

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Unsolicited Investigator Initiated Renewals**

**Priority Number: 1**

Mechanism(s):	<b>RPGs, Centers, Other Research, T</b>
Competing Renewal, New or Expansion:	<b>Competing Renewal</b>
Co-Funding:	<b>0</b>
% of Minority/International:	<b>M 35%, I 10%</b>
Plan Objectives(s):	<b>1A,1B, 1C, 2A, 2B, 2C, 2D, 2G, 2H, 5A, 5B, 5C, 5D, 6A, 6B, 6C, 6D, 6F, 6G, 7A, 7B, 8A, 8B, 8C</b>

**Narrative Justification:**

NIDA supports a broad range of research on the drug abuse aspects of HIV/AIDS in diverse, drug using populations to reduce the acquisition and transmission of HIV associated with sharing injection paraphernalia and/or high risk sexual behavior, to improve HIV treatment including access and utilization of services, and to reduce the consequences of HIV/AIDS. Research on drug abuse treatment as a component of HIV prevention and studies to enhance adherence to drug abuse and AIDS treatment are also a significant component of NIDA's HIV/AIDS research. NIDA also supports research on the natural history, epidemiology, etiology and pathogenesis, prevention, and treatment of HIV/AIDS and AIDS-related co-infections (e.g., hepatitis B virus (HBV), hepatitis C virus (HCV), other sexually transmitted infections (STIs), and tuberculosis (TB)) and other comorbid conditions. Another research area supported by NIDA is basic research, including the use of animal models and in vitro systems to study the role of drugs of abuse in HIV/AIDS etiology and pathogenesis; NeuroAIDS, genetics (host and viral genetic factors), and proteomics are major areas of this program. Because HIV/AIDS associated with drug abuse knows no national boundaries, NIDA supports international research to reduce the intertwined epidemics of HIV/AIDS and drug abuse. NIDA also participates in collaborative efforts with other Institutes and Agencies in order to leverage resources and conduct complementary research.

FY 2011 Plan. This initiative is consistent with all the scientific objectives and emphasis areas in the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research with the exception of Emphasis Areas #3 and 4, Microbicides and Vaccines.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: HIV Prevention in Vulnerable Populations in the U.S.**

**Priority Number: 2**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New and Expansion**  
Co-Funding: **0**  
% of Minority/International: **M 80%**  
Plan Objectives(s): **1A, 1B, 5A, 5B, 5C, 5D**

**Narrative Justification:** As the US AIDS epidemic has evolved, there has been a shift toward increasingly disproportionate representation by ethnic/racial minorities, particularly African-Americans and Hispanic/Latinos in the number of AIDS cases and numbers of new infections. There has also been a resurgence of HIV cases among men who have sex with men (MSM), particularly those who are members of ethnic/racial minority groups. The role of non-injection drug use, particularly use of stimulants and club drugs, in fueling the epidemic has become more salient. Stimulant/club drug users tend to overlap with the emergent MSM groups. Drug use and/or drug using sexual partners are important components of the broad ethnic/racial minority epidemics. These populations are in need of better interventions for HIV prevention and treatment, with consideration of cultural and structural factors which may account for racial/ethnic disparities. While disparities have increased over time, it is apparent that there often are few racial/ethnic differences in sexual risk behavior and some of the most vulnerable populations for HIV infection do not see themselves as being at risk. Sexual networking patterns may be significant contributors to the dissemination of HIV among particular ethnic/racial groups, particularly within defined geographic areas. It is important to consider both individual factors such as co-morbidities or differential distributions of genetic risk or protective factors and contextual and socioeconomic factors .

Examples of research that would further this initiative include:

- Epidemiological research which considers factors such as substances of use, networking patterns, access to care & prevention, and cultural factors which may account for disparities in HIV acquisition between white and ethnic/racial minority populations.
- Research on ethnic/racial disparities in HIV acquisition that address different distributions of co-occurring disorders (e.g., STIs), different distributions of genetic risk and protective factors and other biological variables which may contribute to these disparities.
- Development and evaluation of interventions to reduce HIV risk among racial/ethnic minority MSM, which take into account factors such as substances of use, networking patterns, access to care & prevention, and cultural factors from epidemiological research which may account disparities in HIV acquisition.
- Development and evaluation of interventions to reduce HIV risk among racial/ethnic minority women, which take into account factors such as substances of use, networking patterns, access to care & prevention, and cultural factors from epidemiological research which may account disparities in HIV acquisition.
- Development and evaluation of interventions to reduce HIV risk among drug using MSM, which take into account factors of how sexual risk behavior may be affected by

substances of choice, levels of substance use and abuse, and relationships among sexual, social, and drug use networking.

