

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Investigator Initiated Renewals

Priority Number: 1

Mechanism(s): **R01, D43, P30, P50, R24, U01, U10, P01**
Competing Renewal, New or Expansion: **100% Competing Renewal**
Co-Funding:
% of Minority/International: **M 35%, I 10%**
Plan Objectives(s): **1A,1B, 1C, 2A, 2B, 2C, 2D, 2F, 2G, 3E, 5A, 5B, 5C, 5D, 6B, 6C, 6F, 7A, 7B, 8A**
Roadmap Area (if applicable): **Not Applicable**

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 and 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 is a major focus 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 2010 Plan. This initiative is consistent with all the scientific objectives and emphasis areas in the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research with the exception of Emphasis Area #4, Vaccines.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: HIV Prevention in High-Risk Populations
Priority Number: 2

Mechanism(s): **R01, R21, R03**
Competing Renewal, New or Expansion: **New, and Expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 60% I 3%**
Plan Objectives(s): **1A, 5A, 5B, 5C, 5D**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

HIV Prevention in Criminal Justice Populations: Criminal justice settings are important venues for providing drug abuse and HIV prevention services and for identifying and treating HIV and drug use disorders. African-Americans and other racial/ethnic minorities are disproportionately represented in the increased rates of incarceration associated with drug crimes. Because detection of HIV infection usually occurs later among ethnic/racial minority groups, who also bear a greater burden of disease, criminal justice settings (including community correctional programs) have the potential to address health disparities by providing individual and community-based prevention programming, early screening and identification of HIV and facilitation of treatment and general health care.

The following are examples of the research to be conducted under this initiative:

- Research that addresses how criminal justice involvement affects drug abuse and sexual behaviors at the individual (e.g., partnering among non-incarcerated long-term sexual partners) and community levels (e.g., behaviors related to changes in available sexual and drug use partnerships within communities) over time, to formulate novel, effective interventions.
- Interventions that integrate HIV/AIDS care with drug abuse prevention and treatment strategies and the prevention of HIV/AIDS transmission in criminal justice settings.
- Interventions that address drug use and HIV/AIDS risk among women, especially minority women, with direct criminal justice involvement, or sexual or drug use partnerships with men in the criminal justice system.
- Novel and effective ways to incorporate HIV testing and counseling, HIV prevention, and referral to HIV/AIDS treatment into correctional settings (jails, prisons, community corrections).
- Facility-initiated counseling and testing interventions that include components to maintain risk reduction after release from those facilities.

Integrated HIV Risk Reduction among Young Drug-Using Men Who Have Sex with Men: Men who use drugs and have sex with men (MSM) constitute a major HIV risk group in the US. Young MSM in particular have experienced increased HIV incidence and prevalence in recent years, across all racial/ethnic groups, but more so among minorities, particularly African

Americans. Young MSM have never known a world without AIDS and have grown up with the Internet; prevention interventions must be tailored to their experience. Many young HIV-infected MSM are unaware of their infection and unknowingly expose their partners to HIV. Alcohol, methamphetamine, nitrites (“poppers”), cocaine, and club drug use has been linked to HIV risks in this population, but few HIV prevention interventions have truly and effectively integrated sexual and drug use risk components.

Among the topics this initiative will address are:

- Stigma may prevent minority MSM from accessing HIV services so effective strategies are needed to reduce stigma and enable young minority MSM to find support networks.
- Relationships between use of substances, partner selection strategies, and sexual risk behaviors (risk assessment, risk management, serosorting, prevention, fatigue).
- Culturally appropriate HIV prevention and treatment interventions targeting all racial and ethnic MSM and MSMW drug-using populations.

Reducing HIV incidence by Targeting High Risk Communities: The number of AIDS cases has also remained stable at about 40,000 per year. Despite the stability in the overall number, the epidemic is not static and not uniform across the U.S. There are dramatic disparities in rates of infection—African-Americans and Hispanics have disproportionately high rates. There are also regional differences in rates of AIDS cases, the highest rate for each region is found in metropolitan areas with a population of more than 500,000. The rates of AIDS case in metropolitan areas are not uniform; poorer communities of the cities have the highest rates. This initiative focuses on neighborhoods or other geographically distinct communities with high rates of HIV/AIDS. It will support innovative intervention research tailored to the community. Studies may deal with structural barriers to reducing HIV/AIDS 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, etc. Researchers will be encouraged to identify community resources (e.g., churches, community centers, CBOs) that can form a collaborative partnership with researchers.

