Part I Overview Information

Department of Health and Human Services

Participating Organizations
National Institutes of Health (NIH) (http://www.nih.gov)

Components of Participating Organizations
National Institute on Alcohol Abuse and Alcoholism (NIAAA) (http://www.niaaa.nih.gov)

Title: Alcohol Use Disorders: Treatment, Services Research, and Recovery (R01)

Announcement Type
This Funding Opportunity Announcement (FOA) is a reissue of PA-07-066.

Update: The following updates relating to this announcement have been issued:

- September 29, 2010 (NOT-OD-11-007) - NIH to Require Use of Updated Electronic Application Forms in 2011. Adobe B1 forms are required for due dates on or after May 8, 2011.
- August 16, 2010 - IMPORTANT NOTE! NIH has eliminated the error correction window for due dates of January 25, 2011 and beyond. As of January 25, all corrections must be complete by the due date for an application to be considered on-time. See NOT-OD-10-123.

Program Announcement (PA) Number: PA-10-100

NOTICE: Applications submitted in response to this Funding Opportunity Announcement (FOA) for Federal assistance must be submitted electronically through Grants.gov (http://www.grants.gov) using the SF424 Research and Related (R&R) forms and the SF424 (R&R) Application Guide.

APPLICATIONS MAY NOT BE SUBMITTED IN PAPER FORMAT.

This FOA must be read in conjunction with the application guidelines included with this announcement in Grants.gov/Apply for Grants (hereafter called Grants.gov/Apply).

A registration process is necessary before submission and applicants are highly encouraged to start the process at least four (4) weeks prior to the grant submission date. See Section IV.

Apply for Grant Electronically
A compatible version of Adobe Reader is required for download. For Assistance downloading this or any Grants.gov application package, please contact Grants.gov Customer Support at http://www07.grants.gov/contactus/contactus.jsp.

Catalog of Federal Domestic Assistance Number(s)
93.273

Key Dates
Release/Posted Date: March 17, 2010
Opening Date: May 5, 2010 (Earliest date an application may be submitted to Grants.gov)
Letters of Intent Receipt Date(s): Not Applicable
NOTE: On-time submission requires that applications be successfully submitted to Grants.gov no later than 5:00 p.m. local time (of the applicant institution/organization).

Application Due Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm
AIDS Application Due Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#AIDS.
Peer Review Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward
Council Review Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward
Earliest Anticipated Start Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward
Additional Information To Be Available Date (URL Activation Date): Not Applicable
Expiration Date: May 8, 2013

Due Dates for E.O. 12372
Not Applicable

Additional Overview Content

Executive Summary

- **Purpose.** This Funding Opportunity Announcement (FOA) issued by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institutes of Health (NIH), encourages grant applications from institutions/organizations that propose to support research on behavioral and pharmacological treatment for alcohol use disorders; organizational, financial, and management factors that facilitate or inhibit the delivery of services for alcohol use disorders; and phenomenon of recovery from alcohol use disorders.

- **Mechanism of Support.** This FOA will utilize the NIH Research Project Grant (R01) award mechanism and runs in parallel with two FOAs of identical scientific scope: PA-10-102 that encourages applications under the R21 mechanism and PA-10-101 that encourages applications under the R03 mechanism.

- **Funds Available and Anticipated Number of Awards.** Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. The total amount awarded and the number of awards will depend upon the mechanism numbers, quality, duration, and costs of the applications received.

- **Budget and Project Period.** The maximum project period allowable is five years. Because the nature and scope of the proposed research will vary from application to application, it is anticipated the size and duration of each award will also vary.

- **Application Research Strategy Length:** The R01 Research Strategy section may not exceed 12 pages, including tables, graphs, figures, diagrams, and charts. See http://grants1.nih.gov/grants/funding/funding_program.htm

- **Eligible Institutions/Organizations.** Institutions/organizations listed in Section III, 1.A. are eligible to apply.

- **Eligible Project Directors/Principal Investigators (PDs/PIs).** Individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institution/organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

- **Number of PDs/PIs.** More than one PD/PI (i.e., multiple PDs/PIs) may be designated on the application.

- **Number of Applications.** Applicants may submit more than one application, provided that each application is scientifically distinct.

- **Resubmissions.** Applicants may submit a resubmission application, but such application must include...
an Introduction addressing the previous peer review critique (Summary Statement). See new NIH policy on resubmission (amended) applications (NOT-OD-09-003, NOT-OD-09-016).

- **Renewals.** Applicants may submit a renewal application.
- **Application Materials.** See Section IV.1 for application materials.
- **General Information.** For general information on SF424 (R&R) Application and Electronic Submission, see these Web sites:
- **Hearing Impaired.** Telecommunications for the hearing impaired are available at: TTY: (301) 451-5936

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Part II - Full Text of Announcement

Section I. Funding Opportunity Description

1. Research Objectives

NIAAA Research Objectives

Purpose

The National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institutes of Health (NIH), invites applications to support research on various topics in the field of alcohol treatment and services for alcohol use disorders. The scope of interest is wide-ranging. It includes pharmacologic and behavioral treatments; recovery strategies; interventions for alcohol-induced tissue damage; and the organizational, financial, management, and environmental factors that facilitate or inhibit the delivery of evidence-based services for alcohol use disorders.

Research objectives of this Funding Opportunity Announcement (FOA) include, but are not limited to, research within the following four broad research domains: (1) medications development for the treatment of alcohol use disorders and alcohol-induced tissue damage; (2) behavioral therapies and mechanisms of behavioral change; (3) health services research; and (4) recovery research. Cutting across these domains, NIAAA encourages treatment and health services-related studies on a number of special emphasis populations and topics including: (a) psychiatric/substance abuse/medical comorbidity, (b) adolescents, (c) fetal alcohol spectrum disorders, (d) health disparities/special populations, and (e) use of novel methods and technologies.

Broad Research Domains

1. Medications Development for the Treatment of Alcohol Use Disorders and Alcohol-Induced Tissue Damage

Efforts to develop medications for alcohol use disorders have expanded rapidly in recent years. Three agents—disulfiram, naltrexone, and acamprosate—are now approved for use in the United States and many other countries. Recently, topiramate also has been shown to be effective in treating alcohol-dependent patients. However, because of the heterogeneous nature of alcohol use disorders, many patients have limited or no response to these medications. Therefore, developing new medications and evaluating their use in combination with other medications and with behavioral therapies are important steps toward improving treatment outcomes for all individuals with alcohol use disorders. A variety of new compounds are being investigated in clinical trials, including gabapentin, ondansetron, levetiracetam, quetiapine, baclofen, zonisamide, pregabalin, prazosin, and kudzu.

Alcohol-seeking behavior and drinking are influenced by multiple neurotransmitters, neuromodulators,
hormones, and intracellular networks. Thus, there are many potential targets for drug development. Research to date has focused on opioid, serotonin, dopamine, glutamate, and gamma-aminobutyric acid (GABA); cannabinoids, corticotrophin-releasing factor (CRF), nicotine, adenosine, and neuropeptide systems (e.g., neuropeptide Y); signal transduction pathways (e.g., protein kinase A and protein kinase C); and gene transcription factors (e.g., delta fos B and cAMP response element-binding protein [CREB]). Efforts to define different elements of addiction include reward and motivation, negative affect, cue conditioning/craving/wanting, disinhibition/impulsivity/compulsivity/habituation, memory, executive function/cognitive function, and interoception/self-awareness. It is important to identify the neurocircuits underlying these elements and investigate their interactions and integration. The ultimate goal is to target specific sites in these neurocircuits with compounds that modulate them.

Advances also have been made in understanding the mechanisms of alcohol-induced tissue damage. Oxidative stress and inflammation play a major role in the pathogenesis of alcohol-associated injuries of various organs, including the liver, pancreas, heart, lungs, brain, and peripheral nervous system. Potential therapeutic agents include those that attenuate the actions of pro-inflammatory cytokines (e.g., the tumor necrosis factor (TNF)-a), and antioxidants (e.g., S-adenosyl-L-methionine (SAMe), glutathione, and vitamins A and E). Other potential new treatments of alcoholic liver disease include cannabinoid CB1 antagonists and CB2 agonists, metformin (an insulin-sensitizing agent), antifibrotic agents, prebiotics, probiotics, and zinc.