- Development and evaluation of interventions to increase uptake and adherence to antiretroviral medications among ethnic/racial minorities, with particular attention to cultural and structural factors that may impede antiretroviral use.

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective A) by characterizing risk factors in vulnerable populations and (Objective B) by evaluating factors influencing uptake and adherence to ART. This initiative also supports Behavioral and Social Science (Objectives: A, B, C, and D) in developing, evaluating, and advancing prevention interventions (at both the individual and community level); conducting basic and behavioral research on factors influencing HIV risk behaviors and on the consequences of HIV disease; conducting treatment, health, and social services research for people infected and affected by HIV; and quantitative and qualitative research to enhance HIV prevention and care.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Technology-driven Strategies to Improve Assessment and Adherence**

**Priority Number: 3**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New**  
Co-Funding: **0**  
% of Minority/International: **M 30%, I 5%**  
Plan Objectives(s): **5A, 5B, 5C, 5D, 6B, 6D**

**Narrative Justification:**

Maintaining drug abuse treatment and highly active anti-retroviral therapy (HAART) are important to addressing HIV/AIDS among drug abusers. Relapse to active drug use is often associated with non-adherence or lapses in ART. This priority will examine the feasibility of utilizing and disseminating technologically-driven indices of assessment and adherence (e.g., Ecological Momentary Assessment (EMA), Medication Event Monitoring System, cell phone and/or Digital Assistant Device among others) in the context of delivering treatments to individuals with substance abuse disorder and HIV. There is a growing literature on the use technologies in order to monitor adherence to HAART among HIV+ populations (although not typically including HIV+ active drug users). In addition, there is some emerging data that some of these technologies, such as EMA and electronic diary reports, can be used in the context of treatment for drug-abusing populations, specifically in the recording of real-time cue exposure, cravings, and mood in the hours before cocaine and/or heroin use. As such, the use of technological instrumentation that can assess/monitor behavior and adherence in “real time” offers an innovative approach to target the multiple treatment needs, including adherence to HIV treatment regimens, monitoring of antecedent targets to drug use and/or other HIV-risk behaviors of drug-abusing populations with HIV.

Given the high rates of HIV among active drug users, the high rates of nonadherence with treatment regimens for chronic illnesses (such as HIV) as well as the optimal levels of adherence necessary to maintain virological suppression and avoid the development of anti-retroviral drug resistance, there is a critical need to develop interventions that significantly enhance adherence to HIV treatment regimens and decrease HIV-risk behaviors (e.g., sharing needles). The development of several technological measures might offer promise to address the clinical needs of the underserved population of substance users with HIV.

The topics to be addressed by this initiative include:

1. How feasible is it to develop, utilize, implement, and/or disseminate these technologies among drug abusing populations with HIV? What potential barriers exist to adopting these approaches to this population and what resources/approaches are needed to overcome those barriers?
2. Which groups and approaches are the most likely candidates for efficacious use of these technologies? What subgroups of drug-abusing populations with HIV (e.g., prisoners leaving correction facilities and transitioning back to communities; those already receiving specific behavioral and/or other interventions (e.g., DOT)) are most suitable?

3. What secondary benefits and innovative applications (e.g., HIV prevention) may be developed for and as a result of adherence-related technologies?

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science research (Objectives: A, B, C, and D) behavioral and social science research will be investigate the use of technology to encourage drug users to adhere to treatment intervention regimens, including adherence to HAART therapy and Therapeutics (Objective B and D)by supporting studies to improve adherence to ARV regimens and regimens to treat coinfections.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Use of Incentives and Other Strategies to Improve HIV Testing, Adherence to Medications, and Retention in AIDS Treatment**

**Priority Number: 4**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New**  
Co-Funding: **0**  
% of Minority/International: **M 40%, I 5%**  
Plan Objectives(s): **5A, 5B, 5C, 5D, 6B, 6D**

**Narrative Justification:**

The use of motivational incentives, or “contingency management” as it is commonly called, is one of the most powerful interventions known to promote abstinence from drugs and to promote adherence to medications to treat drug abuse. Incentives have also been used to engage and retain drug users in drug abuse treatment. This initiative will study the use of motivational incentives as a component of the continuum of HIV prevention and treatment including HIV testing, engagement in HIV treatment, adherence to HIV treatment regimens, and retention in HIV care.

