UNIVERSITY of MARYLAND
THE FOUNDING CAMPUS

Date: Tuesday, July 3, 2018 1:42:54 PM
View: v2_Introduction Page

Print Close

Introduction Page

1 * Abbreviated Title:
Galantamine potentiation of nicotine

2 * Full Title:
The Use of Low-Dose Galantamine to Potentiate the Attention-Enhancing Effects of Low-Dose Nicotine

3 * Select Type of Submission:
IRB Application

Note: The Type of Submission cannot be changed after this application has been submitted for review.

4 Original Version #:

ID: VIEW4DF8709A33C00
Name: v2_Introduction Page

View: v2_Research Team Information

Research Team Information

1 * Principal Investigator - Who is the PI for this study (person must have faculty status)? ***Faculty status is defined as being a full-time (>51% effort) faculty member holding one of the following titles at UM: Professor; Associate Professor; Assistant Professor.***
Britta Hahn

1.1 * Does the Principal Investigator have a financial interest related to this research?
Yes **No**

2 Point of Contact - Who is the alternative point of contact for the PI? This person can be a study coordinator or any other study team member. In case the IRB cannot contact the PI, this person is a secondary person to contact:
Jacqueline Kiwanuka

2.1 Does the Point of Contact have a financial interest related to this research?
Yes **No**

3 Other Team Members - list all additional members of the research team for this study. DO NOT include the PI or POC in this list:

Name	Edit Submission	cc on Email	Research Role	Has SFI?
Franklin Blatt	no	no	Research Team Member	no
Marie Yuille	no	no	Research Team Member	no
Robert Buchanan	no	no	Sub-Investigator	no

IMPORTANT NOTE: All research team members (including PI) must have current CITI and HIPAA training completed.

ID: VIEW4DF85C16F2800
Name: v2_Research TeamInformation

View: v2_Resources

Resources

If this study is a collaborative UM/VA study, please clarify which resources are being used at each institution.

1 * Describe the time that the Principal Investigator will devote to conducting and completing the research:
25%, i.e. approximately 10 hours/week on average.

2 * Describe the facilities where research procedures are conducted:
This project will take place entirely at the Maryland Psychiatric Research Center (MPRC), located in Baltimore on the grounds of Spring Grove Hospital. The MPRC is a division of the Department of Psychiatry at the University of Maryland School of Medicine. It is dedicated to conducting research and education of the manifestations, causes, and treatment of schizophrenia and related disorders. Twenty basic science and clinical PIs work in the same facility. The MPRC consists of 4 programs: the Outpatient Research Program (ORP) , the Treatment Research Program, the Neuroscience Program, and the Neuroimaging Research Program. The current study will involve the ORP, headed by Dr. Buchanan. The ORP houses an outpatient clinic for people with schizophrenia. Its research focuses on clinical trials of novel schizophrenia medication including cognitive-enhancing agents, and on neuropsychological and cognitive neuroscience studies of cognition, motivation and

emotion.
Three rooms in the building are dedicated to computer-assisted and neuropsychological cognitive testing. Informed consents and interviews also take place here. Clinical facilities: The ORP houses a nurse's station equipped for performing blood draws, ECGs, vital signs, and physical exams in a private exam area. The lobby houses a large waiting area for patients and research subjects. Two rooms can be used as a participant lounge during drug absorption periods, providing comfortable seating and the opportunity to lie down or watch movies. The ORP has its own pharmacy run by a part-time pharmacist whose effort is fully dedicated to supporting research studies. The research and clinical staff at the ORP have existed as a joint venture for over 20 years.

3 * Describe the availability of medical and/or psychological resources that subjects might need as a result of anticipated consequences of the human research:
A study nurse will be on site and a physician familiar with the study will be on call for the duration of the study interventions (from when drug was administered to discharge of the participant. The availability of medical equipment is as described above. In the case of a severe adverse reaction or other medical emergency, emergency medical services would be called and the participant transferred to a hospital.