Finally, to improve safety, efficacy, and efficiency of medications, it is important to identify and characterize patients who respond positively to the medications and those who experience adverse events. Progress in personalized medicine includes evaluating polymorphisms of the mu opioid gene, such as A118G, which appears to modify responses to naltrexone, and the L versus S allele on the serotonin transporter gene, which may influence responses to ondansetron. These and similar discoveries may someday enable clinicians to tailor treatment to the biological profile of individual patients, and thereby to achieve better treatment outcomes.

Specific areas of research include, but are not limited to, the following examples:

- Discover, develop, and test new, more effective agents to prevent or reduce drinking.
- Discover and develop medications to reduce smoking in alcohol-abusing individuals.
- Discover and develop novel medications to treat alcohol-induced organ damage by attenuating or reversing the tissue damage. Identifying new targets for drug development based on mechanisms underlying the alcohol-induced damage is encouraged.
- Advance personalized medicine by employing approaches of pharmacogenetics, sophisticated modeling of human characteristics, brain imaging, and physiological and biochemical markers.
- Evaluate combinations of medications to increase efficacy with minimal side effects.
- Explore optimal combinations of medications and behavioral interventions. This includes cognitive/memory enhancement medications to augment the efficacy of behavioral therapies.
- Identify barriers to and facilitate integration of pharmacotherapy into alcoholism treatment; develop strategies to offset obstacles and promote facilitators.
- Develop quantitative biochemical markers and alcohol-sensing devices to measure alcohol consumption for pharmacotherapy trials.
- Develop and standardize human laboratory models to screen for promising medications.

2. Behavioral Therapies and Mechanisms of Behavioral Change

Over the past 20 years, research on the behavioral treatment of alcohol use disorders has progressed substantially. Behavioral interventions that have demonstrated efficacy include motivational enhancement therapy, cognitive behavioral therapy, brief interventions, behavioral couples therapy, twelve-step facilitation therapy, and the community reinforcement approach. Interestingly, several studies have suggested that these behavioral therapies appear to have similar efficacies when compared with standard treatments. Currently, very little information is available on how and why these behavioral treatments are effective. Understanding the underlying mechanisms of action of an intervention involves identifying the active processes and their
specific effects on diverse patient groups, including racial/ethnic minority, rural, and low-income populations. Because many individuals with alcohol use disorders change their drinking behavior without help from addiction treatment providers or self-help groups, it is as vital to understand how and why people change their drinking outside of specialized treatment settings as it is within them.

Toward this goal of understanding the mechanisms of behavioral change, new transdisciplinary, multilevel, and collaborative approaches are needed that integrate multiple domains of knowledge, including cognitive, affective, and social neuroscience; neuroimaging; genomics; proteomics and metabolomics; social psychology; economics; and computational science. Progress in this complex and challenging area of treatment research will represent a major milestone for the alcohol treatment community.

Specific areas of research include, but are not limited to, the following examples:

**Behavioral Therapies**

- Identify and evaluate mechanisms underlying the effects of behavioral therapies.
- Develop innovative strategies to promote sustainable, positive drinking behavior change during both the initial phase of treatment and aftercare to maintain improvements in the long term.
- Develop strategies to enhance engagement, retention, and compliance of patients in treatment.
- Evaluate combinations and sequences of behavioral treatment.
- Combine cognitive/memory enhancement medications (e.g., D-cycloserine) to increase the effectiveness of behavioral therapies.
- Evaluate the efficacy of specialized behavioral therapies in understudied populations, including the elderly; racial/ethnic minorities; individuals in the criminal justice system; U.S. military personnel, and veterans and their families; and patients suffering from co-occurring psychiatric disorders.
- Investigate mind–body interventions (e.g., yoga, meditation, and biofeedback exercises) that may be used to reduce or prevent problematic drinking.

**Mechanisms of Behavioral Change**

- Conduct longitudinal studies of the natural history of behavioral change in drinking behavior. Transdisciplinary research—including genetic, electrophysiological, and imaging techniques—is encouraged. Innovative measures of real-time cognitive and affective change also should be developed.
- Reanalyze existing studies (secondary analyses) with new models looking at potential mechanisms of change prior to treatment, and within, outside, and after treatment.
- Conduct experiments to elucidate the causal relationship between proposed mechanisms of behavioral change and treatment outcomes.
- Investigate network theory and analysis and new methods of computational and mathematical modeling to understand the complex interactions among individuals, their social systems, and the treatment settings.
- Add supplemental questions, aims, and measures, such as assessments of behavioral change and social context, to existing alcohol treatment and epidemiological studies.

3. **Health Services Research**

Based on data from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC), a national survey of the non-institutionalized population in the United States, it has become clear that the U.S. population is characterized by a continuum of drinking types, ranging from low-risk drinkers to high-risk and chronic, relapsing alcohol-dependent drinkers. Approximately 65 percent (144 million) of adult Americans drank alcohol at various times during the past year. Of those, 59 million Americans exceeded high-risk drinking limits and 18 million of these had a diagnosis of alcohol use disorders. Only an estimated 13 percent of people identified as alcohol dependent had ever received specialty alcohol treatment. Epidemiological data such as these demonstrate the need to broaden and enhance the continuum of health care for alcohol-related...
problems and disorders. The menu of alcohol services, and the organizations that deliver them, needs to be diversified, enhanced, extended, and provided in a range of settings that meet the needs of underserved groups needing interventions tailored to their specific alcohol-related issues. Treatments that are attractive, affordable, accessible, and effective for different types of drinkers need to be identified, tested, and adopted. For example, stepped care would be appropriate for reducing binge drinking in a college population, whereas collaborative care models that integrate treatments for addiction and co-occurring conditions in primary care would be more appropriate for alcohol-dependent individuals with co-occurring medical and/or psychiatric conditions.

These research challenges provide many exciting opportunities for advancing services research. Barriers to treatment must be identified and effective strategies developed to offset these barriers in a variety of settings, including specialty addiction settings, general medical settings (e.g., primary care and mental health care), and settings outside the medical sector (e.g., the workplace and criminal justice, social welfare, and school systems). At a minimum, services should include screening, brief intervention, and referral, if needed. New approaches to establishing more effective evidence-based practices include adaptive models personalized to subtypes of drinkers, long-term management of chronic alcohol dependence, concurrent management of multiple comorbidities, and the patient-centered medical home model. These and other innovative health care approaches need to be adapted and tested for application in real-world practice settings.

Comparative effectiveness studies are encouraged as a tool for identifying the most effective and cost-effective evidence-based interventions. For example, comparing two or more pharmacological and/or behavioral therapies in the same study can be insightful in determining the better choice in certain populations and settings. In the end, this will make the treatment process more efficient and less costly. Also needed is treatment outcome research that identifies, evaluates, and tests long-term outcome measures in clinical effectiveness trials. This research should focus on how best to measure outcomes including drinking outcomes, quality of life, and alcohol-related consequences as well as measures of treatment quality and process from a multidisciplinary perspective. Applicants are also encouraged to discover and derive robust outcome measures from archival, policy, and other secondary data.

A recent review of the NIAAA health services research portfolio revealed a decade of significant advances in critical research areas while at the same time highlighting several important research gaps. As a result of the review and current trends in research on alcohol-related treatment, NIAAA encourages research from among the following five priority areas: implementation science, disease management, access to care, health disparities, and health economics.

Specific areas of research include, but are not limited to, the following examples:

**Implementation Science**

- Identify, develop, and test models and methods that can enhance the diffusion, implementation, and adoption of evidence-based alcohol-related treatment practices across the full spectrum of services for at-risk, harmful, and dependent drinkers.
- Identify, develop, and evaluate treatment outcomes for models tailored for non-medical settings (e.g., criminal justice, social welfare, workplace, and school settings) as well as models for medical non-specialty treatment settings (e.g., primary care and mental health services).
- Conduct comparative effectiveness studies to ascertain significant variations in the effectiveness and cost-effectiveness of evidence-based practices across client types and settings. Such research can help guide selection of models appropriate for implementation in practice.