A large number of drug abusers are HIV positive due to the increased risk of HIV from drug use associated with drug injection and/or high risk sexual behavior. Many HIV positive individuals are unaware of their serostatus because they have not been recently tested for HIV. The use of incentives may encourage drug using individuals at high risk for HIV to be tested for HIV at more frequent intervals and to participate in risk reduction counseling. This will enable these individuals to initiate treatment earlier in the course of their HIV disease and to modify their behavior to reduce the risk of transmitting HIV to others.

Highly active antiretroviral therapy (HAART) is effective in decreasing viral load to undetectable levels, but people must adhere to their HAART medication in order for the medication to be optimally effective. Poor adherence affects the individual’s prognosis and may lead to the development viral resistance. Incentives may be a useful and cost effective means of improving HAART adherence in substance abusers. Although a handful of small randomized interventions trials have demonstrated promising success in increasing adherence to HIV medications through the use of behavioral interventions, such as contingency management and mDOT (modified Directly Observed Therapy), the feasibility and cost-effectiveness of scaling up such interventions is unclear. In addition, interventions must be sustainable over the long term. Specifically, tailoring and evaluating community-friendly interventions is critical, given the financial constraints faced by resource-limited community-based clinics and treatment centers. In addition to issues of poor adherence to HAART, drug abusers frequently drop out of AIDS treatment altogether. Strategies based on behavioral reinforcement may also be of value in retaining drug users in AIDS treatment and encouraging them to access related services.

The topics to be addressed by this initiative include:

- Assess what factors, information, and incentives would be necessary to motivate high-risk drug-using populations to understand the benefits of early detection of blood-borne viruses and to undergo voluntary counseling and testing.
- Study how to effectively use incentives and other motivational factors to enhance HIV testing, entrance into HIV care, adherence to HAART and other treatment medication regimens, and retention in HIV treatment.
- Develop, implement and evaluate community-friendly interventions to promote: HIV testing, HIV treatment engagement, adherence to HAART and relevant HIV care, and

retention in HIV treatment among substance abusing populations in resource-limited settings (e.g., community or clinic-based treatment centers).

- Develop strategies to maintain HAART adherence long term following cessation of mDOT or voucher incentive programs.
- Evaluate cost benefit of interventions.

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science research (Objectives: A, B, C, and D) and Therapeutics (Objective B and D) emphasis areas. Basic behavioral and social science research will be investigate the use of incentives to encourage drug users to access HIV testing and counseling services, return for follow-up diagnostic results, and enter and adhere to prevention and treatment intervention regimens, including adherence to HAART therapy. Studies will investigate adherence and self-management for ARV and coinfection treatment regimens.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Addressing HIV/AIDS at the Community/Neighborhood Level**

**Priority Number: 5**

Mechanism(s): **RPGs, Centers**  
Competing Renewal, New or Expansion: **New and Expansion**  
Co-Funding: **0**  
% of Minority/International: **M 80%, I 2%**  
Plan Objectives(s): **1A, 1B, 1C, 5A, 5B, 5C, 5D**

**Narrative Justification:**

While the number of new HIV infections has remained relatively stable since the late 1990s, the epidemic is not static and not uniform across the U.S. There are regional differences in rates of AIDS cases—the South is highest with 9.4 cases/100,000; followed by the Northeast with 7.2 cases/100,000; the West with 4.2 cases/100,000; and the Midwest with 2.9 cases/100,000. The highest rate for each region is found in metropolitan areas with a population of more than 500,000.

The highest AIDS case rate, 128.4/100,000 in the nation is in Washington, D.C. Within large metropolitan areas, rates are not uniform. For example, in D.C poorer wards in the east and south of the city have the highest AIDS rates. Other cities show similar variations, an analysis in Chicago plotted HIV rates by ZIP code tabulation areas and had rates ranging from 20.6-47.0/100,000 to 238.2-538.1/100,000. The dynamics of the epidemic also vary by city and within cities. For example, in Washington DC, , heterosexual sex, MSM, IDU, and non-injection drug use all contribute to high HIV rates.. HIV/AIDS cases often are concentrated in specific geographic areas. In some places, specific transmission modes may be localized within geographic areas (e.g., New York City), while in other cities (e.g., DC), transmission modes may overlap in a given geographic area.

There is consensus among HIV prevention experts with experience dealing with concentrated epidemics throughout the world that community mobilization is an essential component of the response to localized, concentrated epidemics and that it is necessary to combat prevention fatigue, diversify HIV testing, and combat stigma and discrimination. The need for multifaceted approaches incorporating epidemiology, ethnography, prevention interventions including: HIV testing, access to care and integration with STI and other infectious disease (hepatitis, TB) services have been highlighted in many recent reviews of the literature. Addressing the needs of specific communities will need to integrate available community resources.

