

# Disease Specific Documents for XII Plan

*HIV/AIDS*



**INDIAN COUNCIL OF MEDICAL RESEARCH**

# Disease Specific Documents for XII Plan

## HIV/AIDS

**High Power Committee to Evaluate the Performance of ICMR, 2012-13**



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1. National AIDS Research Institute (NARI), Pune ( lead institute)
2. National Institute of Medical Statistics (NIMS), New Delhi
3. National Institute for Research in Tuberculosis (NIRT), Chennai
4. National Institute of Epidemiology (NIE), Chennai
5. National Institute of Nutrition (NIN), Hyderabad
6. Regional Medical Research Centre (RMRC), Dibrugarh
7. Regional Medical Research Centre (RMRC), Belgaum
8. Rajendra Memorial Research Institute of Medical Science (RIRIMS), Patna
9. National Institute of Cholera and Enteric Disease (NICED), Kolkata
10. National Institute of Immunohaematology (NIIH), Mumbai
11. National Institute of Research in Reproductive Health (NIRRH), Mumbai

**1. Current situation of Disease with contribution of ICMR**

HIV infection and AIDS pose one of the most formidable challenges to the development, progress and stability of our respective societies and the world at large and require an exceptional and comprehensive global response that takes into account the fact that the spread of HIV is often a consequence and a cause of poverty. Globally, 34.0 million [31.4 million–35.9 million] people were living with HIV at the end of 2011. An estimated 0.8% of adults aged 15-49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions. Worldwide, the numbers of people newly infected continue to fall: the number of people (adults and children) acquiring HIV infection in 2011 (2.5 million [2.2 million–2.8 million]) was 20% lower than in 2001.

The first cases of HIV infection and AIDS in India were detected in 1986 and since then HIV infection has been reported in all states and union territories. India responded promptly to the HIV/AIDS challenge at the initial stage itself by setting up an AIDS Task Force under the Indian Council of Medical Research and a National AIDS Committee headed by the Secretary, Ministry of Health & Family Welfare. ICMR provided leadership for establishment of network of laboratories for HIV testing. The data generated by these centres highlighted the fact that HIV infections were increasing rapidly in the country, transfusion transmitted infection was a serious problem and that there was need for

National efforts to control the epidemic with strong regulation of blood transfusion services. In 1992, the Government of India demonstrated its commitment to combat the disease with the launch of the first National AIDS Control Programme (NACP-I) as a comprehensive programme for prevention and control of HIV/AIDS in India. To strengthen the management capacity, a National AIDS Control Board (NACB) was constituted and an autonomous National AIDS Control Organization (NACO) was set up for project implementation. The rapidly spreading AIDS epidemic underlined the fact that the national efforts for control of HIV infection needed to be backed by quality research. It was also realized that AIDS, being a multifaceted disease, needed multi-disciplinary research involving virology, immunology, microbiology, clinical research, epidemiology, field based trials and social and behavioral research. Thus in the year 1992, the National AIDS Research Institute (NARI), an institute devoted exclusively to HIV/AIDS that could undertake research of such diversity and magnitude was established to meet this requirement. In November 1999, the second National AIDS Control Programme (NACP-II) was launched. Based on the experience gained in Tamil Nadu and a few other states, along with the evolving trends of the HIV/AIDS epidemic, the focus shifted from raising awareness to changing behaviours, decentralization of programme implementation to the state level and greater involvement of NGOs. The third phase of National AIDS Control Programme (NACP-III), implemented during 2007-2012, was grounded on a strong structure of policies, programmes, schemes, operational guidelines, rules and norms. NACP-III aimed at halting and reversing HIV epidemic in India over the five-year period by scaling up prevention effort among High Risk Groups (HRG) and General Population and integrating them with Care, Support & Treatment services. Thus, Prevention and Care, Support & Treatment (CST) formed the two key pillars of all the AIDS control efforts in India. Today, the Strategic Information Management and institutional strengthening activities provide the required technical, managerial and administrative support for implementing the core activities under NACP-III at national, state and district levels.

### **Current scenario of HIV in India**

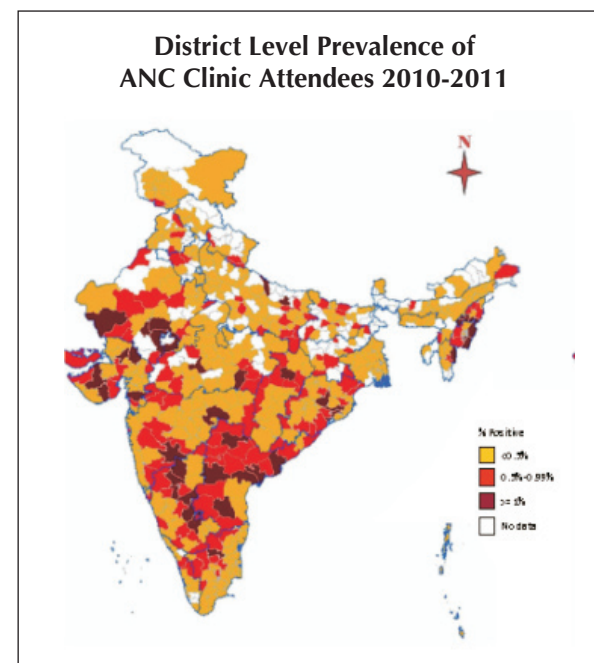
HIV epidemic in India is concentrated among populations at high risk due to their risk behaviours such as female sex workers (FSWs), men having sex with men (MSM), intravenous drug users (IDUs) and the Indian epidemic is driven by interactions within as well as between these groups and the general population. National epidemic projection and modeling based on data from sentinel surveillance and other surveys has revealed that the estimated annual HIV incidence has declined by about 56 percent over the last decade (2000-2009). Wider access to ART has resulted in decline of the number of people dying due to AIDS-related causes. While declining HIV trends are evident at national level as well as in most of the states, some previously low prevalence and vulnerable states have shown rising trends in HIV epidemic, warranting focused prevention efforts in these states. HIV prevalence is showing declining trends among Female Sex Workers both at national level and in most of the states. However, other High Risk Groups such as 'MSM', IDUs and Bridge Population such as 'Single Male Migrants' are emerging as important risk groups in many states.

NIMS, with assistance from NARI, NIE and NICED, has made major contribution to the annual Sentinel Surveillance for HIV among Anti-natal clinic attendees (ANC), sexually transmitted disease (STD) patients and other High Risk groups in India. NIMS (Delhi) has provided leadership for the exercise of estimating the numbers of HIV infected in India and understanding the trends of epidemic. Over the last decade India has

demonstrated an overall reduction of 57% in estimated annual new HIV infections (among adult population) ; from 2.74 lakhs in 2000 to 1.16 lakhs in 2011. Adult HIV prevalence among males and females is estimated at 0.32% and 0.22% respectively. A recent analysis of the impact of targeted interventions showed increase in condom use among FSWs in the high HIV prevalence southern states of India. A significant decline in HIV and syphilis prevalence has occurred in high prevalence southern states among FSWs and young antenatal women. Among young (15-24 years) antenatal clinic attendees significant decline was observed in HIV prevalence from 2001 to 2008 (OR = 0.42, 95% CI 0.28-0.62). In 2011, among the states, Manipur has shown the highest estimated adult HIV prevalence of 1.22%, followed by Andhra Pradesh (0.75%), Mizoram (0.74%), Nagaland (0.73%), Karnataka (0.52%), Goa (0.43%) and Maharashtra (0.42%). Besides these, Odisha, Gujarat, Tamil Nadu, and Chandigarh have shown estimated adult HIV prevalence greater than national prevalence (0.27%). However, rising trends of new infections are noted in some of the low prevalence states. Declines have been achieved among MSM (7.41% in 2007 to 4.43% in 2011) also, though several pockets in the country show higher HIV prevalence among them with mixed trends. Stable trends have been recorded among Injecting Drug Users at national level (7.23% in 2007 to 7.14% in 2011). Besides North Eastern states where declines have been achieved, newer pockets of high HIV prevalence among IDU have emerged over the last few years, in the locations such as Punjab, Chandigarh, Delhi, Mumbai, Kerala, Odisha, Madhya Pradesh, Uttar Pradesh & Bihar. In certain North Indian states, evidence indicates the possible role of migration in fuelling HIV epidemics. Besides high risk migrants, long distance truckers also show high levels of vulnerability and form an important part of bridge population. Prevention strategies for IDU in the newer areas have been initiated recently and are prioritised for further scale up during the next five years. Scale up of Opioid Substitution Therapy and other harm reduction strategies are given focus in the North Eastern states where injecting drug use is identified as the major driver of the epidemic.

In the eight states of North India, where migration is increasingly being identified as playing a role in HIV transmission, NACO is implementing a revised migrant intervention strategy with focus at source, transit as well as destination points. NARI has recently taken up a study on migrants in and around Pune.

**HIV Subtypes and Mosaic Viruses:** HIV-1 infection is common in India while HIV-2 infection is seen infrequently. Among those who are infected by HIV-1, subtype C is the predominant sub-type and other subtypes such as A and B are also reported occasionally. It is likely that the risk of transmission and rate of progression to advanced HIV disease is likely to vary by these sub-types. HIV-1 C subtype has been reported to



have a higher risk of transmission and spread. In order to study biology of Indian HIV viruses NARI has established a virus bank that will enable any scientist within India to study the virus.

The changing patterns in prevalence of the subtypes and emergence of recombinant viral strains can potentially impact HIV vaccine development strategies in India. NARI and NICED have carried out a number of molecular epidemiology studies in India and have documented the presence of recombinant viruses in different parts of the country. NICED documented shift from HIV-1 subtype B to HIV-1 subtype C in Manipur. Manipur also has larger proportion of recombinant viruses. NARI and NICED have documented novel HIV-1 subtype B and Subtype C recombinant viruses in Manipur.

**ART Roll Out:** The total number of people living with HIV/AIDS (PLHIV) in India is estimated at 21 lakh in 2011. Children (<15 yrs) account for 7% of all infections, while 86% are in the age –group of 15-49 years. Of all HIV infections, 39% (8.16 lakh) are among women. The advent of antiretroviral therapy (ART) has transformed the face of HIV/AIDS from a deadly disease to a manageable chronic condition for most infected individuals. Antiretroviral treatment not only reduces the viral load and reconstitutes immune function, but also decreases new infections by limiting viral transmission. Provision of free Antiretroviral Therapy (ART) for eligible persons living with HIV (PLHIV) was launched on 1 April, 2004 by NACO in eight government hospitals located in six high prevalence states. As per the revised National guidelines, ART is initiated in patients with CD4 count less than 350/mm<sup>3</sup> with WHO stage I and II and irrespective of CD4 count in patients with WHO stage III and IV. ART is initiated depending upon the stage of infection. The ARV drugs are available as Fixed Drug Combinations for first line, alternative first line and second line regimens in order to ensure good levels of adherence, ease in logistics related issues and ensure uniformity all across the country. The first line drugs for adults in the National ART roll out programme include Zidovudine, Tenofovir, Lamivudine, Nevirapine and Efavirenz and second line drugs include Atazanavir/ ritonavir and Lopinavir/ ritonavir. It is estimated that the scale up of free ART since 2004 has saved over 1.5 lakh lives in the country till 2011 by averting deaths due to AIDS-related causes. At the current pace of scale up of ART services, it is estimated to avert around 50,000 – 60,000 deaths annually in the next five years. Currently (as on January 2012), there are 342 fully functional ART centres. NARI (Pune) and RMRI (Patna) have full fledged ART centres within ICMR network. A total of 3200 and 4774 patients have been registered at NARI ART centre (Pune) and RIMS ART Centre (Patna) respectively. The ART centres give the opportunity to identify gaps and relevant research are being carried out by a cluster of ICMR institutes to fill these gaps and support the national program.

**Living longer with HIV:** as access to ART improves more and more people with HIV are living longer. Studies will now have to focus on HIV associated conditions like malignancies, and metabolic conditions and complications. The first ever population based HIV and Cancer registry match study in Pune by NARI has shown the association of HIV infection with many non-AIDS defining malignancies. The well regulated ART centers offer opportunities for research studies relevant to the Indian population.

**HIV and Co-infections including Tuberculosis:** Tuberculosis is the commonest opportunistic infection among people living with HIV. NARI published one of the earliest reports on the increase of prevalence of HIV among newly diagnosed TB patients in Pune. As more evidence



of increased TB burden due to HIV emerged, the National AIDS Control Programme (NACP) and Revised National Tuberculosis Control Programme (RNTCP) have established mechanisms for cross-referrals at different levels in the TB and HIV national programmes. Activities for prevention of TB in PLHIV are grouped as 3 “I’s” as follows: Air borne Infection control (Measures to minimize spread of airborne infection in HIV care settings), Isoniazid Preventive Treatment (IPT), and Intensified TB case finding (ICF) at HIV care settings (early detection and treatment, which minimizes mortality and morbidity and also curtails further spread of infection). A total of 73,073 HIV infected TB cases were detected in 2011 through the HIV/TB cross referrals at ICTC and ART centres. To combat HIV-TB co-infecting, a study is being conducted by National Institute of Research in Tuberculosis (NIRT) Chennai, on operational feasibility and efficacy of Isoniazid preventive treatment (IPT) in the Indian ART programme scenario at 12 ART centres. Findings from this study will guide the national programmes on the prospect of adoption of IPT as a programme strategy.