**Disease Management**

- Develop and evaluate cost-effective disease management approaches and algorithms suitable for chronic relapsing conditions.
- Develop and test approaches to individualized care for patients with complex comorbidities.
- Identify or develop and test interventions that enhance the adherence and retention of patients.

Access to Care

- Identify and develop strategies to reduce personal and organizational barriers that prevent people with alcohol use disorders from seeking and receiving appropriate care.

Health Disparities

- Expand research on factors contributing to health disparities to include a broad range of personal characteristics and community settings that may affect health outcomes.
- Assess and evaluate variations in health disparities across a range of treatment settings.
- Develop measures to assess the multiple components and dimensions of personal health disparities models (e.g., health literacy, access to health care, confidence in the proximal health system, socioeconomic status, sociocultural beliefs and practices related to alcohol use, and personal health care).

Health Economics

- Conduct natural history studies on the impact of changes in health care policy on alcohol-related services delivery and quality.
- Employ comparative effectiveness research to map variations in the cost and cost-effectiveness across types of interventions, drinkers, and/or settings that do/do not provide alcohol-related treatment services.
- Use comparative effectiveness research to compare two or more organizational strategies for reducing adverse events such as disability and premature morbidity and mortality.

4. Recovery Research

The term recovery refers to the disappearance of the signs and symptoms of alcohol use disorder accompanied by a state of well-being following an episode of alcohol use disorder. Research indicates that there is a substantial level of recovery from alcohol dependence. Twenty years after the onset of alcohol dependence, about three-fourths of individuals are no longer dependent. Moreover, more than half of those individuals drink at low-risk levels without symptoms of alcohol dependence. Approximately 75 percent of persons who recover from alcohol dependence do so without seeking any kind of help, including specialty alcohol programs and Alcoholics Anonymous (AA). Recovery outside of treatment is more likely in those with fewer symptoms of dependence and fewer comorbid psychiatric disorders. Notwithstanding the high rates of natural recovery from alcohol dependence, in most cases, it is a chronic relapsing illness with serious, often devastating psychological, medical, and social consequences for affected individuals and families over time. In many cases, whether or not affected individuals ever seek treatment, the adverse consequences of alcoholism extend well beyond the period of dependent drinking and may even span multiple generations.

What causes change in drinking behavior that leads to recovery? Because most individuals recover without treatment, it is important to study natural recovery by evaluating mediators and moderators of drinking behavior in subtypes of alcohol users. Biological, psychological, and contextual factors should be considered, including, but not limited to, cultural and socioeconomic milieu, lifestyle, endophenotypes, cognitive functioning, and sleep and other medical disorders.

Specific areas of research include, but are not limited to, the following examples:

- Conduct observational, epidemiological, or natural history studies that lay the foundation for understanding mediators and moderators of recovery in subtypes of alcohol users.
- Conduct systematic studies of natural recovery.
- Identify precipitants of relapse, including components of the protracted withdrawal syndrome, and
evaluate the adverse effects of these precipitants on the course of recovery.

- Identify and evaluate mediators and moderators of recovery in different subtypes of alcohol users, including, but not limited to: variations associated with diverse cultural and socioeconomic milieus, developmental stage, lifestyle, endophenotypes, cognitive functioning, and sleep and other medical disorders.
- Understand the dynamics of both positive and negative changes in quality of life as a function of chronic drinking, recovery, and relapse.

**Special-Emphasis Populations and Topics**

**A) Treatment for Psychiatric/Substance Abuse/Medical Comorbidity**

Alcohol-dependent individuals have exceptionally high rates of co-occurring psychiatric disorders. According to NESARC data, for example, alcohol-dependent individuals, as compared with non-alcohol-dependent individuals, are about four times more likely to have a mood disorder, three times more likely to have an anxiety disorder, seven times more likely to have an antisocial personality disorder, six times more likely to be nicotine dependent, and over thirty times more likely to be dependent on other drugs. Approximately half of individuals with schizophrenia suffer from an alcohol and/or substance use disorder. Similarly, 46 percent of those with bipolar disorder also have an alcohol use disorder. Moreover, in alcohol treatment populations, risk and prevalence rates of co-occurring psychiatric and substance use disorders are often much higher than those observed in the general population. For example, the rate of tobacco use among alcohol-dependent individuals seeking alcohol treatment is approximately 80 percent compared with 26 percent among non-dependent individuals in the general population. In addition, a significant number of alcohol-dependent individuals exhibit two or more comorbidities. Although individuals with comorbid alcohol dependence and psychiatric disorders are most likely to seek treatment, they have a poorer treatment prognosis, a higher risk for treatment dropout, less support for sobriety from family and the work environment, and a higher risk for suicide.

In addition to psychiatric and substance abuse comorbidities, a significant number of alcohol-dependent patients have comorbid medical disorders. For example, in the United States, approximately 20 percent of patients in treatment for HIV have been diagnosed with current co-occurring alcohol use disorders. Rates are even higher for a diagnosis of lifetime alcohol use disorders, with estimates of 26 to 60 percent in people living with HIV/AIDS as compared with 14 to 24 percent in the general population. Recent studies suggest that problematic drinking worsens the clinical course of HIV/AIDS. In addition, over 4 million Americans are living with hepatitis C infection. High-risk drinking also has been associated with hepatitis C, and like HIV/AIDS, drinking may accelerate the progression of this disease. Often HIV/AIDS and hepatitis C are co-occurring conditions that complicate the long-term treatment of this population.

Research on effective strategies to treat alcohol comorbidity is still in its early stages. The appropriate treatment strategy depends on the type and severity of the comorbidity as well as population subtypes within a comorbid population.

Specific areas of research include, but are not limited to, the following examples:

- Evaluate specialized pharmacological and behavioral interventions for alcohol-dependent/abusing patients with psychiatric/substance abuse comorbidity.
- Evaluate specialized pharmacological and behavioral interventions for alcohol-dependent patients who smoke.
- Evaluate medications to prevent or reduce drinking in alcohol-dependent/abusing patients with a comorbid medical disorder including HIV/AIDS and hepatitis C. Determine whether reductions in drinking improve compliance with medications for the medical condition, attenuate the progression of the medical disorder(s), and prevent early mortality.
- Determine the relationship between alcohol and the comorbid condition during treatment. For example, does treatment of either the alcohol or comorbid disorder also concurrently improve the outcome for
Differentiate phenotypes within a type of comorbidity and across comorbidities.
Develop and test theoretical models that underlie comorbidity, integrating biological, genetic, environmental, psychological, and cognitive components.
Establish interdisciplinary partnerships to integrate biological, behavioral, psychological, and social research for the purpose of developing and testing novel treatments for comorbidity.

B) Treatment for Adolescents

Alcohol use remains a pervasive problem for adolescents in the United States, resulting in adverse and sometimes serious consequences. Approximately 12 percent of 12-year-olds, 30 percent of 14-year-olds, 60 percent of 16-year-olds, and over 70 percent of 18-year-olds consumed alcohol. Across all adolescents groups, there are approximately 7.2 million binge drinkers, 2.3 million heavy drinkers, and 1.5 million with alcohol use disorders. Most adolescents in treatment for alcohol and/or drug problems relapse after 6 months of conventional treatment. Researchers have begun to test a variety of behavioral therapies, including cognitive behavioral therapy, family-based interventions, multisystemic therapy, and motivational enhancement therapy. So far, only a few medications studies have been conducted in this population.

Research on adolescent treatment is still in early stages. To design more effective treatments, it is important to develop a multidisciplinary approach that integrates biological, psychological, and social factors across different stages of development. Furthermore, future research needs to focus on subgroups of adolescents, including those with a range of alcohol severities, different comorbidities, racial ethnic groups, and cultural differences. Studies also should evaluate different settings, including rural, community, schools, unemployment programs, and the juvenile justice system.

Specific areas of research include, but are not limited to, the following examples:

- Develop and test pharmacological and behavioral treatments in adolescents with drinking problems. Interventions should be tailored to developmental, biological, psychological, and social needs of adolescents.
- Conduct longitudinal treatment studies of adolescents and develop advanced mathematical approaches that take into account diverse developmental processes and transitions. Explore different types of treatment endpoints for adolescents across the multiple stages of development.