The importance of community is also highlighted in the health disparities literature. Housing segregation by race is associated with premature mortality in areas with large African American populations. Reducing disparities in access, coverage, quality, and intensity of healthcare are important to reducing health disparities but attention must also be paid to the social determinants of health within and outside the health care system. For example, traditional prevention approaches to address disparate rates of STIs among African Americans have not been successful, at least in part, because they have ignored social determinants, and there is now recognition that prevention programs must engage communities and tailor prevention to local communities.

This initiative focuses on neighborhoods or other distinct communities with high rates of HIV/AIDS. It will support innovative intervention research tailored to the community. Given

that HIV and drug use are not evenly distributed among low income or minority neighborhoods, studies may wish to consider factors such as collective efficacy and social capital in providing protective environments in particular communities. Studies should deal with structural and contextual barriers to reducing HIV transmission and improving the lives of people infected with HIV such as: lack of testing and counseling sites within the community, poor linkage of HIV positive individuals to care, lack of coordination of drug abuse treatment and AIDS treatment, stigma and discrimination, etc. Researchers will be encouraged to identify community resources (e.g., churches, community centers, CBOs) that can be utilized to mobilize communities.

Research will be encouraged to incorporate the following areas in their studies:

- Developing approaches for assessing community/neighborhood social and structural environmental protective and risk factors that impact rates of HIV infection, integrating surveillance data, qualitative data and innovative methods such as geomapping.
- Developing approaches for assessing community resources—location of HIV testing and counseling services and drug abuse and HIV/AIDS service providers within the community, community resources for outreach, CBOs in the community.
- Piloting integrated, multifaceted HIV prevention intervention programs tailored to specific community epidemiology and service needs, as well as available resources (e.g., community organizations, clinics).
- Developing, testing, and evaluating interventions that target a range or combination of levels of social organization (i.e., individual, dyad, family, network, neighborhood, community) with consideration of local epidemiology and organizational resources.
- Studying the social, structural, cultural, and demographic factors that influence HIV-related behavior in drug-using populations, with particular attention to factors such as social capital and collective efficacy.
- Studies of how communities adopt, adapt, and implement evidence-based HIV prevention programs.
- Studies on how best to engage underserved minorities, immigrant, and refugee populations in HIV care, including creating community support to bring these populations into care.

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective A, B, C) by characterizing risk factors in communities at high risk for HIV transmission, assessing adherence and access to care, and developing new methodologies to bring interventions to scale. This initiative also supports Behavioral and Social Science (Objectives: A, B, C, and D) in developing, evaluating, and advancing prevention interventions (at both the individual and community level); conducting basic and behavioral research on factors influencing HIV risk behaviors and on the consequences of HIV disease; conducting treatment, health, and social services research for people infected and affected by HIV; and quantitative and qualitative research to enhance HIV prevention and care.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Structural Interventions to Prevent HIV/AIDS**

**Priority Number: 6**

Mechanism(s):	<b>RPGs</b>
Competing Renewal, New or Expansion:	<b>New and Expansion</b>
Co-Funding:	<b>0</b>
% of Minority/International:	<b>M 30%, I 5%</b>
Plan Objectives(s):	<b>1A, 1B, 1C, 5A, 5B, 5C, 5D</b>

**Narrative Justification:** This initiative focuses on distinct communities with high rates of HIV/AIDS and will support innovative intervention research tailored to the community, including structural interventions. To date, most successful HIV prevention efforts have involved large scale mobilization of community sectors or structural interventions. Two examples of such efforts are Thailand's 100% Condom Campaign, which involved coordinated use of policies, sanctions, and mass media activities to reduce risk in particular settings and populations and the prevention effort in the U.S. among MSM in San Francisco, which demonstrated the value of community mobilization. Regrettably, there are relatively few examples of such community-based interventions. Community approaches can occur in geographically distinct areas such as neighborhoods, cities, counties, or other jurisdictional subdivisions (e.g., health districts, planning areas of large cities) as well as highly organized settings such as military installations, or culturally-based communities. Policies and guidelines increasingly foster the adoption of interventions or practices which have evidence of prevention or treatment efficacy in highly controlled studies, but which may have more or less effect when implemented on a wide scale. Questions regarding community and structural intervention and related issues in program implementation need further investigation in order to provide more effective, large scale prevention efforts in the US and in foreign countries.