4 * Describe the process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions:
As part of protocol implementation, a Study Manual will be distributed to all persons involved, detailing Standard Operating Procedures for each person's role in the study procedures, procedures to be followed in the case of an adverse event, and emergency contact numbers. Prior to recruitment, all persons involved will meet, and the Principal Investigator will describe all procedures and sequences of events and answer any questions.

ID: VIEW4DF83CB976400
Name: v2_Resources

View: v2_Sites Where Research Activities Will Be Conducted

Sites Where Research Activities Will Be Conducted

1 * Is this study a:
- ○ Multi-Site
- ◉ **Single Site**

2 * Are you relying on an external IRB (not UM) to be the IRB of Record for this study?
○ Yes ◉ **No**

3 * Are any other institutions/organizations relying on UM to be the IRB of Record for this study?
○ Yes ◉ **No**

3.1 Attach the applicable regulatory documents here (i.e., IRB Authorization Agreement (IAA), FWA, local ethics approval, other IRB approvals, etc.). Final UM approval will be contingent upon final execution of all required regulatory approvals:

Name	Created	Modified Date

There are no items to display

4 * Is UM the Coordinating Center for this study? (Applicable for multi-site studies. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project.)
○ Yes ◉ **No**

5 Is VA the Coordinating Center for this study? (Applicable for Collaborative studies between the VA, UM and other sites. A Coordinating Center is responsible for overall data management, monitoring and communication among all sites, and general oversight of conduct of the project)
○ Yes ○ No

6 * Institution(s) where the research activities will be performed:
Maryland Psychiatric Research Center (MPRC)

ID: VIEW4DF870DF2C000
Name: v2_Sites Where Research Activities Will Be Conducted

View: v2_DHMH

DHMH

You selected "Maryland Psychiatric Research Center" or "DHMH" as a research site. Answer the following questions to determine if Department of Health and Mental Hygiene (DHMH) review is needed.

3.1 * Does this protocol require DHMH IRB review?
○ Yes ◉ **No**

3.2 If Yes, will the DHMH IRB rely on UM IRB as the IRB of record for review of this protocol?
○ Yes ○ No

ID: VIEW4DF86705BB800
Name: v2_DHMH

View: v2_Funding Information

Funding Information

1 * Indicate who is funding the study:
Federal

2 * What portion of the research is being funded? (Choose all that apply)
Drug
Staff
Participant Compensation
Procedures
Other

3 Please discuss any additional information regarding funding below:
All study expenses are covered by an NIH R01 grant to B.Hahn.

ID: VIEW4DF85DF452400
Name: v2_Funding Information

View: v2_DHHS Funded Study

DHHS Funded Study

You indicated that this is a Federally funded study.

1 * Is this study sponsored by a Department of Health and Human Services (DHHS) agency?
(●) **Yes** ( ) No

2 If Yes, indicate the grant number(s):
1R01DA035813-01 - OR - Check here if the grant is not assigned a number. ☐

3 If Yes, upload all grant documents:

Name	Created	Modified Date
Summary Statement	9/11/2013 1:24 PM	9/11/2013 1:24 PM
Application	9/11/2013 1:24 PM	9/11/2013 1:24 PM

ID: VIEW4DF87B9560800
Name: v2_DHHS Funded Study

View: v2_Federal Agency Sponsor Information

Federal Agency Sponsor Contact Information

You indicated that this is a Federally funded study.

1 * Agency Name:
NIH - National Institute of Mental Health

* Address 1:
9000 Rockville Pike

Address 2:

* City:
Bethesda

* State:
MD

* Zip Code:
20892

* Contact Person:
Steven Grant

* Phone Number:
301-443-4877

Grant Number 1 (if applicable):
1R01DA035813-01- OR - Check here if Grant 1 is not assigned a number. ☐

If Grant 1 has no number, please provide the following information:
Title of Grant 1:

PI of Grant 1:
Britta Hahn

Grant Number 2 (if applicable):
- OR - Check here if Grant 2 is not assigned a number.

If Grant 2 has no number, please provide the following information:
Title of Grant 2:

PI of Grant 2:

Grant Number 3 (if applicable):
- OR - Check here if Grant 3 is not assigned a number

If Grant 3 has no number, please provide the following information:
Title of Grant 3:

PI of Grant 3:

Grant Number 4 (if applicable):
- OR - Check here if Grant 4 is not assigned a number.