C) Treatment for Fetal Alcohol Spectrum Disorders (FASD)

The FASD “umbrella” encompasses an array of health consequences of prenatal alcohol exposure including birth defects and neurological abnormalities in children whose mothers consumed alcohol during pregnancy. Fetal alcohol syndrome (FAS), a condition at the most severe end of the FASD spectrum, is characterized by facial dysmorphology, growth retardation, and brain damage, resulting in cognitive and behavioral impairments. Today, FAS remains the leading known preventable cause of mental retardation and other neurobehavioral disabilities. It is estimated that 1 to 2 per 1,000 live births in the United States have FAS, and the incidence of all FASD is on the order of 1 per 100 live births. A host of secondary impairments stem from the behavioral deficits of those with FASD. Their characteristic poor judgment, faulty social skills, and failure to learn from experience commonly lead to complications, such as substance use, arrest/incarceration, failure in school, economic problems, unemployment, and psychiatric comorbidities. Sadly, FASD is frequently not recognized or treated. A major research effort is needed to improve the identification and treatment of children and adults with FASD.

Specific areas of research include, but are not limited to, the following examples:

- Develop effective pharmacological and behavioral treatments for FASD-related problems, including, but not limited to, harmful drinking behaviors among children and adults with FASD.
- Investigate individual, familial, cultural, and/or environmental characteristics that mitigate or exacerbate
the effects of prenatal alcohol exposure.

- Develop and/or validate markers to detect drinking and alcohol cessation interventions that are suited for pregnant women and safe for the developing fetus.

D) Treatment for Health Disparities/Special Populations

NIAAA seeks to elucidate the importance of alcohol treatment, service delivery, and recovery research among racial/ethnic groups and rural and low-income populations. In addition to these populations already experiencing health disparities in the United States, the recent immigration of large numbers of people from diverse cultures requires examination of existing treatment methods for relevance, efficacy, and effectiveness across all levels of adaptation/acculturation. Other subgroups with specific needs that often are understudied include: youths ages 18 to 25 not attending college; youths in the juvenile justice system and/or foster care; adults over the age of 65; youths and adults living in rural or other areas where treatment access is difficult; women residing in shelters for victims of domestic violence; the unemployed; minorities (e.g., Native Americans, African Americans, Hispanic Americans, and Asian American/Pacific Islanders); and adolescents and adults with developmental disabilities due to prenatal alcohol exposure. Of particular interest is comparative effectiveness research in special populations.

Military personnel, veterans, and their families are also an NIAAA priority. In particular, NIAAA seeks research on the development of effective alcohol screening instruments and treatments for this population. Comparative effectiveness research to compare the benefits and harms of different interventions and strategies to prevent, diagnose, treat, and monitor harmful drinking and alcohol use disorders is needed in military settings and in veterans and military family environments. Treatment research should address a variety of comorbid conditions commonly found in this population, including posttraumatic stress disorder (PTSD), traumatic brain injury, depression, anxiety, sleep disturbances, and chronic pain. Of particular interest is research related to individuals who are serving or have served in Operation Enduring Freedom (Afghanistan) and Operation Iraqi Freedom (Iraq). In addition, research related to all phases of the deployment cycle (e.g., pre-deployment, deployment, reintegration, and separation) for all branches of the military and veterans is of interest. National Guard and Reserve service members, Individual Augmentees, and families have been identified as special needs populations that are of particular interest due to limitations in support related to not being attached to a military installation.

Specific areas of research include, but are not limited to, the following examples:

- Develop and implement effective pharmacological and behavioral treatments for understudied special needs populations.
- Identify and develop strategies to reduce personal and organizational barriers that prevent special populations with alcohol use disorders from seeking and receiving appropriate care.
- Investigate the application of evidence-based interventions with populations affected by health disparities and other special populations. Data-based elucidation of the conditions under which standard evidence-based interventions should be adapted with special populations is especially lacking in the literature.
- Explore the influence of culture, gender, race/ethnicity, socioeconomic status, and military service on seeking specialty treatment, remaining in treatment, and maintaining gains post-treatment.
- Investigate potential similarities and differences in mechanisms of behavioral change for problematic alcohol use among racial/ethnic minority, rural, and low-income populations; and military, veterans, and military family populations.

E) Use of Novel Methods and Technologies

Within the last decade, a number of novel methods and technologies have been developed to speed the course of alcohol treatment and related research. For instance, the widespread availability of the Internet, wireless technology, and computers has made possible a number of technological advances that capture important real-time information from patients in the field; synthesize, simulate, and statistically model large
quantities of data in efficient and clinically meaningful ways; and deliver interactive computerized versions of promising behavioral interventions.

With the tremendous promise potentially afforded by these tools, research and development is continually evolving. More research is needed to further develop, refine, validate, and creatively implement these novel methods within alcohol clinical trials and treatment paradigms.

Specific areas of research include, but are not limited to, the following examples:

**Technological Methods**

- Develop and validate ecological momentary assessment (EMA) methods (e.g., interactive voice response technology, cell phones, and transdermal alcohol monitors) for capturing real-time data for use in clinical trials and treatment paradigms.
- Devise novel methods (e.g., Web-mining software of social networking sites) that capture social network information among groups at risk for alcohol dependence and high-risk drinking.
- Develop and validate efficacious computerized behavioral interventions for use in reaching remote or underserved populations of problem drinkers.

**Statistical Methods**

- Evaluate the impact of new statistical models and methods on treatment effectiveness outcomes—for instance, comparing the relative impact of linear models and dynamic models on clinical trial outcomes.
- Use person-centered statistical approaches (e.g., trajectory analysis and growth mixture modeling) to capture changes in outcomes over time and convey results that are more clinically intuitive.
- Develop cross-design synthesis statistical methods to standardize and compare clinical data collected by different methods.
- Use in silico or other computation methods to facilitate development of new compounds for the treatment of alcohol dependence.
- Develop and implement new, efficient adaptive clinical trial designs and statistical analyses that allow for adjustments to treatment based on the changing disease status of the patient.

See [Section VIII, Other Information - Required Federal Citations](http://grants.nih.gov/grants/guide/pa-files/PA-10-100.htm) for policies related to this announcement.

**Section II. Award Information**

**1. Mechanism of Support**

This FOA will use the Research Project Grant (R01) award mechanism. The Project Director/Principal Investigator (PD/PI) will be solely responsible for planning, directing, and executing the proposed project.

This FOA uses “Just-in-Time” information concepts (see SF424 (R&R) Application Guide). It also uses the modular as well as the non-modular budget formats (see http://grants.nih.gov/grants/funding/modular/modular.htm). Specifically, a U.S. organization submitting an application with direct costs in each year of $250,000 or less (excluding consortium Facilities and Administrative [F&A] costs) should use the PHS398 Modular Budget component.

U.S. applicants requesting more than $250,000 in annual direct costs and all foreign applicants must complete and submit budget requests using the Research & Related Budget component.

**2. Funds Available**
Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the financial plans of the IC(s) provide support for this program, awards pursuant to this funding opportunity are contingent upon the availability of funds.

Facilities and Administrative (F&A) costs requested by consortium participants are not included in the direct cost limitation, see NOT-OD-05-004.

NIH grants policies as described in the NIH Grants Policy Statement will apply to the applications submitted and awards made in response to this FOA.

Section III. Eligibility Information

1. Eligible Applicants

1.A. Eligible Institutions

The following organizations/institutions are eligible to apply:

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education
- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Small Businesses
- For-Profit Organizations (Other than Small Businesses)
- State Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- Indian/Native American Tribally Designated Organizations
- U.S. Territory or Possession
- Indian/Native American Tribal Governments (Other than Federally Recognized)
- Regional Organizations
- Non-domestic (non-U.S.) Entities (Foreign Organizations)
- Other(s):
  - Eligible Agencies of the Federal Government
  - Faith-based or Community-based Organizations.

1.B. Eligible Individuals

Any individual(s) with the skills, knowledge, and resources necessary to carry out the proposed research as the PD/PI is invited to work with his/her organization to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support.