Although tuberculosis is the most frequent clinical condition reported in HIV infected, other co-infections like Hepatitis B and Hepatitis C are also a cause of concern. Cervical abnormalities due to high prevalence of Human Papilloma Virus (HPV) infection have been reported in HIV infected females in India making screening and prevention activities for cervical cancer among HIV infected women an important agenda.

**Leishmania:** India has the largest burden of Visceral Leishmaniasis (VL). The WHO has identified co-infection with HIV as a major threat to control of VL. HIV-infected people are particularly vulnerable to VL, while VL accelerates HIV replication and progression to AIDS. The risk of treatment failure for VL is high, regardless of the drug used, and all co-infected patients will relapse with high mortality rates unless they are given antiretroviral therapy (ART). The Rajendra Memorial Research Institute of Medical Sciences, Patna has been involved in research in this field.

**Laboratory support to programme:** NACO launched “National External Quality Assessment Scheme” (NEQAS) in year 2000 to assure standard quality of the HIV tests being performed in the programme. NARI functions as an apex laboratory for conducting the EQAS for HIV serodiagnosis and CD4 cell estimations. The EQAS operates through a chain of National Reference Laboratories and state reference laboratories. The EQAS functions through trainings at different levels and providing proficiency panels. The EQAS has resulted in improving the performance of the laboratories. Besides NARI, other Institutes of ICMR, NICED and NIIH play important role in this activity. While conducting the national EQA to 240 CD4 estimating centers and providing training and troubleshooting has resulted in improved performance of these labs, the % coefficient of variation has reduced from 16% to 6%. The indigenously developed stabilized blood has reduced the cost of EQA by 70%.

**ICMR’s Response to HIV/AIDS:** In the light of the complex dynamics of HIV as sociological and biological disease, taken together, it became increasingly clear that HIV is eliciting dramatic, multilayered effects and shifts both in science and control. While a single or stand alone strategy could not have offered a definitive influence on the myriad issues of HIV/ AIDS, in the year 1992 when NACP-I was being launched, Indian Council of Medical Research established a multidisciplinary institute, the National AIDS Research Institute at Pune, dedicated solely to HIV. This institute endeavored to explore productive new avenues and approaches for investigation and analysis. HIV and AIDS are affecting every region of the country although drivers of the epidemic, vulnerabilities, aggravating factors and the populations that are affected could be



distinctive, and therefore the responses must be uniquely tailored to each particular situation, taking into account the local epidemiological and social context. Realizing the unique epidemiology of HIV, the spread of the disease in specific geographical pockets of the country and facing the challenges of opportunistic infections especially HIV-TB dual infection, several other ICMR institutes and Regional Medical Research Centres (Table 1) initiated work in their respective areas of expertise or epidemic. The various institutes of ICMR are providing scientific back up to NACO in finding solution to outstanding problems in AIDS control through behavioral, basic, applied and operational research.

The United Nations Sixth Millennium Goal targets for halt and begin to reverse the spread of HIV/AIDS by year 2015. This is not achievable without equal emphasis on prevention and treatment and management of HIV/AIDS. While a robust NACP is being implemented, ICMR focused its research agenda on Prevention of HIV infection, Generating new epidemiological data, Care and Treatment of those infected with HIV and understanding the Biology of viruses circulating in India. In the prevention research, studies on HIV vaccines and microbicides have been flagship programmes of ICMR. In addition other prevention options such as circumcision, education and awareness are being explored. Research in HIV treatment and care is focused on supporting clinical trials for optimization of treatment, adherence to treatment and anti-retroviral drug resistance, drug discovery and PK-PD studies on anti-HIV drugs. Studies in HIV biology have focused on understanding the mechanisms of virus entry and factors influencing neutralization potentials, coreceptor usage, molecular characterization of the strains and other immune mechanisms involved in the control of HIV. In addition, the institutes have contributed significantly in the success of NACP through training, quality control, surveillance and other activities.

In view of aforesaid background, research studies related to HIV may be focused on the themes as described below. The research findings from these themes will help in preventing the spread of the disease while improving the lot of those who are already infected.

1. **Care and Support:** Key areas for research related to care and support of HIV infected individuals include studies to identify optimal and simple second and third line antiretroviral treatment regimens; studies to prevent/minimize emergence of drug resistance and improve and measure adherence; optimal management and prevention of co-infections like Tuberculosis, Hepatitis and HPV, screening for HPV related cancers and precancers, neurodementia; HIV associated malignancies; cardiovascular and other metabolic complications of HIV infection and treatment; operations research for implementation of 'early ART' and TB prophylaxis. Low cost diagnostics and validation of POC testing.
2. **Prevention:** Key research areas include tools and options for prevention of HIV and STI's including microbicides, vaccines, PrEP and combination prevention strategies for Indian populations
3. **Epidemiology:** While much work has been done to characterize HIV epidemiology and the national HIV surveillance continues to track the epidemic in different populations- more research is required in the Indian context to focus on the evolving molecular epidemiology of HIV in India, epidemiology of drug resistance, of co-infections (STI, TB, HPV, HHV8, Hepatitis B and C) malignancies and other co-morbid and

metabolic conditions that will impact treatment , care and prevention programming as well as mainstreaming with other disease control activities.

4. **HIV Biology:** Key themes in HIV biology will include research related to acute HIV infection, latent HIV infection, impact of treatment on HIV reservoirs, mucosal immunity and HIV acquisition, interactions of various pathogens with HIV, HIV entry mechanisms and host genetic factors affecting disease progression or susceptibility to HIV infection.
5. **Translational Research:** Programme related needs for translational research in HIV encompass newer and low cost assays for diagnosis and monitoring of HIV 1 and 2; development and validation of point of care diagnostics which will improve provision and access to care; research on biomarkers for HIV progression, co-infections like TB and co-morbid conditions like cardiovascular diseases and malignancies. The focus of research at NARI and NIRT has been on clinical research that has potential for application in the programmes for public good. Other focus with high translation potential is drug discovery.

## 2. MAJOR ACHIEVEMENTS WITH LEADS EMERGED DURING XI PLAN

### Care and Support

ICMR commits to accelerate clinical research efforts to achieve the goal of care and support to individuals infected with HIV. The institutes endeavor to test and find simpler regimens, study drug resistance and strategize to avert it, develop simple affordable diagnostics at point of care, develop community mobilization strategies to retain patients in care continuum, develop strategies and measures to enhance adherence to treatment, improve infant HIV diagnosis, focus on prevention and treatment strategies for co-infections such as tuberculosis and hepatitis, have a long term vision for caring for PLHIVs who would be living longer with HIV and treatment for HIV infected adolescents and youth.

- **Clinical Research/Trials:** NARI established a National Institute of Health supported Clinical Trial Unit where clinical trials for optimization of anti-HIV treatment have been initiated. NARI has conducted several therapeutic and prevention trials with various networks [ACTG, MTN and HPTN]. HPTN 052 was an NIH funded landmark trial where 96% efficacy of ART in preventing secondary transmission among HIV discordant couples was reported.
- **Study on Anti HIV** drug resistance in women receiving single dose Nevirapine as a prophylaxis for PPTCT showed the development of resistance mutations against non-nucleoside reverse transcriptase inhibitor (NNRTI) in a proportion of women. This has an implication on the success of future ART to these mothers. The National policy has been changed to multi-drug regimens for PPTCT.
- **Surveillance for ARV Drug resistance:** Facility for testing for anti-HIV resistance using genotyping was established at NARI. The drug resistance laboratory became the first laboratory in South east and South Asia to get accredited by WHO as well as NIH, USA. The findings

indicated that the drug resistance was seen in less than 5% drug naïve newly infected persons indicating very low level of transmission of drug resistant viruses. Monitoring surveys in patients enrolled in ART programme indicated that one centre achieved desired control of emergence of drug resistance while the second centre failed to do so. Loss to follow up appeared to be major concern.

- **Mental Health needs:** Under NACO sponsored project, Mental Health Needs Scale has been developed to assess mental, social and emotional needs of PLHAs with in Indian context. This is a 42 item scale and it can be used by clinician or social worker.
- **Neurocognitive impairment in HIV infection:** The studies conducted under NIH RO1 project showed that the prevalence of HAND is low in Indian HIV infected patients, amino acid signature of neurocognitive impairment was identified in Tat gene and ART leads to prevention of neurological impairment in people with HIV.
- A qualitative study to identify barriers to ART adherence was conducted by NARI at three regions in Maharashtra in collaboration with MSACS. Retention in ART care continuum was more of a challenge than adherence to ART. Structural interventions were recommended to combat the loss to follow up in program.
- A study to understand barriers to adherence at 30 ART centres were conducted by NIRRH, Mumbai. Data is being analysed.
- With increasing longevity of PLWHAs, care becomes an important issue for the programme. Role of family care provider was studied in collaboration with Maharashtra Association of Anthropological Sciences in Pune. Changing norms of support from the in-laws' family of women PLHIV was witnessed and shared with the program. Family care providers will be an important vehicle for improving treatment adherence and success.
- Nutrition status of HIV-positive and HIV-negative injection drug users in Chennai – a longitudinal study (2006-2011) was conducted by NIE, Chennai. This study identified food security-related issues among drug users. [NIH funded]

## Prevention

ICMR has encouraged prevention research in order to develop evidence based innovative prevention measures comprehensively targeting populations at higher risk and other vulnerable populations. Studies on new prevention technologies and studies to understand population preparedness for deployment of validated new technologies and methods are also undertaken. Microbicides are positioned to realign gender inequalities and women's vulnerability to HIV infection. Therefore, ICMR has established a national level Microbicide Expert Group and Microbicide Society of India that moves forward the research agenda on microbicide, other female controlled options and 'multiple prevention technologies' which includes contraceptives as well as HIV prevention technologies. Multicentric studies have been instituted by ICMR under prevention research agenda. ICMR has joined hands with NACO and IAVI for HIV vaccine research and with DBT and CONRAD for pushing microbicide research agenda. ICMR task force studies also address priority areas in prevention research viz. Male circumcision and PrEP and in India. Studies for prevention of co-morbidity and HPV associated malignancies are also gaining recognition in the prevention agenda

- NARI and NIRT under ICMR- IAVI-NACO programme successfully conducted phase 1 trial of prime (ADVAX-DNA Vaccine) and boost (TBC M4, Modified Vaccinia Ankara vector based multigene construct) HIV vaccine regimen. This vaccine regimen was found to be well tolerated and moderate immune response was noted in most of the volunteers, the vaccine could not go further because of stability issues with TBC-M 4 vaccine candidate. The expertise developed is proposed to be used for Phase I vaccine trial for chikungunya vaccine.
- NARI has initiated studies to identify epitopes targeted by broadly cross-reactive Cytolytic T Lymphocyte and neutralizing antibody response. Role of pDCs and neutralizing antibodies in early HIV infection has been demonstrated.
- A database of 80 full length sequences of HIV viruses from different period and from different geographic locations has been created. This will be important resource for studies related to diagnostics, vaccine development and studying evolutionary trends in HIV virus in India.
- Evaluation of efficacy of a polyherbal (Basant) anti-HIV vaginal microbicide in humanized mouse model and its mode of action was conducted by NARI. Basant was found to inhibit growth of various clades of HIV-1 by direct inactivation of the virus and was found to inhibit post entry steps also.
- With the success of Tenofovir gel as microbicide, there was felt need of exploring whether Phase III clinical trials of Tenofovir gel or other microbicide products can be undertaken in the country. ICMR-CONRAD sponsored study implemented by NARI, NIRRH, NIN and KHPT explored select sites with earlier report of high HIV prevalence to identify possible sites for Phase III trials. Incidence estimation using four different assays for incidence estimates using cross sectional testing has been carried out at these sites besides collecting important behavioral data.
- A qualitative study to understand community perspective on male circumcision as HIV prevention option was conducted in four different regions in India in collaboration with Calcutta University (Kolkata), HRRC (Meerut), TISS (Mumbai) and RMRC (Belgaum). Religious beliefs, the need for stronger and local evidence of protection and involvement of opinion leaders from non-circumcising communities were major findings relevant to the issue of roll out.

### **Epidemiological/Operational Research/STIs and Co-infections**

- Assessment of the Impact of Targeted interventions among groups for high risk of HIV infection in India. This project was under collaboration between NARI, NIE, NICED and PGIMER. This study highlighted the effect of TI among FSW on the decline of India's HIV epidemic. The report was shared with NACO.
- NARI, NICED and NIE are responsible for sentinel surveillance in different parts of the country. They also provide Technical support & guidance to SACS in overall planning & implementation of HSS activities in the allotted states. Involvement of ICMR institutes has led to the qualitative improvement of surveillance.