If Grant 4 has no number, please provide the following information:
Title of Grant 4:

PI of Grant 4:

ID: VIEW4DF8584874400
Name: v2_Federal Agency Sponsor Information

View: v2_Research Protocol

Research Protocol

1 * Do you have a research protocol to upload?
No, I do not have a research protocol and will use the CICERO application to enter my study information

2 If Yes, upload the research protocol:

Name	Created	Modified Date
There are no items to display		

ID: VIEW4E00563F8D000
Name: v2_Research Protocol

View: v2_Risk Level

Risk Level

What is the risk level of your study? (Ultimately, the IRB will determine the appropriate risk level and your designation is subject to change.)

* Choose One:
Greater Than Minimal - Does not meet the definition of Minimal Risk.

ID: VIEW4E02805225800
Name: v2_Risk Level

View: v2_Type of Research

Type of Research

1 * Indicate **ALL** of the types of research procedures involved in this study (Choose all that apply):
Use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol.
Psychological/Behavioral/Educational Method or Procedure (i.e., survey, questionnaires, interviews, focus groups, educational tests).
Sample (Specimen) Collection and/or Analysis (including genetic analysis).

2 * Is this study a clinical trial OR will this study be registered at ClinicalTrials.gov?
A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.
(•) **Yes** ( ) No

ID: VIEW4E0280569E000
Name: v2_Type of Research

View: v2_Lay Summary

Lay Summary

1 * Provide a summary of the background and purpose of the study in language that can be understood by a person without a medical degree.

Drugs that activate the nicotinic acetylcholine receptor (nAChR) such as nicotine enhance cognition, and efforts are underway to develop similar compounds as therapeutic agents. Over the last two decades, drug development efforts have been invested into nAChR agonists. Effects have generally been in the expected direction but tended to be of small magnitude and uncertain clinical significance. A potential way of increasing the effect size ceiling is by co-administering a nAChR allosteric potentiating ligand (APL). APLs do not activate the nAChR on their own but bind to a second, modulatory site and facilitate agonist-induced responses. The acetylcholinesterase inhibitor galantamine used for treating Alzheimer's disease is an APL at nAChRs at concentrations found in CSF at clinical doses. The concentration range for its APL action is slightly below that for AChE inhibition. Low dosing may thus induce a bias towards its APL action, which may potentiate the effects of a nAChR agonist such as nicotine and enhance its attention-enhancing properties.

ID: VIEW4E02805CF7000
Name: v2_Lay Summary

View: v2_Justification, Objective, & Research Design

Justification, Objective, & Research Design

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the purpose, specific aims, or objectives of this research. State the hypothesis to be tested:

The attention-enhancing effects of nicotinic acetylcholine receptor (nAChR) agonists may be of clinical potential. A potential way of raising the effect size ceiling of these effects is by co-administering a nAChR allosteric potentiating ligand (APL). The acetylcholinesterase inhibitor galantamine is an APL at nAChRs and may therefore potentiate the effects of a nAChR agonist and enhance its attention-enhancing properties.
The aim of the present study is to provide a proof of principle of allosteric potentiation of the attention-enhancing effects of nAChR agonists, using low-dose galantamine and low-dose nicotine as research tools shown to be safe in human subjects, even in combination. This proof of concept would stimulate the development of more selective (i.e. devoid of acetylcholinesterase inhibition) APLs for human therapeutic use (these compounds are currently only available for preclinical use). Nicotine is an agonist at all nAChR subtypes, and this non-selectivity makes it an ideal tool for this proof-of concept study. Ultimately, more selective nAChR agonists not currently available for human use would be expected to be employed therapeutically in combination with APL.
We hypothesize synergistic effects of nicotine and galantamine on attention, such that the attention-enhancing effects of low-dose nicotine and low-dose galantamine combined are greater than the attention-enhancing effects of either drug alone.