More than one PD/PI (i.e., multiple PDs/PIs), may be designated on the application for projects that require a “team science” approach and therefore clearly do not fit the single-PD/PI model. Additional information on the implementation plans and policies and procedures to formally allow more than one PD/PI on individual research projects is available at [http://grants.nih.gov/grants/multi_pi](http://grants.nih.gov/grants/multi_pi). All PDs/PIs must be registered in the NIH electronic Research Administration (eRA) Commons prior to the submission of the application (see...

The decision of whether to apply for a grant with a single PD/PI or multiple PDs/PIs is the responsibility of the investigators and applicant organizations and should be determined by the scientific goals of the project. Applications for grants with multiple PDs/PIs will require additional information, as outlined in the instructions below. When considering the multiple PD/PI option, please be aware that the structure and governance of the PD/PI leadership team as well as the knowledge, skills and experience of the individual PDs/PIs will be factored into the assessment of the overall scientific merit of the application. Multiple PDs/PIs on a project share the authority and responsibility for leading and directing the project, intellectually and logistically. Each PD/PI is responsible and accountable to the grantee organization, or, as appropriate, to a collaborating organization, for the proper conduct of the project or program, including the submission of required reports. For further information on multiple PDs/PIs, please see http://grants.nih.gov/grants/multi_pi.

2. Cost Sharing or Matching

This program does not require cost sharing as defined in the current NIH Grants Policy Statement.

3. Other-Special Eligibility Criteria

**Number of Applications.** Applicants may submit more than one application, provided that each application is scientifically distinct.

**Resubmissions.** Applicants may submit a resubmission application, but such application must include an Introduction addressing the previous peer review critique (Summary Statement). Beginning with applications intended for the January 25, 2009 official submission due date, all original new applications (i.e., never submitted) and competing renewal applications are permitted only a single amendment (A1). See new NIH policy on resubmission (amended) applications (NOT-OD-09-003, NOT-OD-09-016). Original new and competing renewal applications that were submitted prior to January 25, 2009 are permitted two amendments (A1 and A2). For these “grandfathered” applications, NIH expects that any A2 will be submitted no later than January 7, 2011, and NIH will not accept A2 applications after that date.

**Renewals.** Applicants may submit a renewal application.

**Section IV. Application and Submission Information**

To download a SF424 (R&R) Application Package and SF424 (R&R) Application Guide for completing the SF424 (R&R) forms for this FOA, use the “Apply for Grant Electronically” button in this FOA or link to http://www.grants.gov/Apply/ and follow the directions provided on that Web site.

**Registration:**

Appropriate registrations with Grants.gov and eRA Commons must be completed on or before the due date in order to successfully submit an application. Several of the steps of the registration process could take four weeks or more. Therefore, applicants should immediately check with their business official to determine whether their organization/institution is already registered with both Grants.gov and the Commons. All registrations must be complete by the submission deadline for the application to be considered “on-time” (see 3.C.1 for more information about on-time submission).

A one-time registration is required for institutions/organizations at both:

- Grants.gov (http://www.grants.gov/applicants/get_registered.jsp) and
- eRA Commons (http://era.nih.gov/ElectronicReceipt/preparing.htm)
PDs/PIs should work with their institutions/organizations to make sure they are registered in the NIH eRA Commons.

Several additional separate actions are required before an applicant can submit an electronic application, as follows:

1) Organizational/Institutional Registration in Grants.gov/Get Registered

http://www.grants.gov/applicants/get_registered.jsp

- Your organization will need to obtain a Data Universal Number System (DUNS) number and register with the Central Contractor Registration (CCR) as part of the Grants.gov registration process.
- If your organization does not have a Taxpayer Identification Number (TIN) or Employer Identification Number (EIN), allow for extra time. A valid TIN or EIN is necessary for CCR registration.
- The CCR also validates the EIN against Internal Revenue Service records, a step that will take an additional one to two business days.
- Direct questions regarding Grants.gov registration to:
  Grants.gov Customer Support
  Contact Center Phone: 800-518-4726
  Business Hours: M-F 7:00 a.m. - 9:00 p.m. Eastern Time
  Email support@grants.gov

2) Organizational/Institutional Registration in the eRA Commons

- To find out if an organization is already Commons-registered, see the "List of Grantee Organizations Registered in NIH eRA Commons."
- Direct questions regarding the Commons registration to:
  eRA Commons Help Desk
  Phone: 301-402-7469 or 866-504-9552 (Toll Free)
  TTY: 301-451-5939
  Business hours M-F 7:00 a.m. – 8:00 p.m. Eastern Time
  Email commons@od.nih.gov

3) Project Director/Principal Investigator (PD/PI) Registration in the NIH eRA Commons: Refer to the NIH eRA Commons System (COM) Users Guide.

- The individual(s) designated as PDs/PIs on the application must be registered also in the NIH eRA Commons. In the case of multiple PDs/PIs, all PDs/PIs must be registered and be assigned the PI role in the eRA Commons prior to the submission of the application.
- Each PD/PI must hold a PD/PI account in the Commons. Applicants should not share a Commons account for both an Authorized Organization Representative/Signing Official (AOR/SO) role and a PD/PI role; however, if they have both a PD/PI role and an Internet Assisted Review (IAR) role, both roles should exist under one Commons account.
- When multiple PDs/PIs are proposed, all PDs/PIs at the applicant organization must be affiliated with that organization. PDs/PIs located at another institution need not be affiliated with the applicant organization, but must be affiliated with their own organization to be able to access the Commons.
- This registration/affiliation must be done by the AOR/SO or his/her designee who is already registered in the Commons.

Both the PD(s)/PI(s) and AOR/SO need separate accounts in the NIH eRA Commons since both are authorized to view the application image.

Note: The registration process is not sequential. Applicants should begin the registration processes for both Grants.gov and eRA Commons as soon as their organization has obtained a DUNS number. Only one DUNS number is required and the same DUNS number must be referenced when completing Grants.gov registration,
eRA Commons registration and the SF424 (R&R) forms.

1. Request Application Information

Applicants must download the SF424 (R&R) application forms and the SF424 (R&R) Application Guide for this FOA through Grants.gov/Apply.

Note: Only the forms package directly attached to a specific FOA can be used. You will not be able to use any other SF424 (R&R) forms (e.g., sample forms, forms from another FOA), although some of the “Attachment” files may be usable for more than one FOA.

For further assistance, contact GrantsInfo -- Telephone 301-435-0714, Email: GrantsInfo@nih.gov.

Telecommunications for the hearing impaired: TTY: (301) 451-5936

2. Content and Form of Application Submission

Prepare all applications using the SF424 (R&R) application forms for this FOA through Grants.gov/Apply and in accordance with the SF424 (R&R) Application Guide (http://grants.nih.gov/grants/funding/424/index.htm).

The SF424 (R&R) Application Guide is critical to submitting a complete and accurate application to NIH. Some fields within the SF424 (R&R) application components, although not marked as mandatory, are required by NIH (e.g., the "Credential" log-in field of the "Research & Related Senior/Key Person Profile" component must contain the PD/PI's assigned eRA Commons User ID). Agency-specific instructions for such fields are clearly identified in the Application Guide. For additional information, see "Frequently Asked Questions – Application Guide, Electronic Submission of Grant Applications."

The SF424 (R&R) application has several components. Some components are required, others are optional. The forms package associated with this FOA in Grants.gov/APPLY includes all applicable components, required and optional. A completed application in response to this FOA includes the data in the following components:

Required Components:
SF424 (R&R) (Cover component)
Research & Related Project/Performance Site Locations
Research & Related Other Project Information
Research & Related Senior/Key Person
PHS398 Cover Page Supplement
PHS398 Research Plan
PHS398 Checklist
PHS398 Modular Budget or Research & Related Budget, as appropriate (See Section IV.6. regarding appropriate required budget component.)

Optional Components:
PHS398 Cover Letter File
Research & Related Subaward Budget Attachment(s) Form

Foreign Organizations (Non-domestic [non-U.S.] Entities)


Applications from Foreign organizations must:
- Request budgets in U.S. dollars;
- Prepare detailed budgets for all applications (that is, complete the Research & Related Budget component of the SF424 (R&R) application forms – not the PHS398 Modular Budget component)(see NOT-OD-06-096);
- Not include any charge-back of customs and import fees;
- Comply with the format specifications, which are based upon a standard U.S. paper size of 8.5" x 11" within each PDF;
- If appropriate, request funds for up to 8% Facilities and Administrative (F&A) costs (excluding equipment) (see NOT-OD-01-028, March 29, 2001);
- Comply with Federal/NIH policies on human subjects, animals, and biohazards; and
- Comply with Federal/NIH biosafety and biosecurity regulations (see Section VI.2., “Administrative and National Policy Requirements”)

Proposed research should provide special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions in other countries that are not readily available in the United States (U.S.) or that augment existing U.S. resources.