Examples of research that would further this initiative include:

- Development and evaluation of interventions to reduce HIV risk in settings, subpopulations, or geographic communities which demonstrate elevated risk for HIV acquisition.
- Development and evaluation of interventions that make use of social structures within communities or large social settings that demonstrate elevated risk for HIV acquisition.
- Consideration of social networks, different organizational characteristics of communities or settings in developing, implementing, and evaluating interventions.
- Assessments of policies and practices affecting populations at increased risk for HIV acquisition (e.g., IDU, MSM, racial/ethnic minorities) to provide bases for structural interventions to alter policies, practices, and related factors
- Evaluations of new policies which are likely to affect HIV risk such as changes in the availability of HIV testing, prevention services, sex education, antiretroviral treatment with consideration of their effects on individuals and communities, and investigation of concepts and properties of behavior that are assumed to be changed by these policies.
- Evaluation of efforts to disseminate prevention and/or treatment interventions on a wide scale in communities defined by social characteristics (e.g., race/ethnicity) or geography.
- Cost-benefit analyses of the implementation of structural interventions for HIV prevention and/or treatment, including the distribution of costs and benefits across participating sectors of society.

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective A, B, C) by characterizing risk factors by employing social network analysis, assessing structural factors affecting adherence and access to care, and developing new methodologies to bring interventions to scale. This initiative also supports Behavioral and Social Science (Objectives: A, B, C, and D) in developing, evaluating, and advancing structural prevention interventions; conducting basic and behavioral research on factors influencing HIV risk behaviors and on the consequences of HIV disease; conducting treatment, health, and social services research for people infected and affected by HIV; and quantitative and qualitative research to enhance HIV prevention and care.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Project Title: ART use and Pre-exposure Prophylaxis in drug-using populations**

**Priority Number: 7**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New**  
Co-Funding: **0**  
% of Minority/International: **M 50%, I 10%**  
Plan Objectives(s): **1A, 1C, 5A, 5B, 5D**

**Narrative Justification:**

With the advent of antiretroviral therapy (ART) and other advances in medicine, HIV/AIDS has become a treatable and chronic disease. In the context of expanding therapeutic availability and coverage, effective and consistent use of ART has prevention potential for effectively lowering community viral load. Pre-exposure prophylaxis (PrEP) or intermittent PrEP may also hold promise for targeted HIV prevention in high incidence settings and populations. Currently, trials to test the efficacy of daily PrEP are underway in international settings, including a trial in IDUs. If efficacy is demonstrated, PrEP faces country/region specific challenges, including its use in the U.S. Better understanding of adherence and risk behaviors associated with ART availability and usage in association with injection and non-injection drug use is important in this changing context in order to assess the potential impact of new treatment prevention approaches.

Questions to be addressed include screening and counseling strategies, patterns of risk behaviors and ART use, selection of optimal drug regimens, development of targeted intermittent or event-driven dosing strategies, and potential effectiveness in various sub-groups.

Research topics of interest include but are not limited to the following:

- Conduct feasibility and effectiveness studies of PrEP or intermittent PrEP as a prevention strategy in different drug using populations within high incidence settings.
- Conduct modeling studies, including cost effectiveness studies, to predict which populations will benefit most from PrEP or intermittent PrEP.
- Determine whether widespread use of PrEP will have unintended consequences (increase in sexual and/or injection risk behavior) in drug using populations.
- Determine how and to what extent the availability of ART affects willingness to engage in risk taking (e.g., sex without a condom, multiple partners) among drug users and their sex partners?
- Does knowledge about ART and specifically PrEP availability influence the likelihood of being tested for the HIV?

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objectives: A and B), in characterizing the risk factors and mechanisms of HIV transmission and methodologies to evaluate PrEP. Behavioral and Social Science Research (Objectives: A, B, and D) emphasis areas are also included in this initiative.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Exploring Epigenetic Regulatory Mechanisms in HIV/AIDS and Drug Abuse**

**Priority Number: 8**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New**  
Co-Funding: **0**  
% of Minority/International: **M 5%, I 2%**  
Plan Objectives(s): **2A, 2B, 2C, 2G**

**Narrative Justification:**

Epigenetic changes (stable, long-term alterations in the transcriptional potential of a cell) may provide protection from or vulnerability to HIV-1 infection and disease progression, and drugs of abuse or a history of drug abuse may impact these mechanisms. Emerging evidence suggests that epigenetic mechanisms influence HIV-1 integration into the host genome, control of viral latency and reactivation, and expression of host factors and receptors critical for HIV-1 infection and progression. Epigenetic factors are known to regulate both innate and adaptive immune responses, so immune control of HIV-1 infection may be influenced by such factors. It is unknown how epigenetic regulation of HIV-1 differs in various organ systems (e.g. lymph nodes, brain, or gut), different cell types, and over time during the course of disease progression. In addition, recent reports show that drugs of abuse such as nicotine and cocaine alter gene expression in the brain via epigenetic mechanisms. Epigenetic changes resulting from drug abuse may impact HIV-1 infection or progression, but this scientific area has not been explored. Studies involving histone modifications, DNA methylation, and non-coding RNAs are appropriate for this initiative. This initiative ultimately will improve our understanding of HIV/AIDS and provide new strategies for treatment.