- Estimates of number of HIV infected persons: NIMS has lead the exercise of modeling surveillance and other data for estimation of HIV infections in India (National and State level) based on the data from sentinel surveillance as well as other sources. More recently other ICMR institutes like NARI and NIE have been involved in state level estimations..
- IBBA :, Size estimation, and Integrated Behavioral and biological Assessment (IBBA) in high prevalence setting in India was conducted as collaborative project involving NARI (Pune), NIMS (Delhi), NIE (Chennai), NIN(Hyderabad), and RMRC (Dibrugarh). The results indicate an overall increase in the programme coverage and decline in HIV and STI prevalence. The project was first in sharing raw data with other scientists for secondary analysis. Over 40 peer reviewed publications have resulted from the data. The data was shared with NACO and was used for size estimation also. NACO is planning to adopt this model to institute a National IBBA.
- Study of Genital ulcer disease in India at NARI focused on etiologies and performance of current syndrome guidelines. Findings of this study suggest a revision of existing national STI treatment guidelines in India to include treatment of syphilis infections of all GUD patients. Periodic studies are required to monitor changing spectrum of GUD etiologies in India.
- A study from NARI showed that mutations in the gyrA and parC genes of quinolone-resistant *Neisseria gonorrhoeae* isolates quinolone target enzymes might be the reason high-level resistance seen in these isolates in India. Another aspect of the study showed that the combination of auxotyping and serotyping is a potential useful method for typing *N. gonorrhoeae* as a result of high discriminatory index, rapidity, ease, and relatively lower cost.
- In an operations research study, prevalence and assessment of clinical management of sexually transmitted infections among female sex workers was studied in Hyderabad and Mumbai indicated presumptive treatment for gonorrhea, chlamydia, and syphilis screening should continue. Presumptive treatment for trichomoniasis should be considered. Consistent condom use and partner treatment need to be reemphasized.
- Establishment of the normal ranges of CD4 counts in Indian health adults: A twelve site study for establishment of normal ranges both among adult and pediatric population was conducted by NARI. 97.5 percentile of CD4 counts in normal males and females were 381-1585 and 447 to 1846 per cmm respectively CD4 normal range.
- NIE, Chennai conducted a study to assess HIV related knowledge and attitude among medical students in Pondicherry.
- NIE, Chennai tried to develop evidence-informed methodology and tools for mapping and size estimation of Hijra and transgender populations in India at the national, state, district and sub-district level by conducting desk review of available methodology and tools and conducting mapping methodology workshop and regional consultations with hijra and transgender communities.[UNDP funded]

- Prevalence of HIV/STIs and associated risk factors among wives of truck drivers in Namakkal, Tamil Nadu (2009-2010) conducted by NIE, Chennai showed the feasibility of use of ACASI for sensitive information from rural population. HIV prevalence higher than the latest sentinel surveillance report. [NIH funded].

## **HIV Biology**

HIV is a unique virus with extreme genetic diversity. It causes pathogenesis by suppressing immune system and promoting immune activation. Correlates of protection from HIV infection are still not known. Institutes of ICMR have been carrying out studies to characterize Indian HIV virus strains, immune response to HIV infection, especially in long term non-progressors and recently infected individuals. Although antiretroviral therapy improves the quality and span of life it has not been effective against HIV reservoirs. The eradication of HIV reservoirs is one of the important research areas for the future and NARI has initiated studies in this area.

- Studies on the HIV reservoir at NARI has revealed reactivation HIV from latent reservoir by HIV antigens and highlighted need of IL-10 blockade when such activation is attempted.
- Inter-subtype recombinant viruses: NARI and NICED have carried out molecular characterization of HIV virus strains from North-East and have reported presence of intersubtype recombinants especially involving HIV-1 subtypes B and C.
- The first report of characterisation of tat gene and LTR region of HIV-1 samples among IDUs from north-eastern India was given by NICED and they confirmed the presence of a unique recombinant HIV-1 strain, emerging as a result of recombination between HIV-1 strains from India and Thailand.
- Identification of the amino acid residues both in env and gag region that are critical for neutralization sensitivity of HIV have been identified by NARI. The findings will assist in developing env immunogen.
- A recently transmitted virus strain that used multiple co-receptors was identified.
- Rev and DDX3X helicase interaction was found to be critical for transport of HIV mRNA across nuclear membrane. This may be another potential target for intervention for HIV multiplication studied at NARI.
- The natural killer cells and dendritic cells are important cells of innate immune response. A study on innate immune response at NARI showed that the natural killer cells are compromised, both qualitatively and quantitatively, in early HIV infections and the dysfunction is related to the viral load set point, the marker of disease progression. The myeloid dendritic cells were decreased in recent HIV infection but the number is restored in case of successful ART, however the plasmacytoid dendritic cells once reduced could not revert to normal even after successful ART. Both these studies indicated importance of restoration of innate cell functions in early HIV infection.



- A mucosal immune response study at NARI showed that the Lactobacillus quantity at vaginal level is important in reducing cervical HIV load and not mere presence of Lactobacillus. The TGF- $\beta$ 1 levels were significantly associated with higher cervical viral load and with lower levels of Trappin-2/Elafin and SLPI. The findings indicate that the increased secretion of TGF- $\beta$ 1 might reduce secretion of Trappin-2/Elafin and SLPI which might be resulting in increase HIV shedding.

### **Translational Research**

- Adolescent Reproductive and Sexual Health intervention study has led to the development of school based ARSHE module which can be used by teachers or non teachers for imparting ARSH to school going adolescent in India.
- NARI has established a facility for testing anti-HIV activity of new drugs. The activity is tested on the cell lines that support the HIV multiplication, transepithelial culture and explant culture models.
- Testing of 136 synthetic NCEs for anti-HIV activity have resulted in identification of four leads with NNRTI activity.
- The raw data from IBBA survey has been shared with NACO and has been used for HIV estimate calculations and formulation of the National IBBA.
- Mental Health Needs Scale for PLWHA has been developed by NARI.
- An in vitro model has been developed for testing the immunogenicity of immunogen/vaccine candidates by sensitizing peripheral blood mononuclear cells from HIV naïve individuals. This could be an important tool for selecting the HIV vaccine candidates for taking to human clinical trials.
- Alteration in sample preparation to increase the yield of multiplex Polymerase Chain Reaction assay for diagnosis of genital ulcer disease was done at NARI. The study results indicated that sample preparation using phenol chloroform extraction and ethanol precipitation, prior to M-PCR helps to eliminate the inhibitors and increase the yield of the assay. However, being a laborious procedure, it may be used for samples giving negative results after the screening by Roche Amplicor specimen preparation kit.
- In House HIV Drug resistance assay has been developed and validated. Training in this assay will be carried out for technologists from different Indian laboratories.
- In vitro-sensitization of PBMCs using DCs pulsed with HIV antigens provided additional tool to study immunogenicity of HIV vaccine constructs before taking them to human studies. This model will be validated during XII plan period.
- The role of miRNAs in the pathogenesis of HIV/AIDS and their utility as biomarkers of disease progression and therapy failure are being studied at NARI as a parameter for predicting the response to ARV.

### 3. RESEARCH PAPERS PUBLISHED: Total: 173

NARI, Pune	:	108
NIE, Chennai	:	9
RMRC, Dibrugarh	:	15
RMRI, Patna	:	4
NIMS, New Delhi	:	12
NICED, Kolkata	:	25

### 4. TECHNOLOGIES TRANSFERRED TO NACO/OTHER HEALTH AGENCIES

- Following four technologies were assessed by NARI and results were shared with NACO: 1) Guava"CD4 Machine 2) Reamatrix dry reagents for estimation of CD4 counts 3) PIMA CD4 Point of Care assay
- NARI Mental Health Needs Scale

### 5. LIST OF PATENTS FILED

Sr. No.	Year of filing	Title of Patent	Institute
2996/MUM/2010	2011	A new pharmaceutical composition in which Serratiopeptidase is found to be potentiating the action of Fluconazole against biofilm forming isolates of <i>Candida albicans</i>	NARI, Pune
563/MUM/2011	2012	A new pharmaceutical composition was designed and developed in which Serratiopeptidase potentiated the action of antibacterial agent, Ciprofloxacin against biofilm forming isolates of <i>Staphylococcus aureus</i> .	NARI, Pune
1342DEL2012	2012	Microbicides from plant extract for protection against HSV-2 infection	NARI, Pune

## 6. MANPOWER TRAINED

The Manpower trained during XI<sup>th</sup> Plan by the various institutes reflect training implemented for supporting Public Health delivery systems in general (MPH and FETP) as well as for Training of Trainers (TOT) specifically focused on HIV Prevention Control and Care and Treatment programs for HIV like ICTC, ART centres, HIV testing and EQUAS and Sentinel Surveillance. The training of trainer activities resulted in percolation of the training to large numbers of individuals at different levels of the program nationally. Additionally training was conducted for MSC and MSW students and Fulbright scholars.

The training activities are briefly summarized below:

1. Public Health Personnel/epidemiologist/physician	: 06 + 12 (NIE)+ 36 (RMRIMS)
2. Scientists	: 24 (NIE)
3. Laboratory Technicians	: 07 (RMRIMS)
4. Counselors	: 09 (RMRIMS)
5. Nurse	: 09 (RMRIMS)
6. Scholars [WHO, Fulbright, ICMR]:	: 04 (NARI)
7. M.Sc. student training	: Total 91 [85(NARI) +6M.Sc students from NICED]
8. MSW students [Block placement]	: 60-65 approx
9. Workshops conducted	: Total 43 [ 38(NARI),+5 NICED] [The workshops include Ethics training, GCP and GLP training, Research Methodology, High end technologies, training of the trainers for counseling, ART Medical Officers, counselors and Laboratory technicians, EQAS training for HIV Serology and CD4 estimations, Biostatistics, Qualitative research for Social & Behavioural Sciences]

## 7. NEW HUMAN RESOURCE GENERATED

- Ph D degree awarded : Total 14 [09 NARI+5 NICED]
- Pursuing for Ph D degree : 19 NARI

**Table 1. Activities of the XI<sup>th</sup> Plan which were completed/initiated during the XI<sup>th</sup> plan itself**

Sr. No.	Type and Title of Research Study	In Case of No Follow Up Planned, Outcome of The Study	If further follow up planned, salient points about outcome & follow-up proposed during XII Plan	Institution
<b>Basic Research : Studies related to immune-pathogenesis of HIV</b>				
1	<p>Studies on HIV Vaccine development and clinical Trials.</p> <p>Under Indo-South Africa programme for vaccine development studies sponsored by DBT were undertaken with objective to identify the CTL and neutralizing antibody epitopes that may have implication for vaccine development.</p> <p>An in vitro model for testing immunogenicity of vaccine construct in human peripheral blood mononuclear cells.</p> <p>Generation of HIV-1 Subtype C based DNA vaccine candidates and assessment of Prime Boost Immunization Strategy in Mouse model.</p>	<p>The model has shown ability to test immunogenicity in human PBMC in vitro. Using three different construct it was shown that it is possible to sensitize peripheral blood mononuclear cells from HIV naïve individuals in vitro. This model once validated can be used to make decision about taking forward vaccine candidates for human clinical trials.</p> <p>This study has been completed. The vaccine construct did not show sufficient immunogenicity and hence the project was concluded and no follow up studies are planned.</p>	<p>The project will be continued. HIV peptides critical for Control of HIV and cross-reacting neutralizing antibodies are expected outcome.</p> <p>Validation of ability of the in vitro immunogenicity testing protocol in predicting human response will be carried out. If validated the model will be important in making decisions on taking vaccine candidates to human trials.</p>	NARI, Pune
2	HIV infection and host genetic mutation among injecting drug users of north-eastern states of India	None of the IDUs had CCR5-mutated gene, a prominent genetic marker of HIV-1 resistance		NICED, Kolkata

3	Studies in HIV biology including neutralizing antibodies, coreceptor usage, virus assembly, mucosal immune response and role of Deadbox helicase DDX3X in HIV replication.	<p>Identified the amino acid residues both in env and gag region that are critical for neutralization sensitivity of HIV.</p> <p>A recently transmitted virus strain that used multiple coreceptors was identified.</p> <p>Rev and DDX3X helicase interaction was found to be critical for transport of HIV mRNA across nuclear membrane. This may be another potential site for intervention for HIV multiplication.</p> <p>Role of vaginal lactobacillus population and TGF<math>\beta</math> at vaginal mucosal level in HIV control identified.</p>	<p>The studies in mucosal immune response are expected to continue in the XII plan with emphasis to study the role of NK cells, DCs, NKT cells and humoral factors in HIV disease progression.</p> <p>Host genetic factors associated with disease progression, neurocognitive impairment and toxicity to antiretroviral drugs will also be studied.</p>	NARI, Pune
4	Training programmes	<p>EQAS training imparted at national level</p> <p>In-vitro methods for testing microbicide candidates with special reference to toxicity testing in epithelial cells and cervical explants cultures</p>		NARI, Pune

Clinical Research : Clinical trials for Vaccines and Microbicides and other Prevention Strategies				
1	<p>HIV Vaccine Trial:</p> <p>Phase I Double-Blind, Placebo-Controlled, Randomized Trial to Evaluate the Safety and Immunogenicity of TBC-M4, a multigenic MVA HIV Vaccine vs ADVAX, a multigenic DNA HIV Vaccine followed by TBC-M4, a multigenic MVA HIV Vaccine.</p> <p>(The trial centre was extramurally funded by IAVAI)</p>	<p>The follow up of the volunteers showing HIV-specific immune response is continued. Two years after the last vaccination, three volunteers showed detectable antibody response while no one showed cellular response</p>	<p>Starting with AAV based HIV vaccine phase one clinical trial initiated in 2004, NARI has established capacity to carry out clinical trials of HIV vaccines following international standards. This second trial of new vaccine (Prime and boost regime) has been completed.</p> <p>While new vaccine regime was found to be well tolerated and moderate immune response was noted in most of the volunteers, the vaccine could not go further because of stability issues with TBC-M 4 vaccine candidate.</p>	<p>NARI,Pune NIRT, Chennai</p>