Research will be encouraged, but not limited to:

- Developing approaches for assessing communities—HIV incidence and prevalence, including transmission routes and demographics, location of HIV testing and counseling services and drug abuse and HIV/AIDS service providers within the community,, community resources for outreach, CBOs in community.
- Piloting intervention programs tailored to specific community strengths and weaknesses.
- 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 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective A) by characterizing risk factors in criminal justice populations. 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 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Incentive-driven Strategies to Improve HIV Testing, Treatment, Adherence, and Retention

Priority Number: 3

Mechanism(s): **R01, R21**
Competing Renewal, New or Expansion: **New**
Co-Funding: **Not Applicable**
% of Minority/International: **M 40%, I 5%**
Plan Objectives(s): **5A, 5B, 5C, 5D, 6B**
Roadmap Area (if applicable): **Not Applicable**

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 HIV prevention and treatment. 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 and has turned AIDS into a chronic disease rather than a terminal disease. However, people must adhere to their HAART medication in order for the medication to be optimally effective. Poor adherence may lead to the development viral resistance, and the individual’s prognosis becomes poorer. Incentives may be a useful and cost effective means of improving HAART adherence in substance abusers. 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 adherence to HAART and other treatment medication regimens.

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science research (Objectives: A, B, C, and D) and Therapeutics (Objective B) 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.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Long Acting, Sustainable Therapies for Addiction and HIV Prevention

Priority Number: 4

Mechanism(s): **R01**
Competing Renewal, New or Expansion: **New, and Expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 40%, I 10%**
Plan Objectives(s): **5A, 5B**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

The UNODC World Drug report of 2007 states that 15 million people are addicted to opiates. Opiate addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use, and by neurochemical and molecular changes in the brain. Intravenous injection continues to be the predominant method of opiate delivery among opiate users. Injection drug use increases the risk of acquiring and transmitting HIV /AIDS through sharing of contaminated injection paraphernalia. Injection drug use is estimated to account for 30% of the new HIV infections worldwide (excluding sub-Saharan Africa). Although there are FDA (Food and Drug Administration) approved medications (methadone, buprenorphine, buprenorphine/naloxone, and naltrexone) available for treating opiate addiction, there are populations for which these treatments are not optimal. Furthermore, in the Eurasian land mass where the majority of opiate addicted individuals live, there are significant policy, regulatory, and logistic challenges to the delivery of these medications to the addicted people. Thus, there is an urgent need to develop alternative strategies for treatment of opiate addiction and for HIV prevention.

This initiative focuses the reduction of HIV/AIDS transmission in opiate addicts through the development and application of immunotherapy and/or other pharmacotherapies with the potential to overcome compliance issues with currently available treatments for opiate dependence. A major emphasis of this initiative is to overcome compliance issues associated with daily dosing and medication self-administration. It is expected that clinical applications will include a behavioral component meant to enhance the effects of the pharmacotherapy, improve adherence to the pharmacotherapy regimen, and improve the effect of treatment on reducing HIV risk behaviors.

The following are examples of the research to be conducted under this initiative:

- Modifying, adapting, or refining existing efficacious HIV prevention interventions to increase their potency, and also to make them more easily administered and used in the community.
- Development of heroin/morphine conjugate vaccines for the treatment of heroin/opiate addiction as a means of reducing or minimizing the potential for acquiring or transmitting HIV.
- Development of clinical systems for the application of currently available long-acting (30-day or longer sustained-release) dosage forms for opiate pharmacotherapies to

optimize these sustained pharmacotherapies to effect the reduction of the risk for acquisition and transmission of HIV.