Topics under this initiative include:

- What host genes/factors are altered epigenetically by HIV infection in different cell populations and different organ systems?
- Do epigenetic changes associated with drug abuse affect HIV infection, integration, latency, or pathogenesis?
- Does HIV latency and/or transcriptional silencing contribute to HIV spread, persistence or level of viremia?
- Can non-human primate or murine models be used to understand epigenetic factors regulating drug abuse-host-virus interactions?
- How can epigenomic information be integrated with other biological information (e.g., genomes, proteomes, metabolomes, interactomes)?
- How can epigenetic studies be integrated with ongoing genetic, epidemiological or clinical studies to monitor long-term effects?

**FY 2011 Plan:** This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Etiology and Pathogenesis (Objectives: A, B, C, G) by delineating the host and viral epigenetic mechanisms involved in the transmission, establishment, and progression of HIV disease, including neurological disease, in drug-using populations.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Acute/Early HIV Infection**

**Priority Number: 9  
DESPR 50%, DPMC 15%, DCNBR 20%, DBNBR 15%**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New and expansion**  
Co-Funding: **0**  
% of Minority/International: **M 15%, I 10%**  
Plan Objectives(s): **1A, 1B, 1C, 2A, 2B, 2C, 2G, 2H, 5A**

**Narrative Justification:**

Early events in HIV-1 infection in humans and SIV infection in macaque models are critical to disease pathogenesis. Early host responses (CTL responses) to acute infection are associated with viral load set point. Depletion of CD4+ T cells in gut occurs early in infection and enteropathy associated with HIV infection leads to microbial translocation and persistent immune activation characteristic of chronic HIV infection. Other sequelae (e.g, CNS effects) may also be determined early in infection. Furthermore, given the high viral loads seen in acute infection, it is important to detect acute infections in high risk groups and in areas with high HIV incidence in order to reduce the spread of HIV. In general, there is more known about early infection following sexual transmission than through intravenous drug use. Comparatively little is known about events following acute HIV infection in IDU and about the effects of drugs of abuse or a history of drug abuse on early events in HIV infection. There has been little research on identifying acutely infected IDU in regions with high incidence and developing interventions for them. This initiative includes:

- Research on IDU to determine if a single founder virus is usually transmitted as in sexual transmission
- Feasibility studies of antigen/antibody HIV tests in high risk drug using populations
- Development of interventions for drug users with acute infection and their sexual and injection partners
- Investigate whether CNS and other end organ effects are determined by events occurring during acute/early infection

**FY 2011 Plan:** This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objectives A, B, C) concerning risk of transmission following acute infection, characterize the consequences of acute infection, test feasibility of methods for detecting acute infection and develop intervention strategies. The initiative also relates to the Etiology and Pathogenesis (Objectives: A, B, C, D, E, F, and G) to expand research to study acute infection, its transmission, its pathogenic sequelae. This initiative also relates to Behavioral and Social Science (Objective A) to develop preventive interventions for drug users with acute infections.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Understanding HIV among Youth and Young Adults**

**Priority Number: 10**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New and expansion**  
Co-Funding: **0**  
% of Minority/International: **M 45%**  
Plan Objectives(s): **1A, 5A, 5B, 5C, 5D**

**Narrative Justification:**

CDC data demonstrate that more new HIV infections (34%) occurred in the 13-29 year old age group than in any other age group. This initiative focuses on the behavioral and neurobiological bases of high risk behavior in youth and young adults.

To better inform prevention efforts, research is needed on the cognitive, affective, and underlying neurobiological processes related to resilience to the common risk factors associated with HIV/AIDS risk behaviors in adolescents and young adults (e.g., unsafe sexual practices, sharing needles). Research is also needed to answer the question, “Why do many adolescents engage in unprotected sex despite warnings about contracting HIV/AIDS?” Adolescents may perceive the rewards for healthy decisions (like abstinence and condom use) as either too deferred in time or too uncertain. In children, ability to delay gratification has been linked to positive psychosocial outcomes, and in adolescents, drug use and other psychosocial indices of general impulsivity have been linked to risky sexual behavior.