SPECIAL INSTRUCTIONS

Applications with Multiple PDs/PIs

When multiple PDs/PIs are proposed, NIH requires one PD/PI to be designated as the "Contact" PI, who will be responsible for all communication between the PDs/PIs and the NIH, for assembling the application materials outlined below, and for coordinating progress reports for the project. The contact PD/PI must meet all eligibility requirements for PD/PI status in the same way as other PDs/PIs, but has no other special roles or responsibilities within the project team beyond those mentioned above.

Information for the Contact PD/PI should be entered on the SF424 (R&R) Cover component. All other PDs/PIs should be listed in the Research & Related Senior/Key Person component and assigned the project role of “PD/PI.” Please remember that all PDs/PIs must be registered in the eRA Commons prior to application submission. The Commons ID of each PD/PI must be included in the “Credential” field of the Research & Related Senior/Key Person component. Failure to include this data field will cause the application to be rejected.

Multiple PD/PI Leadership Plan: For applications designating multiple PDs/PIs, the Research Plan section and the Multiple PD/PI Leadership Plan must be included. A rationale for choosing a multiple PD/PI approach should be described. The governance and organizational structure of the leadership team and the research project should be described, and should include communication plans, process for making decisions on scientific direction, and procedures for resolving conflicts. The roles and administrative, technical, and scientific responsibilities for the project or program should be delineated for the PDs/PIs and other collaborators.

If budget allocation is planned, the distribution of resources to specific components of the project or the individual PDs/PIs should be delineated in the Leadership Plan. In the event of an award, the requested allocations may be reflected in a footnote on the Notice of Award (NoA).

Applications Involving a Single Institution

When all PDs/PIs are within a single institution, follow the instructions contained in the SF424 (R&R) Application Guide.

Applications Involving Multiple Institutions

When multiple institutions are involved, one institution must be designated as the prime institution and funding
for the other institution(s) must be requested via a subcontract to be administered by the prime institution. When submitting a detailed budget, the prime institution should submit its budget using the Research & Related Budget component. All other institutions should have their individual budgets attached separately to the Research & Related Subaward Budget Attachment(s) Form. See Section 4.8 of the SF424 (R&R) Application Guide for further instruction regarding the use of the subaward budget form.

When submitting a modular budget, the prime institution completes the PHS398 Modular Budget component only. Information concerning the consortium/subcontract budget is provided in the budget justification. Separate budgets for each consortium/subcontract grantee are not required when using the Modular budget format. See Section 5.4 of the Application Guide for further instruction regarding the use of the PHS398 Modular Budget component.

3. Submission Dates and Times

See Section IV.3.A. for details.

3.A. Submission, Review, and Anticipated Start Dates

Opening Date: May 5, 2010 (Earliest date an application may be submitted to Grants.gov)

Application Due Date(s): Standard dates apply, please see http://grants.nih.gov/grants/funding/submissionschedule.htm

AIDS Application Due Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#AIDS

Peer Review Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward

Council Review Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward

Earliest Anticipated Start Date(s): Standard dates apply, please see http://grants1.nih.gov/grants/funding/submissionschedule.htm#reviewandaward

3.A.1. Letter of Intent

A letter of intent is not required for the funding opportunity.

3.B. Submitting an Application Electronically to the NIH

To submit an application in response to this FOA, applicants should access this FOA via http://www.grants.gov/applicants/apply_for_grants.jsp and follow Steps 1-4. Note: Applications must only be submitted electronically. PAPER APPLICATIONS WILL NOT BE ACCEPTED. All attachments must be provided to NIH in PDF format, filenames must be included with no spaces or special characters, and a .pdf extension must be used.

3.C. Application Processing

3.C.1 Submitting On-Time

Applications may be submitted on or after the opening date and must be successfully received by Grants.gov no later than 5:00 p.m. local time (of the applicant institution/organization) on the application due date(s). (See Section IV.3.A. for all dates.) If an application is not submitted by the due date(s) and time, the application may be delayed in the review process or not reviewed. All applications must meet the following criteria to be considered “on-time”:

- All registrations must be complete prior to the submission deadline
- The application must receive a Grants.gov tracking number and timestamp (or eRA help desk ticket confirming a system issue preventing submission) by 5:00 p.m. local time on the submission deadline
Any system identified errors/warnings must be corrected and the submission process completed within the "error correction window."

Please visit [http://era.nih.gov/electronicReceipt/app_help.htm](http://era.nih.gov/electronicReceipt/app_help.htm) for detailed information on what to do if Grants.gov or eRA system issues threaten your ability to submit on time.

Submission to Grants.gov is not the last step – applicants must follow their application through to the eRA Commons to check for errors and warnings and view their assembled application!

### 3.C.2 Two Day Window to Correct eRA Identified Errors/Warnings

**IMPORTANT NOTE!** NIH has eliminated the error correction window for due dates of January 25, 2011 and beyond. As of January 25, all corrections must be complete by the due date for an application to be considered on-time. See [NOT-OD-10-123](https://grants.nih.gov/grants/guide/pa-files/PA-10-100.htm).

Once an application package has been successfully submitted through Grants.gov, NIH provides applicants a two day *error correction window* to correct any eRA identified errors or warnings before a final assembled application is created in the eRA Commons. The standard error correction window is two (2) business days, beginning the day after the submission deadline and excluding weekends and standard federal holidays. All errors must be corrected to successfully complete the submission process. Warnings will not prevent the application from completing the submission process.

Please note that the following caveats apply:

- Initial application submission must be "on-time."
- The AOR/institutions is expected to enforce that application changes made within the error correction window are restricted to those necessary to address system-identified errors/warnings. NIH may reject any application that includes additional changes.
- Proof of "on-time" submission (e.g., Grants.gov timestamp and tracking number) and description of all changes made within the window must be documented in the PHS 398 Cover Letter component of the application.

### 3.C.3 Viewing an Application in the eRA Commons

Once any eRA identified errors have been addressed and the assembled application has been created in the eRA Commons, the PD/PI and the Authorized Organization Representative/Signing Official (AOR/SO) have two weekdays (Monday – Friday, excluding Federal holidays) to view the assembled application before it automatically moves forward to NIH for further processing.

- If everything is acceptable, no further action is necessary. The application will automatically move forward to the Division of Receipt and Referral in the Center for Scientific Review for processing after two weekdays, excluding Federal holidays.
- Prior to the submission deadline, the AOR/SO can "Reject" the assembled application and submit a changed/corrected application within the two-day viewing window. This option should be used if it is determined that some part of the application was lost or did not transfer correctly during the submission process, the AOR/SO will have the option to "Reject" the application and submit a Changed/Corrected application. In these cases, please contact the eRA Help Desk to ensure that the issues are addressed and corrected. Once rejected, applicants should follow the instructions for correcting errors in Section 2.12 of the SF 424 (R&R) application guide, including the requirement for cover letters on late applications. The "Reject" feature should also be used if you determine that warnings are applicable to your application and need to be addressed now. Remember, warnings do not stop further application processing. If an application submission results in warnings (but no errors), it will automatically move forward after two weekdays if no action is taken. Some warnings may need to be addressed later in the
process.

- If the two-day window falls after the submission deadline, the AOR/SO will have the option to "Reject" the application if, due to an eRA Commons or Grants.gov system issue, the application does not correctly reflect the submitted application package (e.g., some part of the application was lost or didn't transfer correctly during the submission process). The AOR/SO should first contact the eRA Commons Helpdesk to confirm the system error, document the issue, and determine the best course of action. NIH will not penalize the applicant for an eRA Commons or Grants.gov system issue.
- If the AOR/SO chooses to "Reject" the image after the submission deadline for a reason other than an eRA Commons or Grants.gov system failure, a changed/corrected application still can be submitted, but it will be subject to the NIH late policy guidelines and may not be accepted. The reason for this delay should be explained in the cover letter attachment.
- Both the AOR/SO and PD/PI will receive e-mail notifications when the application is rejected or the application automatically moves forward in the process after two weekdays.