- Development of effective clinical treatment modalities, including behavioral treatment in conjunction with pharmacotherapies, to improve the effectiveness of opiate treatment and reduce the risk behaviors associated with transmission of HIV.
- Conducting basic research to have a better understanding of the impact of HIV therapeutic regimens on adherence to treatment for HIV and co-occurring infections, sexual risk behaviors, drug-related risk behaviors, and psychosocial adaptation (i.e., improved quality of life).
- Research that identifies the social and behavioral factors affecting recruitment, retention, and adherence to prevention and treatment interventions, including clinical trials of HIV-related vaccines, microbicides, and therapeutics.
- Research on the relationship between HIV/AIDS medication adherence and relapse to higher risk behaviors among HIV infected drug users.
- Research on strategies to increase medication adherence, particularly in recovering populations at high risk for relapse to drug abuse and risky sexual behaviors.

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science Research (Objectives: A and B) for conducting research on preventive interventions as well as performing basic and behavioral social science research. By combining behavioral treatment with pharmacotherapy, the effects of pharmacotherapy will be enhanced, reducing HIV risk behaviors and also improving adherence to HAART pharmacotherapy regimens.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: International Research on HIV/AIDS: Regional Networks

Priority Number: 5

Mechanism(s): **R01**
Competing Renewal, New or Expansion: **New**
Co-Funding: **Not Applicable**
% of Minority/International: **M 0%, I 100%**
Plan Objectives(s): **1A, 1B, 2A, 2B, 2F, 5A, 5B, 5C, 5D**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

Illicit drug use and abuse continues to be, linked to the spread of HIV/AIDS around the world. Illicit drug use-related transmission of HIV, includes not only that related to sharing contaminated injection equipment, but also sexual transmission among injection drug users or their non-injecting sex partners, perinatal transmission, and high risk sexual behavior associated with non-injection drug use, such as the use of stimulants. UNAIDS estimates there are 33.2 million people living with HIV. The World Health Organization (WHO) reports that more than 15 million people have been diagnosed with drug use disorders. The United Nations Office of Drugs and Crime (UNODC) reports that 13.2 million people inject drugs and that up to 10% of all HIV infections are attributable to injection drug use (if sub-Saharan Africa is excluded about 30% of HIV infections are associated with injection drug use). Of particular concern are Eastern/Central Europe and Central Asia and Southeast Asia where injection drug use accounts for the majority of new HIV cases.

NIDA's International AIDS research is interested in taking advantage of opportunities to address important research questions that cannot be readily addressed within the US but would have implications for the US. Another goal is to build research capacity in resource limited countries where HIV/AIDS associated with drug abuse is prevalent in order to bring basic and clinical science to bear on public health needs. In FY08, NIDA issued an R21 announcement (DA08-005) to encourage international research on HIV and included in that announcement region specific areas of interest. This was designed to encourage research that could ultimately lead to regional research networks that address HIV/AIDS. Ten applications were funded under this FOA; applications were from Central and Eastern Europe, Russia, Southeast Asia, China, Africa, and Latin America. Additional pilot international studies have been supported through administrative supplements and ongoing program announcements. The present initiative encourages applications to establish regional research networks that bring together researchers from countries with similar drug abuse issues and modes of HIV transmission. Research questions that this initiative will seek to address include:

- How can cross-border and regional research inform us about cultural factors, immigration, and social networks that impact HIV transmission?

- How can the study of HIV subtypes tell us about HIV transmission within and across nations? What are the implications of new subtypes for preventive interventions (microbicides, vaccines) and treatment (antiretroviral resistance)?
- Can interventions (e.g., opioid substitution therapy) that have been demonstrated to be efficacious in one country be more readily tested in other countries in the region?
- Can we predict outbreaks of HIV in countries with relatively low prevalence and incidence?
- How do patterns of migration and relocation and socioeconomic and cultural adjustments in new country settings affect drug use and the spread of HIV?

