1) Clinical Trials Unit at National AIDS Research Institute, Pune, India: (NARI CTU)	
Principal Investigator	Dr. A.R. Risbud, Scientist 'F'
Co-Principal Investigator(s)	Nil
Other Investigator(s)	Nil
Category / Nature	Prevention and Therapeutic Randomized Controlled Clinical Trials
Collaboration / Participating Centers	Nil
Funding Agency(ies) / Sponsors	The study is being funded by the National Institutes of Health of the US government through the Division of AIDS.
Budget	12 crores
Study Period	2007-2014
Objectives	Nil
Description	This study provides support to building clinical, laboratory, data management and community work infrastructure to carry out Phase I, II and III clinical trials with evaluable biological end-points in the areas of HIV prevention and therapeutic research. The clinical trials will be conducted by the Clinical Trials Unit [CTU] located at NARI through the following Clinical Research Sites in Pune city. 1. NARI CRS at National AIDS Research Institute 2. NIV CRS at National Institute of Virology 3. Gadikhana CRS at Dr. Kotnis Municipal Dispensary, Pune 4. Womens' study clinic, Ganesh Peth, Pune National AIDS Research Institute (NARI), Pune, is a NIH designated “Unit for HIV / AIDS Clinical Trials Network” to participate in clinical trials conducted by global networks of HIV / AIDS. This 7-year competitive research grant was awarded to NARI during July 2007 through a global request for application (RFA) process and to participate in three HIV / AIDS global networks of the NIAID / NIH, viz., Prevention of HIV infection [HPTN]; Optimization of clinical management including co-morbidities

	[ACTG]; and Microbicides [MTN]. The award supports a CTU administrative and community component and four clinical research sites (CRSs) to implement network driven protocols. The activities carried out under this project are steered by the CTU Scientific Advisory Group and CTU Internal Evaluation Committee and are regulated by the Institutional Scientific Advisory Committee, Ethics Committee, and Community Advisory Board. Status of clinical trials under different networks at the NARI CTU : • HIV Prevention Trials Network: Ongoing: HPTN 052 study: Antiretroviral therapy for prevention of sexual transmission of HIV in among HIV discordant couples. Enrollment completed, follow-up ongoing • AIDS Clinical Trials Group 1) Completed studies - ACTG 5175, ACTG 5190, ACTG 5199, ACTG 5221 and ACTG 5253 studies 2) Planned Studies - ACTG 5274 • Microbicides Trials Network: Completed studies - MTN 005
Current Status	Nil
Publications	Nil
Presentations	Nil

2) Study to Understand Prevention and Explore Barriers for Women: A multi-stakeholder perspective on vaginal microbicides and other NPTs	
Principal Investigator	Dr. Seema Sahay, NARI
Co-Principal Investigator(s)	Dr. S. Thilkavathi (NIE, Chennai) Dr. Mubashir Angolkar (KLE University, Belgaum)
Other Investigator(s)	NARI Mrs. N. Joglekar, Mrs. S. Sane
Category / Nature	Prevention study Community based multisite qualitative research
Collaboration / Participating Centers	NIE, Chennai JNMC, KLE University, Belgaum
Funding Agency(ies) / Sponsors	Indian Council of Medical Research
Budget	INR 4,430520/-
Study Period	2012-2014
Objectives	To determine social, cultural and behavioral paradigm for access and willingness and barriers to use vaginal microbicides and other new prevention technologies in selected high HIV prevalence districts in India.
Description	The prime objective of this research study is to provide an understanding of the triggers for women's acceptance and willingness for usage of vaginal microbicides (VM) and other new prevention technologies (NPT) to prevent HIV infection in with a focus on different high and low risk women/ population in India. The study is also designed to explore the mindset, needs and concerns of the service providers towards NPTs and VMs and bring in acceptance among women and community across selected high HIV prevalence districts. This qualitative study proposes to feed into designing of BCC strategies and IEC materials which in turn helps in increasing the accessibility and coverage of VM and NPTs. We propose to study a range of stakeholders to explore following issues: • Knowledge, attitudes, beliefs, regarding risk behaviors and threat and consequences of HIV infection especially in context of women

	• Perceptions, beliefs and attitudes towards using VM & NPT and willingness to use • Barriers to potential use VM and NPT
Current Status	Ongoing Project
Publications	Nil
Presentations	Nil