2 * Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.:

A single group of healthy non-smokers will complete 4 test sessions of performing cognitive (mostly attention) paradigms. In each session, a capsule containing placebo or 4 mg of galantamine (Galantamine HBr immediate release tablet, Patriot Pharmaceuticals, Horsham, PA) , and a skin patch containing placebo or 7 mg/24 hrs of nicotine (Nicoderm CQ, GlaxoSmithKline, Moon Township, PA) will be administered. Thus, each participant will be tested with Placebo+Placebo, Placebo+Nicotine, Galantamine +Placebo, and Galantamine +Nicotine, in a 2x2 factorial design. Nicotine is expected to enhance performance as shown previously. Galantamine , at the low dose administered, is expected to have minimal effects by itself, but to potentiate the effects of nicotine, resulting in an interaction of the effects of nicotine with galantamine , and significantly better performance after Galantamine +Nicotine than after Placebo+Nicotine.

3 * Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data:

Potentiation of nAChR agonist responses by APLs have been shown in vitro and in preclinical behavioral assays, but never in humans. The availability of nicotine and galantamine as safe human research tools may allow us to fill this gap.
We have previously shown that the low-dose nicotine patch (7 mg/24 hrs) to be used in the present experiment causes significant improvements in non-smokers in one of the three task paradigms to be employed in the present study.

4 * Provide the scientific or scholarly background, rationale, and significance of the research and how it will add to existing knowledge:

Several disease states marked by cognitive deficits, most prominently schizophrenia, Alzheimer's disease, and ADHD, entail nAChR hypofunction and have been suggested to benefit from nAChR agonist treatment(1,2). Cognitive benefits of the prototypical agonist nicotine that are not restricted to deprived smokers are well established and are reported most consistently in tests of attention(3-5). Over the last two decades, drug development efforts have been invested into more selective nAChR agonists, aiming for more pronounced benefits with reduced side effects. Effects have generally been in the expected direction(6-8) but tended to be of small magnitude and uncertain clinical significance. Many compounds failed clinical trials due to limited efficacy(6;9). Thus, attention-enhancing effects harvested from nAChR agonists to date have not lived up to their expected potential. The current study aims at evaluating a potential way to raise their effect size ceiling.
A potential way of increasing the effect size is by co-administering a nAChR APL. APLs do not activate the nAChR on their own but bind to a second, modulatory site and, through several possible mechanisms, facilitate agonist-induced responses(10). Some, although not all(11), APLs reverse desensitization of a fraction of nAChRs, specifically in the presence of low to intermediate agonist concentrations(10). Desensitization is more pronounced with nicotine than with acetylcholine (ACh)(12) and may limit effects of exogenous agonists in particular. Through partial reversal of desensitization or other mechanisms, combined APL and agonist treatment is expected to enhance nAChR neurotransmission and associated behavioral effects to a greater degree than a larger dose of agonist alone, while being more sparing of native circuit dynamics. The acetylcholinesterase inhibitor galantamine used for treating AD is an APL at nAChRs at concentrations found in CSF at clinical doses(13;14). Galantamine potentiates alpha4beta2, alpha3*, alpha6beta4 and alpha7 nAChR currents induced by ACh, nicotine or epibatidine, causing long-lasting increases in amplitude and frequency of nAChR-mediated responses(15-17). The APL action of co-administered galantamine may therefore potentiate the effects of a nAChR agonist and enhance its attention-enhancing properties. Galantamine has been safely co-administered with nicotine in experimental settings(18;19) and when prescribed to smokers. The concentration range for its APL action is slightly below that for AChE inhibition(14). Low dosing may thus induce a bias towards the APL action. Even at low doses, galantamine will have pharmacological actions besides allosteric potentiation, but an interaction with nicotine effects reflecting potentiation can be explained by allosteric potentiation and not acetylcholinesterase inhibition.