Cohort studies and Clinical trials in HIV infected adults and children				
2	<p>Studies related to diagnosis of opportunistic infections in HIV patients.</p> <p>Role of induced sputum as a non-invasive tool for diagnosis of pulmonary infections in HIV positive patients</p> <p>Evaluation of diagnostic algorithm for HIV Positive Pulmonary TB suspects, who are initially, smear negative. This study was taken up in collaboration with NIRT under WHO funding.</p> <p>Evaluation of ELISPOT assay in the diagnosis of active TB in children.</p>	<p>1. This completed study established the utility of induced sputum for diagnosis of pulmonary infections in HIV patients. The results obtained with induced sputum were comparable with those of pulmonary lavage as the sample. Two manuscripts are under review in peer reviewed journals.</p> <p>2. The study has been completed. Sufficient leads to take forward the study were not found.</p>	<p>3. The diagnosis of pediatric TB is difficult to achieve with certainty. This study is evaluating the ability of Advanced Elispot assay using ESat6 CFP10 and other antigens. The results of the study will inform on whether this assay will improve the diagnosis of pediatric TB.</p> <p>The enrollment needs to be completed. 70% enrollment target is achieved. We expect to complete the enrollment in next six months. The data will be unblinded and analysed after the enrollment is completed.</p>	<p>NARI, Pune</p> <p>BJMC, Pune</p>
3	<p>Anti HIV drug resistance in women receiving single dose Nevirapine as a prophylaxis for prevention of mother to child transmission of HIV.</p>	<p>This study was instituted at request of the NACO to study development of drug resistance mutations in women receiving single dose of Nevirapine for prevention of vertical transmission of HIV as under National programme. Results were submitted to NACO. The results showed the development of resistance mutations against non-nucleoside reverse transcriptase inhibitor (NNRTI) in a proportion of women who received the single dose Nevirapine. This may have implication on the success of future ART to these mothers. The National policy has been changed to multi-drug regimens for PPTCT.</p>		<p>NARI, Pune</p>

4	A Pilot Study to Explore the Association between HIV-1 Lipoatrophy/ Dyslipidemia and Gene Polymorphisms in the TNF- $\alpha$ -gene in An HIV-1 patient cohort in Pune.	Completed. Enrolled 184 patients on ART. The incidence of the TNF- $\alpha$ -238G/A SNP is two folds higher in patients on antiretroviral therapy having lipodystrophy vs those who do not have it. Two manuscripts are being written on it.		NARI, Pune
5	HIV- Kalazar coinfection in Bihar- a hospital based study	Completed		RMRIMS, Patna
6	Treatment response of Kalazar/HIV coinfectd patients with Ambisome and Anti Retroviral Therapy (MSF),	Completed		RMRIMS, Patna
7	Training programme	Training of ART centre's and ICTC's doctors, technician, nurses & counselors		NARI, Pune NACO, Delhi
<b>Epidemiological/Operational Research: Prevalence and Incidence studies in 'at-risk' and vulnerable populations for site identification and preparation</b>				
1	Epidemiology of HIV and sexually transmitted infections in sex workers of West Bengal	The study highlighted that younger sex workers were more at risk of HIV compared to sex workers at large. Secondly, the study revealed that Kolkata & some districts of north-Bengal were high-prevalent Districts		NICED, Kolkata
2	Oncogenic HPV among HIV infected female population in West Bengal	About 53% (23/43) of cases with oncogenic HPV were infected with genotypes other than 16, 18 either as single or multiple or both types. The currently available HPV vaccines offer protection only against HPV 16 and 18 and some cross protection to few associated genotypes. These vaccines are therefore less likely to offer protection against cervical cancer in HIV positive women a high percentage of who were infected with non-16 and non-18 oncogenic HPV genotypes.		NICED, Kolkata NARI, Pune

3	Assessment of the Impact of Targeted interventions among groups for high risk of HIV infection in India.	This completed study highlighted the effect of TI among FSW on the decline of India's HIV epidemic. The report has been submitted to NACO which was important document as a part of mid term evaluation of National AIDS Control Programme III. Two manuscripts have been published and one more submitted to the journal.		NARI, Pune NIE, Chennai NICED, Kolkata PGIMER, Chandigarh
4	HIV Drug Resistance Surveillance and Monitoring (funded by NACO/WHO)	<p>Facility for testing for anti-HIV resistance using genotyping was established at NARI. The drug resistance laboratory became the first laboratory in South east and South Asia to get accredited by WHO as well as NIH, USA.</p> <p>The surveillance is completed. The findings indicated that the drug resistance was seen in less than 5% drug naïve newly infected persons indicating very low level of transmission of drug resistance viruses.</p> <p>The monitoring surveillance showed that while Chennai centre achieved desired suppression of HIV drug resistance, Mumbai centre fell short.</p> <p>The findings were shared with NACO and emphasized that loss to follow up needs to be reduced. The present regimens can be continued.</p>	Although originally planned study is completed, the Institute has proposed studies for developing HIV drug resistance database and carrying out further monitoring of drug resistance among patients enrolled in national ART roll out programme.	NARI, Pune

<b>Observational and interventional studies in social and behavioural aspects of HIV prevention, care, community support, impact of HIV, and issues related to PLHA. Information on efficacy and effectiveness of the ongoing intervention programs</b>				
5	Mapping, Size estimation, and Integrated Behavioral and biological Assessment (IBBA) in high prevalence setting in India (IBBA)	<p>This Bill and Melinda Gates Foundation sponsored study was aimed at assessing the Impact of “Avahan” intervention programme in six HIV high prevalence states.</p> <p>Two rounds of surveys included 50000 respondents selected by probability based sampling in whom 184 behavioural and 7 biological indicators were studied. The results showed overall increase in the programme coverage and decline in HIV and STI prevalence.</p> <p>The raw data has been shared with NACO and has been used for HIV estimate calculations and formulation of the National IBBA.</p> <p>40 manuscripts have been published.</p> <p>Report containing the Survey Methodology and data has been put into public domain for wider use.</p>		NARI, Pune NIE, Chennai NIN, Hyderabad NIMS, New Delhi RMRC, Dibrugarh
6	Statistical Modeling of HIV/AIDS Epidemic	Stochastic models were developed to identify epidemiological parameters of HIV transmission and estimate the incubation period. The simulated results were compared with global models.	The report has been submitted to ICMR with the recommendation of gathering new data on behavioural and biological components of HIV epidemic in order to derive robust estimate of the dynamics of HIV transmission.	NIMS, New Delhi
7	Estimation and Prediction of HIV/AIDS in India Using Deterministic Asian Epidemic Model	Robust deterministic model was developed to determine adult HIV incidence and forecast with difference scenario of programme effects on HIV prevention using both biological and behavioral data. One manuscript publishes		NIMS, New Delhi

8	The Prevention of HIV/STI among Married Women in Urban India	<p>To develop and evaluate culturally appropriate theory driven health facility based intervention utilizing enhanced women's health service to promote primary prevention of HIV/STI among married women.</p> <p>More than 11,500 women were screened and 11025 were recruited for three armed Randomized Control Trial (RCT) for intervention study during XI plan.</p>	Recruitment is completed and theory based intervention will be continued	NIMS, New Delhi
9	Sex-trafficking, violence, negotiating skill and HIV infection in brothel-based sex workers of eastern India, adjoining Nepal, Bhutan & Bangladesh	The sero-positivity rate of HIV was strikingly higher among Nepalese, which could be related to a high number of trafficking of girls from Nepal at their early ages. It is alarming that 24% of the brothel-based sex workers joined their work by being trafficked		NICED, Kolkata
10	Substance use, sexual abuse and HIV/STIs among street children of Kolkata city	Sexual abuse appeared to be the primary contributory factor for acquiring HIV infection in this vulnerable group		NICED, Kolkata
11	Oncogenic Human Papilloma Virus and cervical pre-cancerous lesion in brothel-based sex workers of India	To study the problem of oncogenic HPV among brothel-based sex workers in Bengal	The observation of older sex workers with relative freedom from HPV supports the view of acquired immunity against HPV, which needs further in-depth study	NICED, Kolkata
12	Social/sexual networks of high risk married MSM in Mumbai [I to I funding-Indo-US grant]	<p>This study has been completed.</p> <p>This study has shown certain epidemiologically important findings which will be useful in planning prevention and control strategies in HIV infection. Very low level of disclosure of MSM status to their wives by married MSM is a major challenge for control programme.</p>		NARI, Pune

13	Preparing Sites for Conducting Effectiveness Trials of Microbicides in India	<p>Under this study Enrollment of 1500 sex workers was done at each of the six sites. HIV and syphilis prevalence and CD4 count estimation(for HIV +ve) was carried out on these in FSWs. Incidence estimation using four different assays for incidence estimates using cross sectional testing has been carried out. Important behavioural data has also been gathered.</p> <p>Presently no microbicide is ready for phase III trial. These sites may be useful for future Phase III microbicide trials.</p>		NARI, Pune NIN, Hyderabad KHPT, Belgaum
14	To understand community and health care providers' perspective on male controlled biological options in India (An ICMR task-force study)	<p>Male circumcision is found to be associated with protection from HIV acquisition in many studies including our earlier report on the HIV sero-negative cohort. ICMR set up a task force study to understand the perspectives of different stake holders on circumcision as a HIV prevention strategy.</p> <p>The study underlined the barriers due to religious beliefs, the need for stronger evidence and involvement of opinion leaders from non-circumcising communities. Abstract accepted at IAS 2013</p>		Calcutta University, Kolkata TISS, Mumbai RMRC, Belgaum HHRC, Meerut
15	A qualitative study to understand to non-adherence to ART among defaulting patients at Three NACO ART centers in Maharashtra	<p>Completed. Two manuscripts published.</p> <p>Findings shared with NACO and ICMR</p>		NARI, Pune
16	Sexual behavior and contraceptive use among HIV positive people	Completed		RMRC, Dibrugarh NIRRH, Mumbai



17	Art and testimonial: A Unique Community Based Approach to Reduce HIV/AIDS Stigma	Completed. A World Bank publication titled 'Tackling HIV-Related Stigma and Discrimination in South Asia' (page 137 onwards) describes the intervention in details and it has been made available worldwide through internet.		NICED, Kolkata SPARSHA, Kolkata
18	Identifying factors influencing HIV transmission in married couples - a step towards intervention development	Wives of HIV positive husbands had a significantly higher risk of being HIV positive. Assessment of needs of children infected with or affected by HIV came out as a priority and was voiced by the study participants		NICED, Kolkata SPARSHA, Kolkata
19	Studies related to CD4 count estimation:  Establishment of the range of CD4 count in Normal Health Indian Adults and pediatric populations  Validation of following technologies "Guava" CD4 Machine  Reamatrix dry reagents for estimation of CD4 counts  PIMA CD4 Point of Care assay for CD4 count	1. CD4 Adult reference range: There is no data on the normal ranges of CD4 absolute counts in Indian population. A twelve site study for establishment of normal ranges provided following data. 97.5 percentile of CD4 counts in normal males and females were 381-1585 and 447 to 1846 per cmm respectively.  The pediatric normal ranges will help in making decisions on the initiation of ART for HIV infected children.  2. The results of all four technology assessments were shared with the National AIDS Control Programme.		NARI, Pune
<b>Training Programmes</b>				
20	Training Programmes	Qualitative research methods and analysis workshop was done for ICMR institutes and university staff.  Two workshops on research methodology and quantitative methods at:  National level for junior faculty of medical colleges  Regional level for undergraduates	20 researchers trained in qualitative research from all over the country	NARI, Pune

21	Post Graduate Diploma in HIV Epidemiology (2011-2014)	Develop long-term sustainable human capacity for applied HIV epidemiology in India	First batch of 4 medical officers from Tamil Nadu (2), Manipur and Mizoram graduated in January 2013. Second batch to begin in July 2013.	Tamil Nadu State AIDS Control Society (TNSACS)  Sri Chitra Tirunal Institute Medical Sciences and Technology (SCTIMST), Thiruvananthapuram NIE, Chennai
22	HIV Sentinel Surveillance	NIE, NARI and NICED are is designated by NACO as Regional Institute to monitor and conduct HSS in Southern , eastern and western states in India  To train and orient staff in HSS activities, data collection and Dried Blood Spot (DBS) methodology.	Pre- and post surveillance workshops conducted for personnel involved in HSS activities (State Epidemiologists, Microbiologists, Medical officers and other staff) from 7 southern states of India	NIE, Chennai NICED, Kolkata NARI, Pune
23	Capacity Building Workshop on Operations Research in HIV/AIDS: Focusing Research Methodology (Nov. 2009)	To build capacity of researchers from NIIHAR institutes in operations research	Trained 24 researchers from 12 institutions (NIMHANS, NARI, NIRRH, NICED, TISS, STM, TNMGRMU, TANSACS, SRMC, SJNAHS, BJMC, APAC)	NIE, Chennai
<b>Translational Research : Testing of Candidate Product for anti HiV Activity</b>				
1	Evaluation of efficacy of a polyherbal (Basant) anti HIV vaginal microbicide in humanized mouse model and its mode of action. [I to I funding-Indo-US grant]	<ul style="list-style-type: none"> <li>This study has been completed</li> <li>One manuscript submitted, one in progress. Abstract accepted for 2<sup>nd</sup> Anti-Viral International Congress, 2012</li> <li>Basant was found to inhibit the growth of various clades of HIV-1 by direct inactivation of the virus and was found to inhibit post entry steps.</li> </ul>		NARI, Pune

