the costs used to establish the fixed rate and actual costs.

D. USE BY OTHER FEDERAL AGENCIES:

The rates in this Agreement were approved in accordance with the authority in Title 2 of the Code of Federal Regulations, Part 200 (2 CFR 200), and should be applied to grants, contracts and other agreements covered by 2 CFR 200, subject to any limitations in A above. The organization may provide copies of the Agreement to other Federal Agencies to give them early notification of the Agreement.

E. OTHER:

If any Federal contract, grant or other agreement is reimbursing facilities and administrative costs by a means other than the approved rate(s) in this Agreement, the organization should (1) credit such costs to the affected programs, and (2) apply the approved rate(s) to the appropriate base to identify the proper amount of facilities and administrative costs allocable to these programs.

BY THE INSTITUTION:

University of Alabama at Birmingham

(INSTITUTION)

Stephanie Mullins

(SIGNATURE)

Stephanie Mullins

(NAME)

UAB Chief Financial Officer | Associate VP for Financial Affairs

(TITLE)

9/29/17

(DATE)

ON BEHALF OF THE FEDERAL GOVERNMENT:

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Darryl W. Mayes -S

Digitally signed by Darryl W. Mayes -S
DN: c=US, o=U.S. Government, ou=HHS, ou=PSC, ou=People, 0.9.2342.19200300.100.1.1=2000131669, cn=Darryl W. Mayes -S
Date: 2017.09.19 09:09:50 -04'00'

(SIGNATURE)

For Arif Karim

(NAME)

Director, Cost Allocation Services

(TITLE)

9/13/2017

(DATE) 6985

HHS REPRESENTATIVE: Shon Turner

Telephone: (214) 767-3261