Among the topics this initiative will address are:

- Executive functioning, inhibitory control, attention, and other cognitive processes in youth measured by cognitive and neuropsychological tests, and/or neuroimaging
- Sensitivity to affective interpersonal social-cueing components of peer pressure, as measured by performance on measures of sensitivity to affective stimuli (e.g., facial expressions) and other social cues, such as social referencing
- Studies in youth of mood, emotional reactivity, and emotional regulation
- How do perceptions of risk match risk behavior in youth? How best to convey information about risk, such as risk due to partner selection?
- Do individual differences in quantifiable measures of decision-making relate to adolescent vulnerability to (or diagnosis of) drug abuse or HIV/AIDS?
- In HIV positive youth and young adults, does HIV/drug abuse related cognitive impairment impact risky decision making that can lead to transmission of HIV?
- Assessment of neurocognitive impairments in HIV+ adolescents and how these impairments may inform prevention and treatment interventions.

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research in Natural History and Epidemiology (Objective A) and Behavioral and Social Science Research (Objectives: A, B, C, and D). The goals are to understand risk behavior and to develop and advance preventive interventions for youth and young adults at risk or infected with HIV.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: HIV/AIDS and Human Development**

**Priority Number: 11**

Mechanism(s): **R01, R03, R21, U01**  
Competing Renewal, New or Expansion: **New and Expansion**  
Co-Funding: **0**  
% of Minority/International: **M 60%**  
Plan Objectives(s): **1A, 1B, 1C, 2C, 2H, 5A, 5B, 5C, 5D**

**Narrative Justification:**

Antiretroviral therapy is now the standard of care for preventing mother to child transmission in the U.S. and is available increasingly throughout the world. It is therefore imperative to better understand the effects of fetal and infant exposure to HIV and ARVs on development in children with multiple exposures, including licit and illicit drug use. It is also important to better understand the effects of perinatally acquired HIV on development for children for whom prophylactic ARVs were not available, as well as the long-term developmental outcomes of these multiple exposures, including adolescent drug use vulnerability and resiliency.

Furthermore, given the unique developmental issues of youth between the ages of 12 and 24 years of age and the additional challenges faced by substance using youth, it is crucial that developmentally informed, prevention, treatment, and care interventions for HIV infected and at-risk youth be developed, evaluated, and implemented in a timely manner.

The following topics to be addressed by this initiative include:

1. Substance use and mental health outcomes
2. Effects of maternal drug use on developmental outcomes in infants and children
3. Central nervous system imaging correlates of substance use and substance exposures, neurodevelopment, cognitive, behavioral, hearing, and language outcomes
4. Genetic and epigenetic, including mitochondrial effects of exposure to ARVs
5. Genetics and epigenetics related to HIV, its complications, and its treatment
6. Adherence to antiretroviral therapy
7. Sexual health and HIV-risk behaviors
8. Neurodevelopment, cognitive, academic, vocational, behavioral, hearing, and language outcomes of ARV exposure and HIV infection
9. Cardiovascular complications and cardiovascular disease risk
10. Testing, counseling and linkage to care
11. Primary and secondary prevention interventions targeting minority YMSM.

**FY 2011 Plan:** This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research in Natural History and Epidemiology (Objectives A, B, and C), Etiology and Pathogenesis (Objectives C and H), and Behavioral and Social Sciences (Objectives: A, B, C, and D). The goals are to develop, evaluate, and advance prevention and risk behavior (HIV and substance use) interventions concerning the health and life course of children exposed in utero or as infants exposure to HIV and ARV and for HIV infected and at-risk youth.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Seek, Test, and Treat**

**Priority Number: 12**

Mechanism(s): **RPGs**  
Competing Renewal, New or Expansion: **New and expansion**  
Co-Funding: **0**  
% of Minority/International: **M 40 %, I 4%**  
Plan Objectives(s): **1A, 1B, 1C, 5A, 5B, 5C, 5D**

**Narrative Justification:**

There is growing support for the hypothesis that increasing HIV testing and reducing viral load among HIV+ individuals through effective ART therapy can be effective in reducing the heterosexual route of HIV transmission at a population level. Less is known about intravenous transmission or transmission among MSM. More data are needed on the ability of ART to reduce HIV transmission among drug using populations, particularly IDU and MSM. In addition, while HIV testing and subsequent treatment are important, there are data that indicate the importance of interventions to reach out to high risk groups in order to get them tested and into care. For example, although IDU have low rates of undiagnosed HIV infection, they tend to be late testers so that they are not engaged in ART early in infection. MSM have high rates of undiagnosed HIV. Even if drug users can be recruited for HIV testing, initiating and maintaining ART provide challenges in drug using populations. Active drug use is often associated with non-adherence to ART or lapses in treatment.