2	Testing of herbal extracts, preparation from alternative systems in medicine, new synthetic compounds for inhibition of HIV multiplication. Design, synthesis and biological evaluation of HIV-1 RT-inhibitors 4-Thioazolidinone compounds.		136 synthetic NCEs were tested for anti-HIV activity and have resulted in identification of four leads with NNRTI activity.  Testing for anti-HIV and anti-SI activity will be continued.  Testing of NCEs will be continued as a programme to identify new entities with activity against HIV and that have promise of improving anti-HIV treatment.	NARI, Pune
3	Testing of Plant extracts and leads emerged.	A total of 79 plant extracts and their fractions and antimicrobial peptides were tested for anti-HIV and anti-STI activity using various in-vitro assays. Seven extracts and their fractions have been identified as leads based on the inhibition of primary and lab adapted HIV-1 isolates (CCR5 and CXCR4 strains) and standard HSV-2 strains. Patent filed for one		NARI, Pune NCL, Pune
<b>Translational Research : Observational and interventional socio behavioral studies [Identification of strategies for behavior change and education of HIV prevention among women, children and adolescents]</b>				
1	Adolescent Reproductive and Sexual Health Education (ARSHE): An intervention study [ICMR task force study]	This study has been completed and a manuscript is accepted for publication  Findings were disseminated among stakeholders in a dissemination meeting.  Published ARSHE module for school going adolescents in a book form with CD ROM and being shared with various NGOs/ CBOs on request		NARI, Pune  Safdarjang Hospital, Delhi  Calcutta University, Kolkata  IIHMR, Jaipur  GB Pant institute, Lucknow

Table 2. Activities of The XI <sup>th</sup> Plan which are to be continued to the XII <sup>th</sup> Plan.				
Sr. No.	Type and Title of Research Study	Work done during The XI <sup>th</sup> Plan	Reason for continuation of the activity in XII Plan	Institute
<b>Basic Research: Studies related to immune-pathogenesis of HIV</b>				
1	Immunologic and virologic characterization of Recent HIV -1 infection [DBT funded]	The study as funded by DBT is completed. Impaired dendritic cells seen in early HIV infection and presence of NK cells showing good control over virus multiplication being a need of early HIV infection.	As recommended by SAC, follow-up of these participants for future studies is proposed under XIIth plan.	NARI, Pune
2	Studies on the effect of HIV infection on Dendritic Cells	A dendritic cell based invitro model has been developed which can be used for evaluating / predicting T-Cell response against a vaccine candidate response.  The pDCs showed permanent impairment form early phase of disease.	The studies on dendritic cells in LTNP and patients with recent HIV infection will be continued in XIIth plan.	NARI, Pune
3	Role of Natural killer cells in recent HIV-1 infection.	The NK cell functionality and expression of various markers is ongoing. Manuscript published on interim findings.	This is ongoing Ph.D work	NARI, Pune
4	Emergence of circulating recombinants in Manipur	Ongoing work		NICED, Kolkata RIMS, Imphal
<b>Up gradation and expansion of previous initiative –Virus Repository</b>				
5	Virus Repository	This activity has been very low key due to lack of funding and availability of permanent staff.	NARI would like to reinstate and expand this national research resource in the XIIth plan.	NARI, Pune

<b>Clinical Research : Clinical trials for Vaccines and Microbicides and other Prevention Strategies</b>				
1	Community Involvement for Biomedical Research	This is an ongoing activity bringing visibility to the institute, acceptance of human subject research, recruitment and retention of study participants and pathway for community based studies. This also results in awareness in the community regarding HIV/ AIDS	Will be continued	NARI, Pune
<b>Cohort studies and Clinical trials in HIV infected adults and children</b>				
2	Development of Prospective Long Term Non-Progressors' Cohort	Cohort of 56 prospective LTNP is established. 15 patients were identified as true LTNPs. The immunological characterization is underway.	This is an important cohort. Enrollment and follow up will continue. This cohort will be useful for multiple future studies in XIIth plan	NARI, Pune
3	Cervical cancer and HIV program	Previous studies have shown that women with HIV have an increased risk of developing cervical precancerous lesions and have also shown a high prevalence of high risk HPV infections in these women.	Studies under this program will be undertaken during XII plan.	NARI, Pune NIE, Chennai KLE University, Belgaum
<b>Prevalence and Incidence studies in 'at-risk' and vulnerable populations for site identification and preparation</b>				
1	Modelling and Estimation of HIV/AIDS Epidemic in India	Estimates are extensively used in NACP III and NACP IV for strategic planning, evaluation and monitoring the programme.  NACO has identified NIMS as the nodal Institute to provide technical support by closely working with the programme and refining the tools and providing input to the programme on continuous basis including XII plan.		NIMS, New Delhi

<b>Social &amp; Behavioral Science] :Observational and interventional studies in social and behavioural aspects of HIV prevention, care, community support, impact of HIV, and issues related to PLHA</b>				
2	Process of policy development to combat HIV-TB co-infection in India:	This is Ph.D work on process of policy development in India.  Abstracts published. Manuscript under preparation	Thesis to be submitted in 2013.	NARI,Pune
3	Care needs assessment of children living with or affected by HIV in selected districts of West Bengal	A study among married couple brought the assessment of needs of children infected with or affected by HIV came out as a priority and was voiced by the study participants		NICED, Kolkata SPARSHA, Kolkata AASHA, Kolkata
4	The Prevention of HIV/STI among Married Women in Urban India	This is an ongoing intervention study where recruitment is complete. Intervention and follow up will be ongoing	The study will continue till 2013	NIMS, New Delhi
5	Knowledge Network on Avahan Project on HIV/AIDS in India	To strengthen national capacity to young researchers in documentation and dissemination of Avahan (The India AIDS Initiative) Intervention program by preparing evidence based research articles.  Trained over 60 researchers on scientific paper writing, modelling and data analysis	It is a study to continue in XII Plan and finalize scientific papers that would disseminate the learning of the programme interventions.	NIMS, New Delhi TISS, Mumbai NARI, Pune
6	STIs and HIV prevalence and sexual behaviour among married couples seeking STD care at a major Govt Hospital, Chennai	To find out the sexual behaviour and prevalence of HIV and STDs among married couples seeking care for STDs at the Institute of Venereology, Government General Hospital, Chennai	Manuscript under preparation	NIE, Chennai
7	Current status on HIV/AIDS - related Knowledge and Attitude among Medical students, Pondicherry. (2007 – 2008)	To understand the current knowledge and attitude of the medical students on HIV/AIDS	01 Manuscript published	NIE, Chennai



Translational Research				
1	Development of facility for In-vitro anti-HIV screening and immuno-modulatory testing (GTP)	87 products were tested on request. One product tested: a synthesized RT inhibitor has shown good activity, provisional patent filing in progress	This is a service required for new product development and provided to the nation and will be continued.	NARI, Pune
2	Nevirapine versus Efavirenz-based highly active antiretroviral therapy regimens in antiretroviral-naïve patients with HIV and Tuberculosis infection in India.	No major differences seen so far in either arm.	NACO has suggested that follow-up should be continued this study is of great importance of national importance. The follow up will be continued	NARI, Pune
3	Role of Gelsolin in HIV infection	Levels of gelsolin might have an important role to play in HIV infection	Initial study indicates that level of gelsolin is significantly changed in HIV patients	RMRIMS Patna IMTECH Chandigarh NIPER Hajipur
4	Improving the quality of life among people living with HIV/AIDS through Sudarshan Kriya Yoga(SKY): A Pilot Study (A NARI, Pune –VVMVP, Bangalore collaborative study)	The ongoing pilot study among 61 HIV infected in the intervention arm (30) and control arm (31) showed significant improvement in quality of life scores in the study group as compared to control group with respect to three domains: physical, level of independence and psychological domain.	The qualitative data is being collected and data for changes in bio-markers is being analysed.	NARI, Pune

Table 3. New proposals listed in the XII <sup>th</sup> five year plan				
Sr. No.	New Proposal	Justification		Institute
		Off-Shoot of an earlier completed programme	De Novo idea which is either nationally relevant or it is likely to lead to a new scientific break through.	
Basic Research				
1	National Virus Repository	<p>NARI had established first largest collection of Indian HIV strains and generated national resource for HIV research. The virus strains have been shared both with public institutions as well as private institutions. This activity was initiated with initial grant from DBT. During last five year plan the activity was maintained with intra-mural support, but work was hampered due to lack of human and financial resources. With increase in technical manpower at the Institute it is intended to revive this activity.</p> <p>It is intended to revive this activity during 12<sup>th</sup> five year plan. The activities will be coordinated with other Institutes working on HIV and other viruses.</p>		NARI, Pune

2	System Virology under the title "Centre for Systems Virology"	<p>Molecular epidemiology of AIDS patients to know the prevalence of subtypes of HIV</p> <p>Analysis of drug resistant mutations and its implication in retroviral therapy</p> <p>Role of Viral genotype on host immune response</p>	<p>It would provide information about the types of viral isolates present</p> <p>Drug resistance can be correlated with the mutations, and it would help designing the therapeutic strategies.</p> <p>Would throw light on the relationship between viral genotype and disease progression markers, host cytokine response and other immune response</p>	RMRIMS, Patna ICGEB, New Delhi DMSC, Kolkata
3	Immunopathogenesis of HIV, co-infections and chronic morbidities	<p>Studies in immunopathogenesis of HIV, coinfections and chronic morbidities will generate data that will provide critical information for immune intervention, attempts towards HIV cure and management of coinfections and chronic comorbidities that will become more common as a result of ART scale up. more common</p> <p>Studies on innate immune response at mucosal surfaces.</p> <p>Studies on the latent reservoir of HIV infection and mechanisms of maintaining latency</p>	<p>Impact of HSV-2 infection on acquisition and progression of HIV infection.</p> <p>Host genetic factors on HIV disease progression and role in hepatic toxicity to ART and development of HAND.</p>	NARI, Pune
4	Animal House		<p>The Institute is going to undertake activities related to the anti-retroviral treatments and development and testing of the anti-HIV vaccines. Both these are crucial activities and require animal experimentation for toxicity and immunogenicity studies for new drugs and vaccine candidates.</p> <p>It is proposed to set up a small animal house that will hold the experimental animals.</p>	NARI, Pune

Clinical Research				
1	Pharmacogenetics of AZT related Hematological toxicity- Pilot study	De novo idea	Genetic variations in drug metabolizing pathway enzymes may be associated with ZDV hematological toxicity in HIV cases.  A population specific approach on optimized AZT efficacy and toxicity may be obtained	NIIH, Mumbai
2	<b>Research in HIV-TB co infections: (New)</b>  Studies in New diagnostics, management and prevention:	HIV-TB coinfection has been core research area at NARI. We have for the first time demonstrated high TB burden in HIV infected. Diagnosis and management of TB both in adults and children remains a challenge. Better modalities for diagnosis, treatment and prevention of TB in HIV infected remains important area of research that the Institute intends to follow.  Studies to optimize prevention of TB in HIV infected individuals will be conducted since TB is one of the commonest OI in HIV infected individuals.	Biomarkers are associated with the predisposition to and development of active tuberculosis  Prevalence on MDR / XDR TB among HIV infected individuals in India.  Evaluation of newer diagnostics including biomarkers	NARI, Pune

3	<p>Establishing Center of Excellence for Clinical Trials At NARI, Pune</p> <p>1A) Clinical Trial unit for therapeutic drug and prevention strategies other than vaccine:</p>	<p>Yes.</p> <p>NARI has received funding from NIH, USA to establish a clinical trial unit that has created the capability at NARI for conducting controlled clinical trials adhering to international standards. ICMR has provided manpower support as well as financial support for these studies. Under this project five controlled clinical trials have been carried out.</p> <p>The HPTN052 clinical trial for comparing ART plus standard care vs standard care alone for prevention of transmission of infection from HIV positive partner to HIV-ve partner at CD4 counts above 350/cmm showed 96% efficacy and also showed decline in clinical events, especially tuberculosis. This was termed as the breakthrough of the year by "Science".</p> <p>To sustain the infrastructure and expertise significant support would be needed from the XIIth plan. The expertise developed at NARI should be converted to a national resource.</p> <p>A follow up operational research is planned to study feasibility of implementation of the intervention, ART for preventing transmission in discordant couple setting</p> <p>A study will be undertaken to assess the impact of early treatment on the pool of latently infected cells and immune activation.</p>	<p>A multi-centric clinical trial to study the impact of ART on development of drug resistance to anti-malarials in patients infected with HIV and malaria will be carried out in collaboration with RMRC-NE, RMRC-Bhubaneswar and NIMR.</p> <p>A Phase I clinical trial of a Chikungunya virus vaccine developed by Bharat Biological Ltd will be carried out in collaboration with NIE and NITR.</p> <p>Phase I studies for NCEs (anti-retrovirals, microbicides and vaccines) will be initiated if new candidate becomes available during the study period.</p>	<p>NARI, Pune</p> <p>National network for clinical trials</p> <p>( ICMR and non ICMR institutions)</p>
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4	<p>HIV drug resistance database and network:</p> <p>The database will be made available to all researchers and policy makers in the country</p>		<p>Surveys for HIV Drug Resistance will be required to be carried in different parts of the country to ensure that the Free ART programs in the country use the optimum ART regimens.</p> <p>Hence, a network of HIV Drug Resistance testing centers would be required to generate the data for the country.</p>	NARI, Pune
5	<p>Pharmacokinetics, Pharmacodynamics and Pharmacogenomics :</p> <p>Studies on pharmacokinetics, pharmacodynamics and pharmacogenomics will be a new initiatives in the XIIth plan.</p>	Previous work has highlighted the need for establishing the facilities for all three activities in the pharmacy at NARI.	<p>NARI is conducting clinical trials for anti-HIV drugs. There is a need for establishment of facility to support clinical trials.</p> <p>Establishment of Pharmacokinetics, Pharmacodynamics and Pharmacogenomics laboratory.</p> <p>Initiation of studies related to interaction of anti TB medication with anti HIV drugs.</p> <p>Metabolism of Ist line and IInd line ART medication in PLHAs from different genetic background in India.</p>	NARI, Pune NIRT, Chennai
6	Establishment of HIV infected and HIV exposed pediatric cohort.	De novo idea	A pediatric HIV infected cohort would be established under the XIIth five year plan to study the host, viral and social factors which influence the HIV disease progression in Indian setting.	NARI, Pune
7	Living Longer with HIV	De novo idea	<p>The use of ART has immensely improved survival of PLHIV. However, sufficient data on the impact of HIV and ART on the health and chronic and metabolic diseases does not exist. Hence, the next five years will focus on “living longer with HIV”.</p> <p>Initiation of studies to address psycho bio-behavioral challenges of living longer with HIV</p> <p>Studies on HIV and metabolic disorders</p> <p>Studies on HIV and cancer</p> <p>National HIV-Cancer registry Match</p>	NARI, Pune