Upon receipt, applications will be evaluated for completeness by the Center for Scientific Review, NIH. Incomplete applications will not be reviewed.

There will be an acknowledgement of receipt of applications from Grants.gov and the Commons. The submitting AOR/SO receives the Grants.gov acknowledgments. The AOR/SO and the PI receive Commons acknowledgments. Information related to the assignment of an application to a Scientific Review Group is also in the Commons.

**Note:** Since email can be unreliable, it is the responsibility of the applicant to check periodically on their application status in the Commons.

The NIH will not accept any application in response to this FOA that is essentially the same as one currently pending initial merit review unless the applicant withdraws the pending application. The NIH will not accept any application that is essentially the same as one already reviewed. However, the NIH will accept a resubmission application, but such application must include an Introduction addressing the critique from the previous review.

### 4. Intergovernmental Review

This initiative is not subject to intergovernmental review.

### 5. Funding Restrictions

All NIH awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement.

Pre-award costs are allowable. A grantee may, at its own risk and without NIH prior approval, incur obligations and expenditures to cover costs up to 90 days before the beginning date of the initial budget period of a new or renewal award if such costs: 1) are necessary to conduct the project, and 2) would be allowable under the grant, if awarded, without NIH prior approval. If specific expenditures would otherwise require prior approval, the grantee must obtain NIH approval before incurring the cost. NIH prior approval is required for any costs to be incurred more than 90 days before the beginning date of the initial budget period of a new or renewal award.

The incidence of pre-award costs in anticipation of a competing or non-competing award imposes no obligation on NIH either to make the award or to increase the amount of the approved budget if an award is made for less than the amount anticipated and is inadequate to cover the pre-award costs incurred. NIH expects the grantee to be fully aware that pre-award costs result in borrowing against future support and that such borrowing must not impair the grantee's ability to accomplish the project objectives in the approved time frame or in any way adversely affect the conduct of the project. See NIH Grants Policy Statement.
6. Other Submission Requirements

PD/PI Credential (e.g., Agency Login)

The NIH requires the PD(s)/PI(s) to fill in his/her Commons User ID in the “PROFILE – Project Director/Principal Investigator” section, “Credential” log-in field of the “Research & Related Senior/Key Person Profile” component.

Organizational DUNS

The applicant organization must include its DUNS number in its Organization Profile in the eRA Commons. This DUNS number must match the DUNS number provided at CCR registration with Grants.gov. For additional information, see “Frequently Asked Questions – Application Guide, Electronic Submission of Grant Applications.”

PHS398 Research Plan Component Sections

All application instructions outlined in the SF424 (R&R) Application Guide are to be followed, incorporating “Just-in-Time” information concepts, and with the following additional requirements:

- Introduction (required for a resubmission or revision application) is limited to 1 page.
- Specific Aims is limited to 1 page.
- Research Strategy, including tables, graphs, figures, diagrams, and charts, is limited to 12 pages. See Table of Page Limits.

Budget Component

U.S. applicants submitting an application with direct costs in each year of $250,000 or less (excluding consortium Facilities and Administrative [F&A] costs) must use the PHS398 Modular Budget component.

U.S. applicants requesting more than $250,000 in annual direct costs and all foreign applicants must complete and submit budget requests using the Research & Related Budget component.

Specific Instructions for Applications Requesting $500,000 (direct costs) or More per Year

Applicants requesting $500,000 or more in direct costs for any year (excluding consortium F&A costs) must carry out the following steps:

1) Contact the IC program staff at least 6 weeks before submitting the application, i.e., as plans are being developed for the study;

2) Obtain agreement from the IC staff that the IC will accept the application for consideration for award; and,

3) Include a cover letter with the application that identifies the staff member and IC who agreed to accept assignment of the application.

This policy applies to all new, renewal, revision, or resubmission applications. See NOT-OD-02-004.

Appendix Materials
Applicants must follow the specific instructions on Appendix materials as described in the SF424 (R&R) Application Guide (See [http://grants.nih.gov/grants/funding/424/index.htm](http://grants.nih.gov/grants/funding/424/index.htm)).

Do not use the Appendix to circumvent the page limitations. An application that does not comply with the required page limitations may be delayed in the review process.

**Resource Sharing Plan(s)**

NIH considers the sharing of unique research resources developed through NIH-sponsored research an important means to enhance the value and further the advancement of the research. When resources have been developed with NIH funds and the associated research findings published or provided to NIH, it is important that they be made readily available for research purposes to qualified individuals within the scientific community. If the final data/resources are not amenable to sharing, this must be explained in the Resource Sharing section of the application (see [http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm](http://grants.nih.gov/grants/policy/data_sharing/data_sharing_faqs.htm)).

(a) **Data Sharing Plan**: Investigators seeking $500,000 or more in direct costs in any year are expected to include a brief 1-paragraph description of how final research data will be shared, or explain why data-sharing is not possible. Applicants are encouraged to discuss data-sharing plans with their NIH program contact (see Data-Sharing Policy or [http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html)).

(b) **Sharing Model Organisms**: Regardless of the amount requested, all applications in which the development of model organisms is anticipated are expected to include a description of a specific plan for sharing and distributing unique model organisms and related resources, or state appropriate reasons why such sharing is restricted or not possible (see Sharing Model Organisms Policy, and NIH Guide NOT-OD-04-042.)

(c) **Genome-Wide Association Studies (GWAS)**: Regardless of the amount requested, applicants seeking funding for a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. A genome-wide association study is defined as any study of genetic variation across the entire genome that is designed to identify genetic associations with observable traits (e.g., blood pressure or weight) or the presence or absence of a disease or condition. For further information see [Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies (NOT-OD-07-088)](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html) and [http://grants.nih.gov/grants/gwas/](http://grants.nih.gov/grants/gwas/).

**Foreign Applications (Non-domestic [non-U.S.] Entities)**

Indicate how the proposed project has specific relevance to the mission and objectives of the NIH/IC and has the potential for significantly advancing the health sciences in the United States

**Section V. Application Review Information**

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1. **Criteria**

Only the review criteria described below will be considered in the review process.

2. **Review and Selection Process**

**Review Process**

Applications submitted for this funding opportunity will be assigned on the basis of established PHS referral guidelines to the ICs for funding consideration.
Applications that are complete will be evaluated for scientific and technical merit by (an) appropriate scientific review group(s) in accordance with NIH peer review procedures (http://grants.nih.gov/grants/peer/) using the review criteria stated below.

As part of the scientific peer review, all applications will:

- Undergo a selection process in which only those applications deemed to have the highest scientific and technical merit, generally the top half of applications under review, will be discussed and assigned an impact/priority score;
- Receive a written critique; and
- Receive a second level of review by an appropriate advisory council or board

The mission of the NIH is to support science in pursuit of knowledge about the biology and behavior of living systems and to apply that knowledge to extend healthy life and reduce the burdens of illness and disability. As part of this mission, applications submitted to the NIH for grants or cooperative agreements to support biomedical and behavioral research are evaluated for scientific and technical merit through the NIH peer review system.

**Overall Impact**

Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five scored review criteria, and additional review criteria (as applicable for the project proposed).

**Scored Review Criteria**

Reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

**Significance.** Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

**Investigator(s).** Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

**Innovation.** Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

**Approach.** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?
Environment. Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?

Additional Review Criteria

As applicable for the project proposed, reviewers will consider the following additional items in the determination of scientific and technical merit, but will not give separate scores for these items.

Protections for Human Subjects. For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials.

Inclusion of Women, Minorities, and Children. When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children.

Vertebrate Animals. The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information, see http://grants.nih.gov/grants/olaw/VASchecklist.pdf.

Biohazards. Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmission Applications. When reviewing a Resubmission application (formerly called an amended application), the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Renewal Applications. When reviewing a Renewal application (formerly called a competing continuation application), the committee will consider the progress made in the last funding period.