ID: VIEW4E02805EA0C00
Name: v2_Justification, Objective, & Research Design

View: v2_Supporting Literature

Supporting Literature

1 * Provide a summary of current literature related to the research: ***If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.***

1. Levin ED, Rezvani AH. Nicotinic treatment for cognitive dysfunction. Curr Drug Targets CNS Neurol Disord. 2002;1:423-431.
2. Singh A, Potter A, Newhouse P. Nicotinic acetylcholine receptor system and neuropsychiatric disorders. IDrugs. 2004;7:1096-1103.
3. Stolerman IP, Mirza NR, Shoaib M. Nicotine psychopharmacology: addiction, cognition and neuroadaptation. Med Res Rev. 1995;15:47-72.
4. Newhouse PA, Potter A, Singh A. Effects of nicotinic stimulation on cognitive performance. Curr Opin Pharmacol. 2004;4:36-46.
5. Heishman SJ, Kleykamp BA, Singleton EG. Meta-analysis of the acute effects of nicotine and smoking on human performance. Psychopharmacology (Berl). 2010;210:453-469.

6. Haydar SN, Dunlop J. Neuronal Nicotinic Acetylcholine Receptors - Targets for the Development of Drugs to Treat Cognitive Impairment Associated with Schizophrenia and Alzheimer's Disease. Current Topics in Medicinal Chemistry. 2010;10:144-152.
7. Radek RJ, Kohlhaas KL, Rueter LE, Mohler EG. Treating the cognitive deficits of schizophrenia with alpha4beta2 neuronal nicotinic receptor agonists. Curr Pharm Des. 2010;16:309-322.
8. Wallace TL, Ballard TM, Pouzet B, Riedel WJ, Wettstein JG. Drug targets for cognitive enhancement in neuropsychiatric disorders. Pharmacology Biochemistry and Behavior. 2011;99:130-145.
9. Hurst R, Rollema H, Bertrand D. Nicotinic acetylcholine receptors: From basic science to therapeutics. Pharmacology & Therapeutics. 2012;in press.
10. Williams DK, Wang JY, Papke RL. Positive allosteric modulators as an approach to nicotinic acetylcholine receptor-targeted therapeutics: Advantages and limitations. Biochemical Pharmacology. 2011;82:915-930.
11. Gronlien JH, Hakerud M, Ween H, Thorin-Hagene K, Briggs CA, Gopalakrishnan M, Malysz J. Distinct profiles of alpha 7 nAChR positive allosteric modulation revealed by structurally diverse chemotypes. Molecular Pharmacology. 2007;72:715-724.
12. Paradiso KG, Steinbach JH. Nicotine is highly effective at producing desensitization of rat alpha 4 beta 2 neuronal nicotinic receptors. Journal of Physiology-London. 2003;553:857-871.
13. Villarroya M, Garcia AG, Marco-Contelles J, Lopez MG. An update on the pharmacology of galantamine. Expert Opinion on Investigational Drugs. 2007;16:1987-1998.
14. Coyle JT, Geerts H, Sorra K, Amatniek J. Beyond In Vitro data: A review of In Vivo evidence regarding the allosteric potentiating effect of galantamine on nicotinic acetylcholine receptors in Alzheimer's neuropathology. Journal of Alzheimers Disease. 2007;11:491-507.
15. Santos MD, Alkondon M, Pereira EFR, Aracava Y, Eisenberg HM, Maelicke A, Albuquerque EX. The nicotinic allosteric potentiating ligand galantamine facilitates synaptic transmission in the mammalian central nervous system. Molecular Pharmacology. 2002;61:1222-1234.
16. Samochocki M, Hoffle A, Fehrenbacher A, Jostock R, Ludwig J, Christner C, Radina M, Zerlin M, Ullmer C, Pereira EFR, Lubbert H, Albuquerque EX, Maelicke A. Galantamine is an allosterically potentiating ligand of neuronal nicotinic but not of muscarinic acetylcholine receptors. Journal of Pharmacology and Experimental Therapeutics. 2003;305:1024-1036.
17. Dajas-Bailador FA, Heimala K, Wonnacott S. The allosteric potentiation of nicotinic acetylcholine receptors by galantamine is transduced into cellular responses in neurons: Ca2+ signals and neurotransmitter release. Molecular Pharmacology. 2003;64:1217-1226.
18. Sofuoglu M, Herman AI, Li Y, Waters AJ. Galantamine attenuates some of the subjective effects of intravenous nicotine and improves performance on a go no-go task in abstinent cigarette smokers: a preliminary report. Psychopharmacology. 2012;in press.
19. Sacco KA, Creeden C, Reutenauer EL, George TP. Effects of galantamine on cognitive deficits in smokers and non-smokers with schizophrenia. Schizophrenia Research. 2008;103:326-327.
20. Hahn B, Ross TJ, Stein EA. Neuroanatomical dissociation between bottom-up and top-down processes of visuospatial selective attention. Neuroimage. 2006;32:842-853.
21. Hahn B, Ross TJ, Yang Y, Kim I, Huestis MA, Stein EA. Nicotine enhances visuospatial attention by deactivating areas of the resting brain default network. J Neurosci. 2007;27:3477-3489.
22.. Hahn B, Harvey AN, Concheiro-Guisan M, Huestis MA, Holcomb HH, Gold JM. A test of the cognitive self-medication hypothesis of tobacco smoking in schizophrenia. Biological Psychiatry. 2013;74:436-443.
23. Koelega HS. Stimulant drugs and vigilance performance: a review. Psychopharmacology (Berl). 1993;111:1-16.
24. Wesnes K, Warburton DM. Effects of scopolamine and nicotine on human rapid information processing performance. Psychopharmacology (Berl). 1984;82:147-150.
25. Revell AD. Smoking and Performance - A Puff-By-Puff Analysis. Psychopharmacology. 1988;96:563-565.
26. Warburton DM, Arnall C. Improvements in Performance Without Nicotine Withdrawal. Psychopharmacology. 1994;115:539-542.
27. Warburton DM, Mancuso G. Evaluation of the information processing and mood effects of a transdermal nicotine patch. Psychopharmacology. 1998;135:305-310.
28. Foulds J, Stapleton J, Swettenham J, Bell N, McSorley K, Russell MAH. Cognitive performance effects of subcutaneous nicotine in smokers and never-smokers. Psychopharmacology. 1996;127:31-38.