Epidemiological/Operational Research				
1	School of Public Health	The need of trained public health experts cannot be overemphasized. NARI has been identified as one of the three ICMR Institutes that would function as an "ICMR School of Public Health". NIE has already initiated the School of Public Health and is functioning for several years. NARI has not initiated the activity for want of sufficient staff to carry out academic coordination activities. The Institute will initiate this activity once the manpower becomes available.		NIE, Pune NARI, Pune
2	Establishment of ART naïve and ART experienced HIV infected cohorts :	NARI has initiated development of cohort of ART naïve HIV infected patients under the umbrella of the "NARI care protocol." This cohort besides providing longitudinal data, has been resource for participants in different clinical trials at the Institute.  The cohort of PLHIV on ART will provide the backbone for NARI studies on "living longer with HIV".	An exploratory study to understand the role of immune activation and innate immune responses in Immuno-virological discordance will be taken up.	NARI, Pune
3	Development and maintenance of high risk HIV negative cohort inclusive of most at risk and bridge populations:	NARI had established a seronegative cohort earlier which could not continue because of shortage of funds and man power.  To re-establish such cohort in the XIIth plan period for Prevalence and Incidence Studies in various Sub-populations		NARI, Pune



4	Epidemiology of HIV, HCV and STIs among IDUs in NE India with male injecting drug users in Churachandpur District of Manipur	De novo idea	It is believed that FSWs in Manipur have acted as bridge population through their sexual partners hence it is important to explore possible interactions between FSWs and male IDUs in terms of sexual and injecting risk behaviours. The study will help in providing inputs to existing intervention programmes and also help in designing further quantitative studies to measure and track risk behaviours among IDUs & FSWs	RMRC, Dibrugarh
5	Patterns of disclosure of HIV diagnosis to adolescents/ children: A facility based exploratory study	De-Novo idea	Disclosing HIV status to children is a very sensitive issue. No disclosure module exists for pediatric population. The outcome from this study will fulfill this critical need.  Patterns of HIV disclosure and development of 'HIV Disclosure Module' [Intramural]	NARI, Pune
6	Rural Research Facility	De novo idea  The Community advisory Board has been suggesting NARI to expand its base.	NARI has been primarily focused in urban areas in and around Pune. NARI Scientific Advisory Committee has recommended that NARI expands its activities in rural areas.  With this in mind the establishment of a satellite rural unit of NARI has been proposed in XII plan.	NARI, Pune KIMSU, Karad RMRC, Belgaum KLE University, Belgaum
7	Research on Preventive Strategies: (New)	Yes  It builds on previous experience and specifically directed towards new efficacious prevention products or strategies.	1. Clinical and Epidemiological studies for HIV prevention <ul style="list-style-type: none"> <li>Identifying factors impacting HIV transmission like sexual networks,</li> <li>Migration and</li> <li>Adolescents.</li> </ul> 2. Behavioral disinhibition studies	NARI, Pune

8	Conducting Mapping and Size Estimation of Hijras and other Transgender Populations	Yes Developing Methodology and Initial Assessment for conducting Mapping and Size estimation of Transgender/ Hijra populations in India (2011-12)	Map areas in which hijras and other transgenders reside and/or where they can be potentially reached for providing information about HIV prevention/ treatment and services. Estimate size of hijras and other transgenders in 17 States of India.	NIE, Chennai
9	Improving Cervical Cancer Prevention among HIV-Infected Women Using Novel HPV Based Biomarker Assays: An 'Intramural-to-India' study	Yes Off-shoot of an earlier completed programme (Cancer Cervix Screening among HIV + women)	Evaluate the clinical performance of two novel biomarker assays for detection of histologically-confirmed cervical intraepithelial neoplasia grade 2/3 or more severe ( $\geq$ CIN2 and $\geq$ CIN3) among HIV-infected women and also study the association of risk factors and biomarkers with specific HPV genotypes and studying the interaction of HIV and HPV in cervical disease categories.	NARI, Pune, NIE, Chennai KLE University, Belgaum
10	Modeling the impact of Newer Prevention Technologies for HIV control using Goals Model	De novo idea	Use 'Goals Model' to assess the impact of vaccine, microbicide, pre-exposure prophylaxis, circumcision on HIV incidence in three high HIV prevalent States of India- Tamil Nadu, Karnataka and Maharashtra.	NIE, Chennai NARI, Pune NIMS, New Delhi
<b>Translational Research</b>				
1	Testing for Anti HIV activity In vitro	Leads showing anti-HIV and anti-STI activity have been identified, which would be isolated, characterized and studied for determining mode of action Provisional patent for the leads filed in collaboration with NCL, Pune. Identification of anti-HIV leads from plant sources and determination of mechanism of action Identification of Potential Anti-HIV Natural Product Analogs Using Molecular Docking and Medicinal Chemistry Approaches. 150 analogues of identified lead molecules will be synthesized, evaluated for anti-HIV activity and the mechanism of action would be determined.		NARI, Pune

## EXTRAMURAL RESEARCH

### Achievements

**The Indo-US Joint statement on 'Prevention of HIV/AIDS & STDs' was signed in 2000 for 5 years and was renewed in 2006.**

The Joint statement completed its 2<sup>nd</sup> term in XI<sup>th</sup> plan.

The Statement has been again renewed in October 2011 for the 3<sup>rd</sup> term during 11<sup>th</sup> Plan period and the activities will be continued in the XII<sup>th</sup> plan for a period of another five years.

### 1. Major Achievements

#### 1. Collaborative projects:

- A total of 42 research projects (through three call for Joint Indo-US proposals made in 2007, 2008 and 2010 on different aspects of HIV/AIDS,) have been jointly funded and of which 24 have been successfully completed in 11<sup>th</sup> Plan period.
- **Publications:** The researchers have published a total of 45 articles in international and national peer reviewed journals and another 42 have been submitted for publication. There have been 39 talks and posters at international and national conferences and workshops.
- Pilot data from these studies have led to over 12 large grants with another 25 grant applications submitted to various funding agencies.

#### 2. Technology transfers/novel interventions developed and Capacity Building

The collaborative projects supported under the auspices of this JWG have significantly advanced AIDS research in India and the U.S. Technology transfer has resulted in the training of numerous U.S. and Indian Fellows, postdoctoral graduates, early-stage scientists and physicians, and junior level staff members in a wide range of sophisticated techniques and assay systems including:

- Ligand-based nanosensors to detect HIV;
- Rapid diagnostic platforms and molecular techniques for the detection of HIV-associated co-infections including TB;
- Novel biomarkers for HIV-associated cancers including HPV genotyping, cytopathology, histopathology, immunohistochemistry, and High Resolution Anoscopy;
- Tissue microarray construction and analyses;
- Explant techniques to test potential microbicide candidates;
- Multi-color flow cytometry; and
- Bead-based multiplex of cytokines.

Novel behavioral interventions have been developed and are being tested in these projects including:

- Reducing the risk of the acquisition/transmission of HIV and other STIs
- Decreasing stigma and discrimination associated with HIV infection
- Increasing adherence to treatment and prevention strategies using mobile and social media technologies; and
- Increasing access to health care for at risk and HIV-infected individuals.

Several of these projects have resulted in the establishment of critical specimen and tissue repositories that will be extremely useful for future clinical studies on cervical cancer and pre-malignant lesions in HIV-infected individuals. In addition, several studies have been supported that tested the safety of new microbicide candidates in animal models, the acceptability of various formulations of potential microbicides in cohorts of high risk women, and the first clinical study of the quadrivalent HPV vaccine in women.

### **3. Capacity building**

These projects have resulted in significant capacity building at both U.S. and Indian research institutions in the design, conduct, and analyses of clinical studies and basic research on HIV, topical microbicides, HIV and TB coinfection, HIV/AIDS-related malignancies, and prevention interventions targeted to high risk, hard to reach populations (including MSM, injection drug users, adolescents, male and female commercial sex workers, transgenders, and other populations).

#### **Workshops convened under this joint statement.**

- i. Indo-U.S. Workshop on Drug Abuse and HIV/AIDS in North-East Region of India, 27-29 October, 2005, ICMR National Institute of Drug Abuse (NIDA).
- ii. Indo-U.S. Workshop on Clinical and Translational Research for Prevention and Treatment of Co-Morbidities Associated with HIV Infection, 24-25 September, 2007
- iii. Indo-U.S. Workshop to Develop a Social and Behavioral Research Agenda to Prevent the Spread of HIV and Sexually Transmitted Diseases in India, 27-28 Oct 2010.
- iv. A “Grantsmanship and Peer Review Workshop”, held in India Oct 28-29, 2010 at NIHFWD, Delhi
- v. A “Grantsmanship Workshop”, held in India February 6-7, 2013 at India International Centre
- vi. Indo-U.S. Joint Workshop on HIV Database and Cancer Registry Match, held in India February 11-13, 2013 at NARI, Pune.

Total number of publications from studies completed during 11<sup>th</sup> plan period : 64 {19 (adhoc projects) +45 (Indo-US projects)}

Table 1: Status of Completed Extramural Research Studies undertaken during XI Plan					
Sr. No.	Thematic Area & Title of the Study	Objective	Completed with out come of the study	If off shoot, Refer to XII plan study	Institution
<b>Basic Sciences</b>					
1	Evaluation of efficacy of a polyherbal (Basant) anti-HIV vaginal microbicide in humanized mouse model and its mode of action	The study aimed to confirm anti-HIV activity of Basant in preventing HIV transmission in humanized mouse model and gainst different clades.	The study has been completed. The results have shown safety and efficacy against both T-cell tropic and M-cell tropic HIV in vitro cell culture and vaginal tissue model experiments. The results showed that the product is safe. Successfully developed a humanized mouse model for testing of Basant's efficacy.	Future research this study may lead to the development of novel antiviral microbicides with public health significance.	National AIDS Research Institute, Pune
2	Genotypic analysis of pol gene for drug - resistance associated mutations in antiretroviral- naive patients with HIV infection	The study was initiated with the aim of affordable in house technique to determine the genotypic drug resistance in the pol gene from isolates of HIV-1 naïve drug individuals.	The study has been completed. The results revealed that subtype C HIV-1 was predominant in the North Indian infected population. Results also indicated a transmission of resistant variants to newly infected individuals. The PI has developed an in-house protocol for the detection of DR mutation in HIV-1.	Further research to validate the in house protocol for detection of DR mutation in HIV 1 on a larger number of sample size and efficacy needs to be compared with commercially available kits.	Postgraduate Institute of Medical Education and Research, Chandigarh

3	Comparative analysis of diffuse large B cell lymphoma in HIV/AIDS vs. in immune-competent patients from India.	The study aimed at looking at pathogenetic mechanisms for DLBL in AIDS related lymphomas (ARL) in Indian Patients, comparing the Immunohistochemistry Indian patients, comparing these results in ARL with that in immune-competent Indian patients and DLBL ARL in India with those recorded in the US.	The study has been completed. The investigators identified significant differences among cases of ARL from India and the U.S., which impacts the way these should be diagnosed and treated. In particular, India has a higher proportion of PBL, which are very aggressive EBV-associated lymphomas, frequently occurring in the oral cavity. Thus, it is now known that PBL, while extremely rare in the U.S. and Europe, may be a more common health problem in India and warrants further attention with hope for better treatment approaches.	----	TATA Memorial Hospital & Cancer Research Institute, Mumbai
4	To evaluate the role of innate immune responses in HIV infection and disease progression: with special reference to NK cells and plasmacytoid dendritic cells	The study aimed at evaluating the role of natural killer cells in exposed HIV seronegative individuals and study the role of Plasma dendritic cells.	The study has been completed. Plasma cytoid cells showed significant recovery in terms of frequency and their ability to produce IFN $\gamma$ after 12 weeks of ART, justifying their use as surrogate markers for monitoring HIV disease progression and response to treatment. This is the first study to compare innate response in ESNs with group of recently infected HIV individuals.	--	Postgraduate Institute of Medical Education & Research, Chandigarh