Revision Applications. When reviewing a Revision application (formerly called a competing supplement application), the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

Additional Review Considerations
As applicable for the project proposed, reviewers will address each of the following items, but will not give scores for these items and should not consider them in providing an overall impact/priority score.

Applications from Foreign Organizations. As applicable for the FOA or submitted application, reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Select Agents Research. Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).


Budget and Period Support. Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research.

Selection Process

Applications submitted in response to this funding opportunity will compete for available funds with all other recommended applications submitted in response to this FOA. The following will be considered in making funding decisions:

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.

3. Anticipated Announcement and Award Dates

Not Applicable

Section VI. Award Administration Information

1. Award Notices

After the peer review of the application is completed, the PD/PI will be able to access his or her Summary Statement (written critique) via the NIH eRA Commons.

If the application is under consideration for funding, NIH will request "just-in-time" information from the applicant. For details, applicants may refer to the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General.

A formal notification in the form of a Notice of Award (NoA) will be provided to the applicant organization. The NoA signed by the grants management officer is the authorizing document. Once all administrative and programmatic issues have been resolved, the NoA will be generated via email notification from the awarding component to the grantee business official.
Selection of an application for award is not an authorization to begin performance. Any costs incurred before receipt of the NoA are at the recipient's risk. These costs may be reimbursed only to the extent considered allowable pre-award costs. See Section IV.5., “Funding Restrictions.”

2. Administrative and National Policy Requirements

All NIH grant and cooperative agreement awards include the NIH Grants Policy Statement as part of the NoA. For these terms of award, see the NIH Grants Policy Statement Part II: Terms and Conditions of NIH Grant Awards, Subpart A: General and Part II: Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities.

3. Reporting

When multiple years are involved, awardees will be required to submit the Non-Competing Continuation Grant Progress Report (PHS 2590) annually and financial statements as required in the NIH Grants Policy Statement.

A final progress report, invention statement, and Financial Status Report are required when an award is relinquished when a recipient changes institutions or when an award is terminated.

Section VII. Agency Contacts

We encourage your inquiries concerning this funding opportunity and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research (program), peer review, and financial or grants management issues:

1. Scientific/Research Contact(s):

Page Chiapella, Ph.D.
Division of Treatment and Recovery Research
National Institute on Alcohol Abuse and Alcoholism
5635 Fishers Lane, MSC 9304
Bethesda, MD 20892-9304
(For express mail, use Rockville, MD 20852-1705]
Phone: (301) 443-4715
FAX: (301) 443-8774
Email: pchiapel@wilco.niaaa.nih.gov

2. Peer Review Contact(s):

Not Applicable

3. Financial/Grants Management Contact(s):

Judy Fox
Chief, Grants Management Branch
Office of Extramural Activities
National Institute on Alcohol Abuse and Alcoholism
5635 Fishers Lane, Room 3023
Bethesda, MD 20892-9304
(For express mail, use Rockville, MD 20852-1705]
Phone: (301) 443-4704
Section VIII. Other Information

Required Federal Citations

Use of Animals in Research:

Human Subjects Protection:
Federal regulations (45 CFR 46) require that applications and proposals involving human subjects must be evaluated with reference to the risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained (http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm).

Data and Safety Monitoring Plan:
Data and safety monitoring is required for all types of clinical trials, including physiologic toxicity and dose-finding studies (Phase I); efficacy studies (Phase II); efficacy, effectiveness and comparative trials (Phase III). Monitoring should be commensurate with risk. The establishment of data and safety monitoring boards (DSMBs) is required for multi-site clinical trials involving interventions that entail potential risks to the participants ("NIH Policy for Data and Safety Monitoring," NIH Guide for Grants and Contracts, http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

Sharing Research Data:
Investigators submitting an NIH application seeking $500,000 or more in direct costs in any single year are expected to include a plan for data sharing or state why this is not possible (http://grants.nih.gov/grants/policy/data_sharing). Investigators should seek guidance from their institutions, on issues related to institutional policies and local institutional review board (IRB) rules, as well as local, State and Federal laws and regulations, including the Privacy Rule.

Policy for Genome-Wide Association Studies (GWAS):
NIH is interested in advancing genome-wide association studies (GWAS) to identify common genetic factors that influence health and disease through a centralized GWAS data repository. For the purposes of this policy, a genome-wide association study is defined as any study of genetic variation across the entire human genome that is designed to identify genetic associations with observable traits (such as blood pressure or weight), or the presence or absence of a disease or condition. All applications, regardless of the amount requested, proposing a genome-wide association study are expected to provide a plan for submission of GWAS data to the NIH-designated GWAS data repository, or provide an appropriate explanation why submission to the repository is not possible. Data repository management (submission and access) is governed by the Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies, NIH Guide NOT-OD-07-088. For additional information, see http://grants.nih.gov/grants/gwas/.

Sharing of Model Organisms:
NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants.nih.gov/grants/policy/model_organism/index.htm). At the same time the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding.
pursuant to the Bayh-Dole Act (see the NIH Grants Policy Statement). Beginning October 1, 2004, all investigators submitting an NIH application or contract proposal are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

**Access to Research Data through the Freedom of Information Act:**
The Office of Management and Budget (OMB) Circular A-110 has been revised to provide access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are: (1) first produced in a project that is supported in whole or in part with Federal funds; and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment.

NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm. Applicants may wish to place data collected under this funding opportunity in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

**Inclusion of Women And Minorities in Clinical Research:**
It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43). All investigators proposing clinical research should read the "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research" (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the SF424 (R&R) application; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

**Inclusion of Children as Participants in Clinical Research:**
The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all clinical research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects (http://grants.nih.gov/grants/funding/children/children.htm).

**Required Education on the Protection of Human Subject Participants:**
NIH policy requires education on the protection of human subject participants for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. The policy is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.
Human Embryonic Stem Cells (hESC):
Criteria for Federal funding of research on hESCs can be found at http://stemcells.nih.gov/index.asp and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-116.html. Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (http://escr.nih.gov/). It is the responsibility of the applicant to provide in the project description and elsewhere in the application as appropriate, the official NIH identifier(s) for the hESC line(s) to be used in the proposed research.

NIH Public Access Policy Requirement:
In accordance with the NIH Public Access Policy, investigators funded by the NIH must submit or have submitted for them to the National Library of Medicine's PubMed Central (see http://www.pubmedcentral.nih.gov/), an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication. The NIH Public Access Policy is available at (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html). For more information, see the Public Access webpage at http://publicaccess.nih.gov/.

Standards for Privacy of Individually Identifiable Health Information:
The Department of Health and Human Services (HHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information", the "Privacy Rule", on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the HHS Office for Civil Rights (OCR).

Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

URLs in NIH Grant Applications or Appendices:
All applications and proposals for NIH funding must be self-contained within specified page limitations. For publications listed in the appendix and/or Progress report, Internet addresses (URLs) or PubMed Central (PMC) submission identification numbers must be used for publicly accessible on-line journal articles. Publicly accessible on-line journal articles or PMC articles/manuscripts accepted for publication that are directly relevant to the project may be included only as URLs or PMC submission identification numbers accompanying the full reference in either the Bibliography & References Cited section, the Progress Report Publication List section, or the Biographical Sketch section of the NIH grant application. A URL or PMC submission identification number citation may be repeated in each of these sections as appropriate. There is no limit to the number of URLs or PMC submission identification numbers that can be cited.

Healthy People 2010:
The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This FOA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

Authority and Regulations:
This program is described in the Catalog of Federal Domestic Assistance at http://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR Part 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement.
The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

**Loan Repayment Programs:**
NIH encourages applications for educational loan repayment from qualified health professionals who have made a commitment to pursue a research career involving clinical, pediatric, contraception, infertility, and health disparities related areas. The LRP is an important component of NIH’s efforts to recruit and retain the next generation of researchers by providing the means for developing a research career unfettered by the burden of student loan debt. Note that an NIH grant is not required for eligibility and concurrent career award and LRP applications are encouraged. The periods of career award and LRP award may overlap providing the LRP recipient with the required commitment of time and effort, as LRP awardees must commit at least 50% of their time (at least 20 hours per week based on a 40 hour week) for two years to the research. For further information, please see: [http://www.lrp.nih.gov/](http://www.lrp.nih.gov/).