2 If available, upload your applicable literature search:

Name	Created	Modified Date
There are no items to display		

3 * Provide a list of 3 keywords or search terms (1 per line) relevant to your research that would help potential participants find your study using search engines:

Keyword 1: cognition

Keyword 2: nicotine

Keyword 3: galantamine

ID: VIEW4E02805A7E400
Name: v2_Supporting Literature

View: v2_Study Procedures

Study Procedures

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below. (If this study is a collaborative UM/VA study please list each procedure that is being conducted and the locations where it is being conducted.)

1 * Describe all procedures being performed for research purposes only (these procedures would not be done if individuals were not in the study) and when they are performed, including procedures being performed to monitor subjects for safety or to minimize risks:

1. Consent and Screening visit: After Informed Consent is obtained, participant will undergo the following screening procedures: - Medical history and physical exam targeted at the physical, neurological, and cognitive inclusion and exclusion criteria. This includes taking body weight, a BP and heart-rate reading to check exclusion criteria of hyper- or hypotension, and an electrocardiogram (12-lead with 3-5 minute rhythm strip). Exclusionary conditions documented on ECG include: □ Wolff-Parkinson-White syndrome □ Myocardial ischemia and infarction □ Complete left bundle branch block □ PR interval < 120 ms or > 200 ms □ Prolonged QT interval (corrected) > 500 ms □ Cardiac arrhythmias as defined by PACs > 3 per min or PVCs > 1 per min - Standard clinical laboratory screening (urinalysis, chemistry, hematology incl. complete blood count) including tests for heart, kidney, and liver function, diabetes and anemia. - Urine drug test, as a possible indication for substance abuse or dependence - Urine pregnancy test for females - Alcohol breathalyzer test, as a possible indication for alcohol abuse or dependence - Breath CO reading, to verify non-smoking status - Targeted questions about smoking history and caffeine use - The SCID, to determine the presence/absence of psychiatric conditions. The disorders assessed include mood disorders, anxiety disorders, substance use disorders, psychotic disorders, somatoform disorders, and eating disorders. - Listing of all currently taken medication - Vision test - A short training version of the Rapid Visual Information Processing Task (RVIPT, described below). Our experience has shown that around 15% of volunteers are unable to perform this task at any level. These volunteers will not be invited for any study sessions