3) HIV Vaccine Immunogen Design: Identification of T-cell epitopes associated with control of viral replication in Indian and South African HIV-1 infected individuals	
Principal Investigator	• Dr. Udaykumar Ranga Molecular biology & Genenitic Unit Jawaharlal Nehru Centre for Advanced Scientific Research • Dr. Carolyn Williamsaon Division of Medical Virology Institute for Infectious Diseases & Molecular Medicine University of Cape Town Health Sciences Faculty
Co-Principal Investigator(s)	• Dr. Madhu Vajpayee, Laboratory Head, HIV & Immunology Divison (Incharge VCTC) Department of Microbiology All Indian Institute of Medical Science • Dr. Madhuri Thakar, Scientist 'D' National AIDS Research Institute • Dr. Gray Clive, Chief Specialist Scientist, AIDS Research Unit, NICD • Dr. Sengeziwe Sibeko Project Director , Centre for the AIDS Programme of Research in South Africa
Other Investigator(s)	Nil
Category / Nature	Prevention Research
Collaboration / Participating Centers	• National Institute for Communicable Diseases (NICD) • Centre for the AIDS Programme of Research in South Africa (CAPRISA) • Jawaharlal Nehru Centre for Advanced Scientific Research • All India Institute of Medical Science • Institute for Infectious Diseases and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town

Funding Agency(ies) / Sponsors	INDO-SA DST
Budget	Rs. 22,66,600/-
Study Period	2011 to 2014
Objectives	HIV Vaccine Immunogen Design: Identification of T-cell epitopes associated with control of viral replication in Indian and South African HIV-1 infected individuals
Brief description (one paragraph)	In response to a mandate of the Indo South Africa joint committee on S&T Cooperation, this application proposes a joint project from Indian and South African scientists on HIV vaccine immunogen design. The development of a safe and effective HIV-1 vaccine is a critically important global health priority. Much of the recent effort has focused on the generation of effective cytotoxic T lymphocyte (CTL) responses as studies have shown that HIV-specific T cells can control the initial burst of viremia during acute infection, and in experimental monkey models it has been demonstrated that CTLs are important for clearing circulating levels of simian immunodeficiency virus. Despite recent failures of a proof-of-concept T-cell based clinical trial in the USA and South Africa, as well as modest success in an CTL/antibody-based clinical trial in Thailand, a CTL-based vaccine is still considered important for protection, mitigating disease in those who become infected, and reducing secondary HIV transmission. The first step towards improving current T-cell based vaccine immunogen design is the identification of T cell responses in HIV-infected individuals associated with the control of viral replication. HIV-1 has extraordinary diversity, both at an inter- and intra-clade level, and this diversity together with the capacity of the virus to evade adaptive immune responses, represents unprecedented challenges for vaccine development. At an individual level, studies have shown that the effectiveness of T cell responses in natural infection is a complex interplay between viral diversity, the Human Leukocyte Antigen background of the infected individual, and epitopes recognized by T cells. It is therefore important to study T cell immunity in conjunction with the infecting viral sequences being targeted, and the HLA type of the infected host. At a population level, HIV-1 subtype C is the dominant virus in both India and South Africa and, although there have been numerous studies which have characterized dominant epitope regions,

	there is a need for further studies as: firstly, T cell responses may differ between populations due to diverse HLA backgrounds that are found between South Africans and Indians; and secondly there are new developments in methodological approaches that will allow greater insights into the functionality of T cell immunity and the effect of CTL escape on viral fitness. Through characterization of clinical disease progression, together with a detailed evaluation of immune responses and viral evolution we will: i) identify immunodominant epitopes recognized by T cells in South African and Indian HIV-1 infected individuals; ii) assess the in vitro function of the identified epitopes by the ability of epitope-specific T cells to inhibit virus replication; iii) monitor viral evolution and compare patterns of CTL escape in South African and Indian HIV infected individuals and iv) determine the impact of viral escape on viral replication kinetics using infectious molecular clones. The overall goal is to define antigens that are known to be associated with control of HIV replication for inclusion into HIV vaccines.
Current status	Ongoing
Publications	Nil
Presentations	Nil

4) Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Sero-discordant Couples [HPTN 052 study]	
Principal Investigator	Dr. Sanjay Mehendale Scientist 'G' (National Institute of Epidemiology)
Investigator of Record	Dr. Sheela V. Godbole M.D
Category / Nature	HIV Prevention Research, Randomized Controlled Clinical Trial
Collaboration / Participating Centers	Family Health International and Johns Hopkins University, USA.
Funding Agency(ies) / Sponsors	The study is being funded by the National Institutes of Health of the US government through HIV Prevention trials Network and Family Health International; funded by the Division of AIDS.
Budget	Nil
Study Period	Nil
Objectives	Primary Objectives: The primary objective of the study is to compare the rates of HIV infection among partners of HIV-infected participants in the two study arms below: (1) Antiretroviral therapy upon enrollment plus HIV primary care. (2) HIV primary care, without initiation of antiretroviral therapy until the participant has two consecutive measurements of a CD4+ cell count within or below the range of 200-250 cells/mm^3, or develops an AIDS-defining illness. Secondary Objectives: To determine the long-term safety of two ART regimen strategies (ART immediately upon enrollment vs, ART when the participant has two consecutive measurements of a CD4+ cell count within or below the range of 200-250 cells/mm^3 or develops an AIDS-defining illness) for the treatment of HIV-1 infection. To characterize and compare the patterns and rates of antiretroviral drug resistance of two antiretroviral treatment strategies. To assess factors associated with and to compare adherence of two antiretroviral treatment strategies. To evaluate the usefulness of measures of virologic and immunologic efficacy, and measures to detect antiretroviral drug resistance. To determine, characterize, and compare the rates of AIDS-defining