5	Curcumin: a multi-mechanism HIV microbicide	The study aimed to determine the ability of a novel curcumin formulation to inhibit transmission via the intravaginal route in a murine model of HIV infection.	The study has been completed. The results support the potential utility of nano formulated curcumin as an intravaginal anti-HIV microbicides. The molecular action of the curcumin action has been assessed. The knowledge gained from this study may thus lead to development of novel antiviral microbicides formulation that would greatly reduce the risk of infection following vaginal exposure.	----	University of Hyderabad, Hyderabad
6	Design, synthesis and biological evaluation of HIV-1 RT inhibitors- 4-thiazolidinone compounds	The study aimed at evaluation of thiaolidinone compounds for anti-HIV activity.	The study has been completed . Out of 92 new chemical entity tested, 2 compunds showed the anti-HIV potential. The study has revealed that thiazolidinone compound has anti-HIV activity.	----	National AIDS Research Institute, Pune
7.	Investigation of the emergence of polymorphisms indicating drug resistance in the reverse transcriptase (RT) gene of HIV -1 strains.	To investigate the emergence of polymorphisms indicating drug resistance in the reverse transcriptase (RT) of HIV-1 strains isolated from plasma of pregnant women before administration of prophylaxis to prevent mother-to –child transmission of HIV-1.	The study has been completed and has identified the polymorphism in RT gene of HIV pregnant mothers.	----	Christian Medical College, Vellore
8	N-Terminal region of mycobacterium avium KATG protein: role in identification of M .Avium complex (MAC) disease in HIV patients.	The study aimed to study the role of mycobacterial KATG protein in identification of MAC in HIV patients.	KATG protein has been identified, which can help in identification of MAC in HIV patients.	----	Postgraduate Institute of Medical Education & Research, Chandigarh



9	Optimization of the performance of DNA vaccines by engineering molecular strategies: use of HIV -1 tat as a model antigen	The study aimed at optimization of EF1 $\alpha$ promoter to drive expression of Tat & comparison with CMV promoter, engineering T-helper epitopes into Tat and engineering a synthetic intron into Tat to enhance Tat transcript expression and stability to enhance Tat- specific immune responses in the mouse model. The study also aimed at evaluation of the protective potential of the immune responses generated using virus challenge in the mouse model.	The study has been completed. The investigators devised and evaluated molecular strategies and by delivering Tat as a genetic vaccine, addressed an important problem of antigen access to the MHC class I compartment that is critical for inducing cellular immune response and viral control. The study data ascertains the role of Tat as a potential HIV vaccine candidate.	----	JNCASR, Bangalore
10	Dyslipidemia among HIV infected patients receiving antiretroviral therapy: a prospective observational study	To study the incidence of dyslipidemia among HIV infected patients on WHO based Antiretroviral Therapy (ART).	The study has been completed. There was a high incidence of dyslipidemia associated with use of ART	----	All India Institute of Medical Sciences, New Delhi
11	Reservoirs of drug-resistant HIV-1: impact of drug-resistant HIV-1 reservoirs on efficacy of childhood art	The study aimed to determine the nevirapine resistant mutations in PBMC in NNRTI based ART therapy.	The study was withdrawn by the PI.	----	The Tamilnadu Dr. M.G.R. Medical University, Chennai
<b>Epidemiological/Operational Research</b>					
1	Prevalence of multiple drug resistant (MDR) tuberculosis in HIV infected individuals	The aim was to study isolation rate susceptibility pattern and to determine the prevalence of initial and acquired drug resistance of <i>M. tuberculosis</i> in HIV infected individuals.	The study has been completed. The prevalence of acquired MDR-TB (29.6%) is found to be approximately 3 times that of primary MDR-TB. High prevalence of acquired drug resistance reveals that magnitude of drug resistance problem to a large extent is due to acquired resistance. This emphasizes the importance of high quality DOTS strategy and importance of providers to follow good practices.	----	Postgraduate Institute of Medical Education & Research, Chandigarh

2	Systemic mycoses in HIV positive patients: a study of species spectrum of etiologic agents, antifungal susceptibility pattern and epidemiologic aspects	The study aims to isolate the fungi causing systemic mycoses in HIV positive patients and to characterize their species spectrum, to determine the susceptibility pattern of the etiologic agents isolated against antifungal agents and to utilize the results for more efficacious chemotherapy of patients afflicted with fungal infections.	The study has been completed. The study revealed that overall prevalence of systemic mycoses was high 65% indicating a rising trend in their prevalence in HIV-positive patients in Delhi. The results provided an early diagnosis of mycoses in HIV-positive patients which facilitated their successful therapy. Also, the investigators evaluated a novel media hypertonic SGA with 6.5% NaCl and it was shown to be a highly reliable inexpensive medium for routine differentiation of <i>C.dubliniensis</i> from <i>C.albicans</i> .	----	Vallabhbhai Patel Chest Institute University of Delhi Delhi
3	Study of fungal opportunistic infection and their correlation with immunological status in HIV/AIDS patients in North India	The study aimed to evaluate the clinical profile of the patients with HIV infection and AIDS, to investigate occurrence of common opportunistic infections in these patients and to evaluate the degree of immunodeficiency in these patients. The study also aimed to correlate the clinical and laboratory profile in these patients and to establish the AIDS defining indicator disease, if any.	The study has been completed. A total of 234 patients attending OPDs, ART clinic, along with 30 Symptomatic HIV negative and 30 Asymptomatic HIV positive patients were studied. A decline in type-1 cytokines (IFN- $\gamma$ , IL-2) and rise in type-2 cytokines (IL-4, IL-10) was observed in patients with HIV infection suggesting a shift from Th1 to Th2 type cytokine response, more pronounced in presence of opportunistic infections suggesting a more severe immunosuppression and a prompt recognition and treatment of these infections is essential to prevent the progression to AIDS.	----	Maulana Azad Medical College, New Delhi

Socio-Behavioral Research					
1	Adaptation of an effective us adolescent HIV prevention programme for Goa	The study aimed to apply evidence based adolescent HIV risk reduction intervention, f\‘Focus on Kids (FOK) and youth health risk behavior instrument to assess its impact and develop risk reduction interventions.	The study indicated that youth in rural areas appear to be in greater need of basic facts in addition to skills. Rural youth appear to be at higher risk of onset of sexual activity in absence of sufficient knowledge. There is a need for HIV education that is sensitive to the youth, while simultaneously providing skills to those youths already engaging in risk behavior,	----	Directorate of Health Services Campal, Goa
2	Reducing HIV Risk in Vulnerable Populations: Rapid Policy Assessment & Response	The study aimed to evaluate the risk factors for the HIV in vulnerable HIV population.	DMSC and the CAB produced extensive findings and conclusions based on data and analysis in the areas of drug use, HIV/AIDS, and sex work that will be useful in local efforts to influence law, policy and practice.	----	Tata Memorial Hospital & Cancer Research Institute, Mumbai
3	Alcohol use and transactional sex among HIV-infected adults in India	The aim of the study was to characterize alcohol consumption patterns of HIV infected Indian adults reporting a history of transactional sex involvement.	The study has been completed. The study revealed a strikingly high prevalence of heavy drinking among HIV infected female sex workers and their HIV infected male clients. Heavy drinking by these men appears to be associated with lower rates of condom use. These findings raise the possibility that efforts to reduce alcohol use among HIV infected men who purchase heterosexual sex in India may be an important component of secondary HIV prevention initiatives. Interventions to reduce drinking among HIV infected men and women involved in transactional sex may improve the health of this vulnerable group in India.	----	Network of Maharashtra by People Living with HIV & AIDS, Pune

4	"Acceptability of HIV risk-reducing strategies among Indian couples"	The study aimed to identify the cultural, social and psychological factors that influence acceptability and use of sexual barrier methods and assess feasibility of enrolling at risk couples in sexual barrier study.	The study has been completed. This pilot study supports the feasibility of "translating" evidence-based intervention strategies across cultural, ethnic and political boundaries, and provides the foundation for the recently submitted application for increasing sexual barrier use among "at risk" heterosexual couples in Northern India.	----	PGIMER, Chandigarh
5	Youth alcohol use and risky sexual behaviour in India	The study aimed at collecting the data on the Youth alcohol use and risky sexual behaviour	The study has been completed. The results have indicated that it is possible to engage parents and youth in collecting data about the risk and protective framework for youth risky behaviors such as alcohol use, delinquency, and sexual behaviors. The results also highlight the importance of family rituals to youth in India, as some aspects of rituals are protective but family rituals with risky behaviors are related to adolescent problem behaviors. The study also suggests the value of including families as part of prevention strategies to address youth problem behaviors.	----	Tata Institute of Social Sciences, Mumbai

6	Reducing adolescent HIV- infection in Maharashtra ,India a family based approach	The study aimed to elicit Indian parents perspectives related to the content, acceptability, and feasibility of a family-based HIV prevention intervention, design & delivery as well as factors related to their participation in, family based prevention intervention and to identify the social, psychological, & cultural determinants of adolescent HIV-related sexual risk behavior, and acceptability of biomedical HIV prevention strategies in rural Maharashtra.	The study has been completed. The study provided useful information on perspectives of rural Indian parents and adolescents for involving them in family based interventions aimed at reducing adolescent vulnerability to HIV infection, the acceptability of biomedical prevention strategies.	----	TISS, Mumbai
7	Formative study of HIV prevention needs of HIV - infected persons in Gujarat, India	The study aimed at studying the factors for preventing the HIV in the vulnerable population	The study has been completed. The identified barriers and facilitators can be used to augment training of counselors. Knowledge about correct use of condoms does not appear to be translating into correct and consistent condom use. Consistent and correct use of condoms should be stressed when counseling about safer sex practices.	----	Medical College & SSG Hospital Baroda Anandpura, Vadodara
8	Raising HIV awareness among non-infected wives	The study aimed to do the formative research in at risk wives, risky husbands and providers working with at risk wives, from an urban Indian slum and determine the feasibility and acceptability of RHANI wives, a community based multisession HIV prevention intervention.	The study has been completed. The results indicated that with the intervention there was a decrease in the at risk behavior in the women and increase in the use of safety measures for prevention of HIV.	----	National Institute for Research in Reproductive Health, Mumbai

9	<p>Social and sexual networks of high risk married MSM in Mumbai</p> <p>Addressing psychosocial needs and HIV risk in Indian men</p>	The study aimed at identifying the psychosocial need and HIV risk in Indian MSM through RDS (respondent Driven sampling)	The study has been completed. The findings suggest that men who are both MSM and married to women may encounter greater stigma and stress because of conflicting roles and the need to conceal their behaviors from their partners. Prevention interventions through RDS may benefit from an increased awareness of this population and their specific needs.	----	National AIDS Research Institute, Pune
10	Assessing willingness to participate and methods for improving adherence and self- reporting among high risk women in India: a simulated microbicides trial	The study aimed at finding out the willingness to participate and use of and methods for improving adherence and self reporting among high risk women in India	The study has been completed. The results of the study indicated that coital diaries (CDs) and interactive voice response surveys (IVRS) do not appear to be feasible for the reporting of gel use or sexual behaviors among a sex worker population in Southern India.	----	YRG Centre for Aids Research & Education Voluntary Health Services Hospital Campus, Chennai
11	Communitization and its impact on HIV/AIDS intervention among the sex workers and their clients in Kolkata, India	The study aimed to find out co-relation between major developmental activities undertaken under communitization process (e.g. micro credit, organization building, reduction of violence, education program, anti trafficking, cultural activities etc) and its possible impact on behavior change, service utilization including condom use vis-à-vis HIV transmission among the sex workers and their clients.	The study has been completed. The results indicated that various programs organized by the investigators helped in having an impact on the FSWs and led to the increase in the use of various protective methods for prevention of HIV/AIDS and STDs.	----	Sonagachi Research & Training Institute, Kolkata

Clinical Research					
1	"The Madras Injection Drug User and AIDS Cohort Study"	The study aimed to characterize the incidence of HIV and natural history of drug abuse among cohort of drug users and estimates prevalence of correlates of HIV, HCV and and HBV among spouses, sexual partners of IDUs.	The study has been completed. A heavy burden of HIV, HCV and HBV among cohort of IDUs was observed. There was a dramatic impact of voluntary counseling and testing (VCT) on risk behavior and subsequent HIV incidence. These declines in injection drug use were accompanied by increases in alcohol use. A lower than expected HIV prevalence among the spouses of IDUs and an alarmingly high occurrence of intimate partner violence was seen. There is a low prevalence of condom use among these couples, highlighting the need for female controlled preventive methods.	----	YRG Centre for AIDS Research & Education Voluntary Health Services Hospital Campus, Chennai
2	HPV infection in Indian HIV - seropositive men who have sex with men (MSM) : a trial of the AIDS malignancy clinical trials consortium (AMC)	The study aimed at identifying the prevalence of HPV infection in the Indian HIV positive MSM	The study has been completed. The study has shown that HPV infection in the anus and penis is remarkably common in the HIV-seropositive MSM, and is similar to that seen among MSM in developed countries. Oral HPV infection is not as common but still detected in a substantial proportion of the men. Based on the very high prevalence of anogenital HPV infection it is likely that Indian HIV-seropositive MSM will be at high risk of HPV-related cancers.	----	Christian Medical College And Hospital Ida Scudder Road, Vellore



3	"HIV cervical cancer prevention research training program in India"	The study aimed at evaluating the impact of screening program in prevention of cervical cancer in HIV positive females.	The study has been completed. The results indicated that HIV-infected women are at substantially higher risk for CIN and need adequate monitoring and care, especially as they are living longer on ART. VIA based screening can be implemented and nurses can be trained for undertaking appropriate preventive care for HIV-infected women. It may be possible to integrate VIA or HPV based screening as alternatives to cytology (Pap smears) and to increase utilization of services for high-risk HIV-infected women.	----	NARI, Pune
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**Table 2: Important and Essential Activities which need to be continued in XII<sup>th</sup> Plan (ongoing studies)**