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 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 in international settings. The Etiology and Pathogenesis (Objectives: A, B, and F) areas include delineating the viral, host, and immune mechanisms involved in the transmission and spread of HIV infection as well as the pathogenesis of immune dysfunction and disease progression in ethnic, culturally, and gender diverse populations. All Behavioral and Social Science Research (Objectives: A, B, C, and D) emphasis areas are also included in this initiative.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Drug Abuse and Early Immune Responses to HIV/SIV Infection

Priority Number: 6

Mechanism(s): **R01, R21**
Competing Renewal, New or Expansion: **New**
Co-Funding: **Not Applicable**
% of Minority/International: **M 15%, I 3%**
Plan Objectives(s): **2A, 2B**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

Recent studies have highlighted the importance of events early in HIV/SIV infection on subsequent pathogenesis. Research is needed to understand whether exposure to drugs of abuse affects the regulation of early events following HIV/SIV infection. Immune activation appears to play a critical role in AIDS pathogenesis. Mucosal- and gut-associated lymphoid tissue (MALT and GALT), are important early targets of HIV and SIV replication followed by severe CD4 T-cell depletion. Specifically, the loss of T effector-memory cells in these tissues seems to be a critical determinant of AIDS progression. Although the kinetics of viral suppression and CD4 T-cell restoration in peripheral blood have been extensively investigated in HIV-infected patients undergoing HAART, our understanding of the impact of HAART on the restoration of the gastrointestinal mucosal immune system and function is limited, and the effects of substance abuse on this process is unknown.

Examples of research studies to address this initiative include:

- Assess the impact of drug abuse on HAART restoration of the gut mucosal immune function and suppression of viral reservoirs.
- Investigate whether chronic exposure to drugs of abuse or being a drug user/abuser affects: 1) SIV/HIV replication in gut-associated lymphoid tissue, 2) depletion of CD4+ cells in GALT, 3) the development of enteropathy and translocation of microbial products, 4) sustained immune activation and pathogenic sequelae
- Expand on and develop new interdisciplinary, collaborative, and multidisciplinary research to gain a better understanding the role of drugs of abuse in regulating immune system responses to HIV/AIDS.

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Etiology and Pathogenesis (Objectives: A and B) by delineating the viral, host, and immune mechanisms involved in the transmission, establishment, and spread of HIV infection in drug-abusing populations across the spectrum of age and gender.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Environmental, Host, and Viral Genetic Factors in HIV Disease

Priority Number: 7

Mechanism(s): **R01, R21**
Competing Renewal, New or Expansion: **New and expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 15%, I 10%**
Plan Objectives(s): **1B, 2A, 2B, 2C, 2D, 2F, 2G**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

HIV-1 in humans and SIV infection in macaque models and AIDS progression are processes affected by a variety of environmental, host, and viral factors, and interactions among these factors, which impact on disease susceptibility, disease progression, and response to therapy. Host genetic variation may play a substantial role in terms of susceptibility to HIV/SIV infection, circulating virus (viral load), time to onset of AIDS, development of neuroAIDS, hepatic and cardiovascular diseases, and the effect of substance abuse on these parameters. Polymorphisms in genes encoding chemokines and their receptors are associated with altered rates of disease progression after HIV-1 infection. Recent genome-wide association studies and siRNA approaches have identified additional host factors that may impact the outcome of HIV infection at multiple stages, and ongoing research is likely to identify additional host factors. There are different viral subtypes and population mixing has led to new recombinant forms of the virus, some of which confer antiretroviral resistance (ARV) to ARV naïve subjects. In addition both HIV and SIV have been shown to mutate in response to host MHC (HLA) proteins. In addition, pharmacogenetic factors may lead to unfavorable drug-drug interactions among ARV medications and medications to treat comorbid conditions and either drugs of abuse or pharmacotherapies used to treat drug addiction.

Research on the contribution of environmental, host, and viral factors on various aspects of HIV disease may include studies in human populations, macaque models, and in vitro systems.

Examples of research questions that may be addressed are:

- Comprehensive approaches to identify genetic variants that contribute to HIV-1 vulnerability, and AIDS progression in drug abusing individuals.
- Identification of host and viral genotypes associated with development of neurological complications of HIV-1 infection among individuals using drugs of abuse.
- Identification of genetic factors that impact initial immune or inflammatory responses to viral infection.
- HAART-induced reconstitution of immune responses, inflammation resulting from immune reconstitution, or HIV-1-induced neuroinflammation and oxidative stress in the presence of drugs of abuse.

- Studies to explore the role epigenetics in HIV-1 infection and drug abuse; examination of changes in epigenetic host response to viral infection through DNA methylation, chromatin modification, and/or non-coding RNAs.