	illnesses, sexually transmitted diseases, opportunistic infections, and immune reconstitution syndromes, with regard to outcomes and survival as observed in different geographic settings and by antiretroviral treatment strategies. To determine and characterize the rates of antiretroviral drug-associated toxicities observed in different geographic settings and by treatment strategies. To evaluate the effectiveness of couples HIV counseling and characterize the patterns of sexual behavior in couples in both arms of the study. To characterize and compare Quality of Life (QOL) indicators in different geographic settings and by antiretroviral treatment strategies.
Description	Brief description of the study: Multicentre, Randomized (1:1), Open Label, Phase III two arm Randomized Controlled Clinical Trial. The study is being conducted in different parts of the world at sites in India, Thailand, Malawi, Zimbabwe, South Africa, Brazil Study rationale: Sexual Transmission of HIV is the commonest mode of transmission especially in India. Plasma HIV-1 RNA levels can be correlated with the sexual transmission of HIV. ART decreases the concentration of HIV-1 RNA not only in blood but also in male and female genital secretions, rectal mucosa, and saliva, thereby reducing the levels of HIV innoculum to which the susceptible partner is exposed. Hence reducing Plasma HIV-1 levels may decrease transmission of HIV-1. Thus, this study will assess the use of Anti Retroviral Therapy for Prevention of HIV Transmission in HIV discordant couples [one partner is HIV seropositive (INDEX) and the other is HIV seronegative (PARTNER)]. The study will also try to provide evidence in an RCT setting on when is it better to initiate antiretroviral therapy in HIV-1 infected persons: early or later. The Participants would be randomized to two Arms in this study: Arm 1: Immediate ART + Primary Care and Arm 2: Delayed ART + Primary HIV Care with initiation of ART when 2 consecutive CD4 counts are < 250 per cumm or AIDS defining illness occurs. Protocol Status: Closed to Accrual, Follow up Ongoing Study Size: 175 couples enrolled at NARI and approximately 1762 couples enrolled across all sites, Study Design: The study is a Phase III, two-arm, randomized, controlled,

	multi-center trial. Study Population: HIV serodiscordant couples in which the HIV-infected partner is ART naïve and has a CD4+ cell count of 350-550 cells/mm^3. Study Duration: All couples will be followed until the last couple enrolled completes their 60-month follow-up visit (2015). Treatment Regimen: HIV-infected index cases will be assigned at random in a 1:1 ratio to one of two treatment arms: ARM 1: ART upon enrollment plus HIV primary care. ARM 2: HIV primary care without initiation of ART until the participant has two consecutive measurements of a CD4+ cell count within or below the range of 200-250 cells/mm^3, or develops an AIDS-defining illness. The ART drugs available for the study are Combivir [3TC/ZDV], ATV, EFV, NVP, TDF, 3TC, ddI-EC, d4T, Kaletra/Aluvia [LPV/r], and Truvada [FTC/TDF].
Current Status	Closed to Accrual, Follow up Ongoing
Publications	1. Prevention of HIV-1 infection with early antiretroviral therapy. NEJM. 2011, 365: 493-505 PMCID: 3200068 Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, Hakim J, Kumwenda J, Grinsztejn B, Pilotto JH, **Godbole SV, Mehendale S**, Chariyalertsak S, Santos BR, Mayer KH, Hoffman IF, Eshleman SH, Piwowar-Manning E, Wang L, Makhema J, et al. 2. Analysis of genetic linkage of HIV from couples enrolled in the HIV Prevention Trials Network 052 trial. J Infect Dis. 2011, 204: 1918-26 PMCID: 3209811 Eshleman SH, Hudelson SE, Redd AD, Wang L, Debes R, Chen YQ, Martens CA, Ricklefs SM, Selig EJ, Porcella SF, Munshaw S, Ray SC, Piwowar-Manning E, McCauley M, Hosseinipour MC, Kumwenda J, Hakim JG, Chariyalertsak S, de Bruyn G, Grinsztejn B, et al. 3. HIV treatment as prevention and HPTN 052. Curr Opin HIV AIDS.2012, 7: 99-105 PMCID: 3486734 Cohen MS, McCauley M, Gamble TR 4. Establishing HIV treatment as prevention in the HIV Prevention Trials Network 052 randomized trial: an ethical odyssey. Clin Trials. 2012, 9: 340-7 PMCID: 3486723 Cohen, MS, McCauley, M, Sugarman, J **Abstracts** presented at the XIX International AIDS Conference, 22-27 Washington DC USA July 2012