Sr. No.	Thematic area and title of the study	Work done in XI <sup>th</sup> Plan/Justification for continuation	Time frame	Deliverable outcome with public impact	Institution
<b>Basic Sciences</b>					
All 24 adhoc projects and one TF project (with 7 centers) initiated in XI <sup>th</sup> plan will be continued in the XII <sup>th</sup> Plan and will be completed in XII <sup>th</sup> plan period.					
1	Rapid Diagnosis of early TB in HIV+ patients	The study aimed to evaluate a simple, rapid and cost effective antibody based diagnostic assay for the intensive screening for TB in HIV+ patients.	2 yrs	The rapid test will be useful for rapid screening of TB in HIV patients.	PGL, Chandigarh
2	An Accurate Point-of-Care Diagnostic for HIV Detection without Follow-Up.	The study aimed to develop most effective PNA probe for accurate Point-of-Care Diagnostic for HIV Detection without Follow-Up.	2 yrs	The rapid point of care test will help in detection of HIV in the field areas.	National Chemical Laboratory, Pune
3	HIV, Intestinal Microbiota and ART	The study aimed to elucidate the association between the intestinal microbiota profile and immune, virologic and nutritional status in HIV – infected patients with normal and increased intestinal permeability , immediately prior to the initiation of ART , compared to that of non- HIV infected controls of similar age and gender from the same community with normal permeability.	2 yrs	Identification of unhealthy intestinal microbiota in HIV patients will allow to further understand the pathogenesis of inflammation in HIV and allow to develop and test targeted interventions, such as the use of pro or probiotics or dietary interventions.	Christian Medical College And Hospital, Vellore
4	To study the nature of cellular immune response directed towards RD1- encoded secretory antigens of <i>M. tuberculosis</i> by non CD4 T lymphocytes, in patients of tuberculosis (TB) with & without HIV coinfection				Himalayan Institute of Medical Sciences, Dehradun

5	Immune Reconstitution Inflammatory Syndrome (IRIS) in Human Immunodeficiency Virus (HIV)/ Acquired Immune Deficiency Syndrome (AIDS) patients with & without tuberculosis (TB) co-infection receiving Highly Active Antiretroviral Treatment (HAART)	The study aimed to study the incidence & risk factors of TB-IRIS, to study the frequency & functional dynamics of effector T-cells & regulatory T cells in TB-IRIS and the cytokines & chemokines during TB-IRIS.	2 yrs	The research on immunopathogenesis of IRIS can be helpful in developing better diagnostic tests and effective therapies against IRIS.	All India Institute of Medical Sciences New Delhi
6.	Molecular Mechanisms & therapy for cocaine abuse in HIV Associated Neurocognitive Disorder	The study aims to investigate clade specific effect of HIV-1 Tat B & C protein with cocaine alterations in properties of human brain derived neural progenitor cells & if they are mediated via alterations in PDGF levels and to determine whether HIV-1 Tat B & C along with cocaine alters neuron-glia crosstalk in human neuron – astrocyte co-cultures derived from human neural progenitor cells.	2 yrs	The results so far indicate that cocaine along with HIV along with Tat attenuates hNPCs proliferation and ability to form neurons. The understanding can help in developing treatment therapies for such cases.	NBRC, Manesar
7.	Determine Immune Based Interventions that can enhance NK cell & T cell in HIV+ persons with TB	The study aims to determine if NK cell responses to <i>M. tuberculosis</i> are reduced in HIV+ persons with LTBI and if immune-based interventions can enhance NK cell & T cell function in HIV+ persons with LTBI & active TB.	2 yrs	Results so far indicated that there was no difference in IL-21 production between HIV+ & healthy LTBI+ donors. Further experiments will be performed with additional donors & divide these donors in to HIV+LTBI+ & HIV+LTBI- & compare the expression of IL-21+ cells.	BPRC& D.L.R.C. (Lepra India), Hyderabad
<b>Clinical Research</b>					
1	Growth and development of children with human immunodeficiency virus (HIV)	The study aims to determine the physical growth of children infected with HIV according to their age, sex, socio-demographic factors, and health status and to assess the intellectual and social maturity of children infected with HIV.	3 yrs	The research will provide clues to improving the quality of life of the infected children as well as to the staff, in terms of counseling or providing the necessary opportunities to help the parents and children	ASHA Foundation, Bangalore

2	Studies on Antiviral Therapy that limits the Emergence of Resistance in HIV/HBV co-infection	The study aims to comparatively evaluate the effectiveness of 3 antiretroviral regimens in treatment naïve HIV/HBV co-infect chronic hepatitis B patients, to analyze the prevalence and pattern of HBV mutations in HIV/HBV co-infected individuals on long-term Lamivudine (3TC) therapy as part of anti retroviral Treatment and to compare incidence of antiviral mutants developed in HIV/HBV co-infected with HBV mono infected individuals on long term 3TC therapy.	3 yrs	The study will provide information about the ART regimen that prevents emergence of resistance in HIV/HBV co-infection.	Calcutta school of tropical medicine, kolkata & ICMR virus unit, Kolkata
3	Predictors and immunologic characterization of tuberculosis-associated immune reconstitution inflammatory syndrome in hiv in a prospective clinical trial cohort in chennai, india	The study aims to identify clinical predictors of IRIS-TB Patients who develop IRIS will be compared to those who did not, based on baseline clinical characteristics for prediction and identify laboratory predictors of IRIS-TB in patients co-infected with HIV and TB.	2 yrs	The project will help to understand pathogenesis and predictors of IRIS, henceforth help in predicting and reducing the incidence IRIS and ascertaining the time of ART initiation in HIV-TB co-infected patients. This may pave a way to reduce its incidence and morbidity and mortality by devising preventive strategies at a later date.	NIRT, Chennai.
4	Immunological Correlates Of Immune Reconstitution Inflammatory Syndrome (IRIS) IN subjects with HIV-1/ tuberculosis co-infection after initiating highly active anti-retroviral therapy	The study aims to identify immunological predictors of IRIS-TB Patients	3 yrs	The project will help to understand immunological predictors of IRIS, henceforth help in predicting and reducing the incidence IRIS and ascertaining the time of ART initiation in HIV-TB co-infected patients.	AIDS Research & Education Voluntary Health Services Hospital, Chennai
5	Role of various herpes viruses (HHVS) & cytokines in male to female HIV transmission	The study aims to determine the role of various herpesviruses (HHVs) and cytokines in male-to-female HIV transmission.	2 yrs	The system developed will be used for preclinical testing of various already established or novel anti-HIV strategies, including candidate microbicides.	AIIMS, New Delhi

6	Characterization of genetic diversity and neutralizing antibody response in hiv-1 infected indian children	The study aims to characterize genetic diversity and neutralizing antibody response in HIV infected children	3 yrs	The study will provide data on the genetic diversity in HIV infected children in India	AIIMS, New Delhi
7	Association of cryptosporidium genotypes and presence of intracellular viruses with clinical features of cryptosporidiosis in hiv/aids patients	The study aims to see the correlation of cryptosporidium and presence of intracellular viruses in HIV patients.	3yrs	The study will provide information about the opportunistic co-infection with cryptosporidium in HIV patients.	PGIMER, Chandigarh
8	Genetic and functional characterization of natural HIV-1 Tat, VPR and VPU variants circulating in North India	The study aims to characterize the HIV-1 variants prevalent.	3 yrs	The study will provide data on the various strain variants circulating in Northern India.	NII, New Delhi
<b>Socio-Behavioral Research</b>					
1	HIV prevention via mobile phones among male sex workers in India	The study aims to fully develop an HIV risk reduction counseling intervention for MSWs in India, using mobile phone technology, and to assess if potential mediators of intervention differentially change in the intervention group and if these changes are associated with the primary outcome (reduced sexual risk taking)	2 yrs	It is hypothesized that intervention will also show an effect on increases in Motivations to engage in safe sex, HIV risk reduction information, Harm reduction strategies and Problem solving behavioral skills.	NIRT, Chennai
2	SHAKTI- Stigma reduction, Health care provider Awareness & Knowledge enhancement on Transgender issues in India	The study aims to conduct formative research necessary to develop an innovative and culturally relevant intervention, to develop a provider-focused cognitive-behavioral stigma- reducing intervention and obtain feedback from the community and experts and to pilot test and evaluate preliminary effect of the intervention.	2 yrs	The study is likely to develop a n innovative intervention for stigma reduction in transgenders.	MGMS, Mumbai.

3	Internet-based HIV prevention for MSM in India	The study aims to document how MSM in Mumbai use the internet to meet male sex partners & test the feasibility of conducting online focus groups to reach this population, Collect recommendations for adapting Sex pulse to Indian MSM, & identify content and design features needed to develop an mHealth intervention for Indian MSM at risk of HIV/STI infection	2 yrs.	The significance of this study includes its potential public health impact in averting HIV infections among MSM in India. Based on the results an online intervention targeting Indian MSM can be developed and tested to reduce risky beliefs and behaviors, and hence, to prevent the spread of HIV.	TISS, Mumbai
4	Expanding research capacity in rural Maharashtra NARI-AIDS rural research in Maharashtra	The study aims to setup a rural research unit in rural area of Mahatashtra for future AIDS trial.	1 yr		NARI, Pune
5	Adherence and prevention support for PLHIV in kolkata by use of mobile telephone - a pilot project	The project aims to evaluate the role of mobile Phone Program in increasing adherence, plus reducing transmission acts and improving quality of life	2 yrs.	The study is expected to show that PLHIV on ART will have improved ART and other medical treatment adherence, reduced HIV transmission acts and substance use, and improved mental health and quality of life compared to individuals on ART but not receiving mobile messages.	Sonagachi Research and training instratute, Kolkata
<b>Clinical Research</b>					
1	HPV-related neoplasia among HIV-seropositive Indian men who have sex with men	The study aims to determine the prevalence and incidence of HPV-associated premalignant lesions in the anus and penis in Indian HIV-seropositive men MSM; describe risk factors for prevalent premalignant lesions in the anus and penis in Indian HIV-seropositive MSM; and describe the incidence of penile and anal HPV infection in Indian HIV-seropositive MSM.	2 yrs.	The data collected on the occurrence of HPV-associated anal and penile disease among HIV-infected MSM in India, will be critical to determining the need for anal and penile cancer prevention planning services in this population.	Christian Medical College and Hospital, Vellore

2	Improving cervical cancer prevention among HIV-infected women using novel hpv-based biomarker assays {an 'intra-mural-to-india' (i-to-i) program initiative}	The goal of this study is to evaluate the clinical performance of two novel biomarker assays for detection of histologically-confirmed cervical intraepithelial neoplasia grade 2/3 or more severe (>CIN2 and >CIN3) among HIV-infected women.	2 yrs	This study may demonstrate the usefulness of the new biomarker assays –which if shown to be promising would have practical or policy implications for care and support for HIV-infected women in India and other low and middle income countries.	NIE, Chennai
3	Incidence of HIV and other sti among indian men who have sex with men	The goal of the study is to obtain critical preliminary data needed to design a definitive prospective study on the role of HPV infection in HIV acquisition	2 yrs	The study will yield important information on anal and penile disease and HPV infection among HIV-negative MSM in India. The data will be useful for planning services for this group of men and also to in comparison to HIV-positive MSM in India.	CMC, Vellore
3	HIV and HPV co-infection among female sex workers	The aim of the project is to study the prevalence and type distribution of cervical, anal and oral HPV among HIV positive and HIV negative female sex workers	3 yrs	The study will help in evaluating test performance of VIA and cytology in detecting high grade lesions and safety of cold coagulation in FSWs.	HCJMRI ,Pune & ICPO, Noida
<b>Task Force Epidemiological Study</b>					
1	A multicentric TF study to establish the network of <i>N. gonorrhea</i> surveillance center is ongoing at 7 centers.	The study is a spillover activity of the XI <sup>th</sup> plan	3 yrs.	The study is likely to result in establishing a network of surveillance centers for <i>N. gonorrhea</i> and provide the data on the prevalence of <i>N.gonorrhea</i> which is an important TI and needs surveillance across the country.	Co-ordinating center, AIIMS, New Delhi



Table 3. New proposed Research activities to be undertaken in XII<sup>th</sup> Plan

Sr. No.	Thematic area and Title of the study	Off-shoot/De novo/New study	Justification	Time frame	Deliverables	Institution/ Centre
<b>Basic Sciences</b>						
1	IN-SILICO molecular design of anti-HIV Microbicides and pre-clinical evaluation	New study	The study will help in providing the newer potential anti-HIV microbicide for future.	3 yrs		Bharathiar University, Coimbatore
2	Genetic variants of matrix metalloproteinase enzyme in HIV related neurological disease	New Study	The study will provide information about the association of HIV associated neurological disease with MMP genotypes	3 yrs		NARI, Pune
<b>Epidemiological Research</b>						
1	Armed Forces Cohort Studies: People living with HIV/AIDS (AFCS/PLHA)	New Study	The study will provide data on people living with HIV in the Armed forces for the 1 <sup>st</sup> time.	1 yr		Armed Forces Medical College And Command Hospital, Southern Command, Pune
<b>Other Activities</b>						
1	A total of 11 adhoc projects approved under the Indo US Joint statement on 'prevention of HIV / AIDS and STDs will be initiated in the 12 <sup>th</sup> Plan period.	New Study	These studies are invited as joint projects under the Indo-US Joint Working Group on identified priority areas.	2 yrs	The studies result in development of a newer diagnostic, therapeutic or socio-behavioral intervention in the areas of HIV/AIDS and also results in technology transfer and the training of scientists in both countries.	Studies to be conducted at India and US at various centers jointly