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective B) specific to AIDS progression in humans due to environmental, host, viral factors, and other interactions which impact on disease susceptibility and disease progression in drug-users. The initiative also relates to the Etiology and Pathogenesis (Objectives: A, B, C, D, E, F, and G) to expand research to study viral and host genetic factors to better understand pathogenic progression of HIV and the potential for drug-drug interactions through therapeutic interventions.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Early Developmental Interventions as HIV/AIDS Prevention

Priority Number: 8

Mechanism(s): **R01**
Competing Renewal, New or Expansion: **New and expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 45%, I 0%**
Plan Objectives(s): **1A, 5A, 5B, 5C, 5D**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

In the U.S., a growing proportion of new HIV/AIDS cases are linked to sexual exposure. Adolescents and young adults have the highest rates of sexually transmitted infections (STI), likely due to their higher levels of sexual activity and greater physiologic susceptibility (among women and adolescent girls). Despite numerous prevention efforts, these rates are on the rise. Research has shown links between behavioral and emotional problems occurring in childhood and subsequent high risk sexual behavior. Problem behavior and early involvement with deviant peers predicted risk for adolescent sexual intercourse. NIDA has supported longitudinal studies of childhood interventions designed to reduce early drug use. Results from some of these cohorts, whose subjects have reached adolescence, suggest that these early prevention interventions are associated with reductions in behaviors associated with HIV risk (e.g., early sexual debut). In contrast, most prevention interventions are designed to change proximate factors associated with HIV acquisition (e.g., condom use, partner number, partner characteristics) and ignore factors that occur in early life that may drive high risk behavior. Clearly, interventions that target precursors to high risk behavior and provide sustainable effects over time are needed. Typically, NIDA's cohort studies following childhood interventions comprehensively measure a broad range of behaviors including substance use patterns, risky sexual practices, deviant peer affiliation, antisocial and criminal behaviors, parental involvement, and other sociobehavioral and contextual data. These data provide a unique opportunity to examine individual and contextual dynamics associated with behaviors linked to HIV risk in late adolescence and early adulthood. This examination will further inform our understanding and lead to refining of early interventions to maximize their effects on HIV risk behavior.

The topics to be addressed by this initiative include:

- Research that integrates analysis of new longitudinal data regarding intervention studies beginning in childhood to determine impacts on subsequent drug use and abuse, HIV/AIDS risk behaviors and antisocial behavior for the purpose of formulating novel intervention approaches to effectively target drug abuse and HIV risk and antisocial behavior.
- Evaluate the relationship between sexual risk behavior and potential individual determinants of risk behavior such as rebelliousness, sensation seeking, antisocial behavior, mental health and stressful life events.

- Study the protective effects of individual characteristics (resilient temperament, prosocial orientation, assertiveness, sociability), family structure and dynamics (rewards/costs, attachment and commitment, sibling behaviors, family transitions, and mobility), and parent-child characteristics (parental skills and involvement in children, parent-child attachment), in addition to the traditionally examined peer support.
- Explore the role of the school and neighborhood environment in the development of risk for HIV.
- Studies that build upon, develop, or improve and expand knowledge about HIV risk and/or strategies to mitigate risk in one or more specific and developmentally characterized populations of young people;

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 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 develop, evaluate, and advance prevention and risk behavior interventions, concerning the health and life course of drug-using children at risk for HIV.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Therapeutics: Drug Interactions

Priority Number: 9

Mechanism(s): **R01**
Competing Renewal, New or Expansion: **New and expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 15%, I 4%**
Plan Objectives(s): **1B, 6C**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

Treatment of HIV infected drug abusers is a significant challenge for clinicians. Interactions between antiretroviral medications, addiction pharmacotherapeutic agents and/or drugs of abuse and medications to treat coinfections and comorbid conditions pose significant problems for the successful medical management of HIV-infected drug abusers. The following topics are examples of research supported by this initiative:

- Studies of the nature and characteristics of adverse reactions to therapies in HIV infected drug abusers, taking into account racial/ethnic differences (pharmacogenomics);
- Studies of pharmacokinetic and pharmacodynamic interactions between drugs of abuse and medications used in the treatment of: (a) addiction (e.g., methadone, buprenorphine, or others), (b) comorbid mental disorders (e.g., benzodiazepines) and (c) HIV (antiretroviral medications, e.g. PIs, NNRTIs, NRTIs, CCR5 inhibitor), OIs of HIV such as hepatitis C (interferon, ribavirin), or bacterial infections such as sexually transmitted infections (STIs) and tuberculosis (TB).
- Examination of methodological issues/development of methods of detection of drug-drug interactions;
- Studies of drug pharmacodynamics and effect of interactions on therapeutic efficacy, including mechanisms of drug induction;
- Development of protocols for the clinical management of drug interactions;
- Studies of correlation/extrapolation of in-vitro and in-vivo studies of interactions;
- Studies on the impact of drug interactions on adherence to antiretroviral medications in drug abusers;
- Development of translational/clinical models to assess the pharmacokinetic and pharmacodynamic consequences of gastrointestinal or blood-brain transport induction and/or inhibition that results from administration of drugs of abuse, drug addiction treatment medications and prescribed psychoactive medications.

FY 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective B) by studying the effects of drug abuse treatment (including smoking cessation) on the effectiveness and consequences of ART, HIV disease progression, morbidity and mortality and Therapeutics Research (Objective C) by encouraging research the interactions between antiretroviral

medications, addiction pharmacotherapeutic agents and/or drugs of abuse and medications to treat co-infections and co-morbid conditions.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

Project Title: Training, Infrastructure, and Capacity Building

Priority Number: 10

FY 2009 President's Budget without Roadmap:
FY 2009 Commitment Base:
-2% Level:
0% Level:
+3.6% (BRDPI) Level:
-2% Level:
PJ level:
Mechanism(s): **R03, T32, F31, F32, DP1,
Supplements**
Competing Renewal, New or Expansion: **New and expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 20%, I 3%**
Plan Objectives(s): **7A, 7B**
Roadmap Area (if applicable): **Not Applicable**

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.

A-START 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.

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 2010 Plan: This initiative is consistent with the NIH/OAR FY 2010 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.

**FY 2010 NIH AIDS IC Request
Narrative Justification
National Institute on Drug Abuse**

**Project Title: Translating/Blending Drug Abuse Research Results and Findings into Practice
Priority Number: 11**

Mechanism(s): **R01, R03, R21, F31, F32, T32**
Competing Renewal, New or Expansion: **New and Expansion**
Co-Funding: **Not Applicable**
% of Minority/International: **M 80%, I 15%**
Plan Objectives(s): **1C, 5A, 5D, 8A**
Roadmap Area (if applicable): **Not Applicable**

Narrative Justification:

A report by the Institute of Medicine in 1998 stated that it takes 17 years on average for research results to affect treatment delivery. As a result, NIDA has made it a priority to substantially shorten this wide gap in bringing science to practice to improve drug abuse and HIV prevention and treatment in the community settings in which programs are delivered.

Examples of science relevant to this initiative include:

- Development of mechanisms for improving the transfer of effective HIV interventions among communities. Emphasis is placed on research on the adoption and adaptation of efficacious HIV interventions by communities (including studies of diffusion processes and the exchange of knowledge between service providers and researchers).
- Conducting HIV policy research, including economic studies, necessary for translating epidemiological and clinical studies into policy.
- Implementing research training and career development opportunities for medical and health professionals from communities disproportionately affected by the AIDS epidemic, both in developing countries and domestically with regard to training on translational research to promptly bring basic science results to clinical care and clinical results to health policy and implementation.

FY 2010 Plan. This initiative is consistent with the NIH/OAR FY 2010 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology Research to train medical and health professionals to bring basic science results into clinical care and to have impact on health policy. It also supports the Behavioral and Social Science Research by translating and applying basic science research to optimize the development of innovative and effective intervention strategies; and translating basic research to clinical practice, health care providers, and service communities and for receiving and evaluating community or constituent feedback. In addition, it is consistent with Information Dissemination for establishing and promoting mentorship research training programs where interdisciplinary and translational AIDS-related research guidance is provided to trainees by more than one educator.