The following topics are examples of research supported by this initiative:

- Evaluate strategies to engage IDU and other drug users in frequent HIV testing in order to link them to care earlier.
- Evaluate novel strategies to engage, retain and support IDU and other drug users in care.
- Evaluate morbidity and mortality and by HAART use and adherence and drug use/abuse.
- Test novel strategies to enhance retention and adherence to HAART among IDU and other drug users.
- Characterize HAART uptake, health outcomes, and adherence by HAART regimen among IDU and other drug users.
- Evaluate the concept of community viral load and HIV incidence among IDU and other drug users.
- Evaluate/develop effective interventions for those at high risk who test negative

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objectives A, B, and C) and Behavioral and Social Sciences (Objectives A, B, C, and D) to understand whether frequent HIV testing and linkage to and maintenance in care can reduce HIV transmission and improve health outcomes.

**FY 2011 NIH AIDS IC Request  
Narrative Justification  
National Institute on Drug Abuse**

**Project Title: Training, Infrastructure, and Capacity Building**

**Priority Number: 13  
Across NIDA**

Mechanism(s): **RPGs, training**  
Competing Renewal, New or Expansion: **New and expansion**  
Co-Funding: **0**  
% of Minority/International: **M 20%, I 3%**  
Plan Objectives(s): **7A, 7B**

**Narrative Justification:**

**INVEST Fellowship Program and Humphrey Fellowship Program:** The INVEST program brings foreign postdoctoral fellows to the U.S. for one year of research training and also includes professional development activities and grant-writing guidance. NIDA has added additional slots to this program dedicated to training investigators with an interest in HIV/AIDS research. This expansion of the INVEST program complements other efforts by NIDA to increase international research on HIV/AIDS. The Humphrey program is a partnership with the U.S. Department of State to support a unique training program for midcareer drug abuse professionals; some of NIDA's Humphrey fellows have an interest in HIV/AIDS. In addition, NIDA participates in the national Humphrey Fellowship seminar and has organized sessions focusing on HIV/AIDS and invited participation of fellows from Emory Humphrey Program, which has an HIV/AIDS concentration. Through contacts with NIDA staff, further interactions between foreign HIV/AIDS researchers and U.S. investigators have been facilitated.

**IAS/NIDA Fellowships in HIV and Drug Abuse:** This joint International AIDS Society/NIDA program was initiated in FY09 and provides support for one junior fellow (18 months post-doctoral training) and one senior fellow (eight months professional development) to receive training at leading institutes excelling in research in the HIV-related drug use field. Awardees are announced at the IAS biannual meeting.

**A-START:** To facilitate the entry of newly independent and early career investigators into the area of AIDS research, NIDA has developed the AIDS-Science Track Award for Research Transition (A-START) mechanism. This program supports feasibility studies using the R03 mechanism and providing up to \$100,000 direct costs for two years to facilitate the entry of new investigators into drug abuse and HIV/AIDS research.

**NIDA Director's Avant-Garde Award:** In FY08, NIDA introduced the Avant-Garde award to encourage cutting edge, high-risk, high payoff HIV/AIDS research. It uses the DP1 mechanism; the same mechanism as the NIH Director's Pioneer award. This ongoing program selects 2-3 awardees each year.

**Research Training:** This program supports research efforts through institutional training research grants (T32), pre-doctoral (F31), post-doctoral (F32) mechanisms. NIDA also funds minority supplement at the pre-doctoral and post-doctoral level to train minority investigators in HIV/AIDS research. To increase the numbers of underrepresented minorities in research careers in drug abuse, including HIV/AIDS, NIDA supports a program of diversity supplements. The purpose of all of these programs is to help ensure that a diverse and highly trained workforce is

available to assume leadership roles related to the Nation's biomedical and behavioral research agenda in the areas of substance abuse and HIV/AIDS.

FY 2011 Plan: This initiative is consistent with the NIH/OAR FY 2011 Trans-NIH Plan for HIV-Related Research for Training, Infrastructure, and Capacity Building (Objectives A and B) by supporting predoctoral, postdoctoral, and advanced research training across a broad range of AIDS-related disciplines. It is also consistent with the goal of establishing and maintaining the appropriate infrastructure needed to conduct HIV research domestically and internationally.