	1. Sustained treatment as prevention: continued decreases in unprotected sex and virological suppression after HAART initiation among participants in HPTN 052 (Oral Poster Presentation). 2. Time-to-ART-Initiation: A Risk Factor Analysis of the HPTN 052 HIV-infected Partners on Delayed Therapy. (Poster TUPE083). 3. Effect of early versus delayed initiation of antiretroviral therapy (ART) on clinical outcomes in the HPTN 052 randomized clinical trial. (Late-Breaker Presentation THLBB05). 4. The cost effectiveness of treatment as prevention: analysis of the HPTN 052 trial. (Late-Breaker Presentation FRLBC01).
Presentations	Presented as a Poster at CROI, 2013 3-6 March 2013 Atlanta USA. Acceptance of ART in the Delay Arm after Notification of Interim Study Results: Data from HPTN 052. • The decision not to initiate ART in almost 20% of the population notified of the study results persists even a year after notification. As this is a population that was originally willing to be randomized to initiate ART at higher CD4 cell counts (inclusion criteria of 350/mm3 < CD4 ≥550/mm3), this result implies that the propensity to decline ART could be higher in the general population. • In addition, this result is critical to researchers modeling and testing the “test and treat” approach to community-based HIV prevention, as the approach cannot be successful without very high uptake of ART.

5) Understanding and quantifying domestic violence among married women in India	
Principal Investigator	Dr. Seema Sahay, NARI
Other Investigator(s)	Dr. Ameeta Kalokhe, Global Health fellow, Emory University
Category / Nature	Community based prevention study
Funding Agency(ies) / Sponsors	*National AIDS Research Institute and the Fogarty International Center Global Health Program for Fellows and Scholars*
Budget	$15,000 (USD)
Study Period	2012-2013
Objectives	To better understand the determinants, circumstances, acceptability, levels of physical, sexual, and emotional DV and control across geographically and culturally distinct regions of India. To develop a culturally-tailored scale to measure DV in married women across geographically and culturally distinct regions of India using insight gained from Aim 1. To test and validate the culturally-tailored DV scale in a diverse cohort of married women in Pune, India
Description	Recent Indian literature demonstrates that domestic violence (DV) and cultural norms that propagate social subordination play significant roles in determining the capacity of a woman to protect herself from HIV and other STIs.[4-8] Women who experience abuse are less likely than non-abused counterparts to report safe-sex negotiation and condom use, and experience increased abuse when they negotiate condom use or refuse sexual intercourse. Furthermore, abused women are more likely to have partners who report high-risk behaviors (i.e. having multiple sexual partners, engagement in transactional sex, and substance abuse). According to data from the 2006 Indian National Family Health Survey approximately one-third of married Indian women experience physical DV

	with or without sexual DV from their current husband. In a study by Silverman et al, women who experienced both physical and sexual DV had an almost four-fold higher odds of being HIV-infected compared to those who denied experiencing abuse. Higher frequencies of STIs have also been reported among women who are abused. **This data suggests that HIV and STI preventive interventions targeting Indian women should incorporate a component of DV screening and management.** A scale that effectively measures the DV experiences of married women in India is greatly needed. While over 80 studies in the Indian DV literature have emerged in the past decade, all utilized either non-validated screening tools or scales that were developed for use in Western culture. Due to cultural differences, such adapted scales likely fall short in characterizing the DV experiences of Indian women. For example, women who live in joint families may be subject to DV perpetration by in-laws in addition to the intimate partner. Second, screening of severe forms of physical violence may fail if questions are limited to the use of guns and knife violence rather than tools more readily available in India such as kerosene and chemical-induced burning, sticks, stones, and belts. Third, DV through exertion of control and isolation is commonplace and often considered a societal norm rather than violence; therefore, screening questions must address specific controlling behaviors to elicit such histories. **Thus the development and validation of a culturally-tailored scale is necessary to screen for, measure, and accurately characterize the DV experiences of married Indian women.**
Current Status	Ongoing Project
Publications	Nil
Presentations	Nil