because the effects of interest of the study depend on the ability to perform the cognitive tasks. Participants who meet all inclusion and exclusion criteria will be invited for the training visit. 2. Training visit: Participants will receive instructions and perform a full-length version of each of the cognitive computer tasks. Participants who cannot perform any of these tasks cannot continue with the study; however, with the exception of the RVIPT, this is extremely unlikely. Participants are instructed to abstain from caffeine use on the day of testing and from alcohol use on the day of and the day prior to the test sessions, and are reminded to discontinue any other psychoactive substances (such as recreational THC use) for the duration of the study. 3. Test days (x 4): Upon arrival (around 9 am), a urine drug test, a urine pregnancy test, an alcohol and a CO breathalyzer test are performed, all of which have to be negative for the session to proceed. Participants will be tested for fever and asked about recent diarrhea or vomiting, all of which would lead to discontinuation of the study session. Next, a baseline resting blood pressure and heart rate measurement is taken, after which a patch is applied by a study nurse or physician and covered with tape. The patch will not be applied and the test day postponed if resting systolic blood pressure <90 or >145, resting diastolic blood pressure <55 or >90, or resting heart rate <55. The patch may be a nicotine patch (7 mg/24 hrs; Nicoderm CQ) or a placebo patch (a size-matched bandaid). The participant is then asked to rate their subjective state on the Profile Of Mood States (POMS), an adjective rating questionnaire considered a standardized mood state inventory (McNair et al. 1971). Next, the participant performs a brief refresher training on each of the cognitive tasks to be performed later. The participant is then led to a day room where they may read, watch movies, or use the internet. They are instructed to notify study staff immediately should they not feel well at any time. Every hour, their blood pressure and heart rate will be measured, and they will be asked about subjective side effects that may occur with nicotine or galantamine (see "Side-effects Checklist"). Parameters for discontinuing the study are resting BP >160/100, heart-rate >120 x 2 (measurement repeated after 10 min if first heart-rate >120), vomiting, or if at any time drug effects are perceived as subjectively too unpleasant for the participant to want to continue (in which case the patch will immediately be removed). Unless systolic blood pressure <90 mmHg, diastolic blood pressure <55 mmHg, or heart rate <55 bpm 3 hours post patch (in which case the study session would be aborted), participants will be given a capsule (p.o.) that may contain 4 mg of galantamine or inactive filler 3.5 hours after patch application. Immediately after the capsule is ingested, the participant is served lunch. The participant is also provided with ad libitum drinking water throughout the test day. Adequate fluid intake and administration with food have been shown to reduce the likelihood of gastrointestinal side effects of galantamine, and this will be stressed to the participant. Every half hour after capsule ingestion, the participant's blood pressure and heart rate will be measured, and they will be asked about subjective side effects that may occur with nicotine or galantamine (see "Side-effects Checklist"). An additional parameters for discontinuing the study now is resting heart-rate <50 x 2 (measurement repeated after 10 min if first heart-rate <50 bpm). Five hours after patch application (1.5 hours after capsule administration), participants are asked to complete the POMS again and will be led to a testing room and will perform the following 3 cognitive tasks in the sequence shown here (after the SARAT, blood pressure, heart rate and subjective side effects will be measured): - The SARAT is a human stimulus detection paradigm (Fig.1) first described and validated by Hahn et al.(2006) and found to be sensitive to the performance-enhancing effects of nicotine(21,22, and preliminary results). Participants fixate a central circle and respond to a 500-ms target signal presented randomly at one of 4 peripheral locations. A trial begins with the presentation of a cue in a central circle; target presentation follows after a variable stimulus onset asynchrony. The cue consists of 1 or 4 quarters of the circle turning black, indicating that the target will appear in one of the corresponding quadrants of the display. One cued location allows a precise prediction of the target location, resulting in a narrow and intense attentional focus. Four cued locations create the need to monitor broadly. The cue is not followed by a target on 20% of trials to discourage anticipatory responding to the cue. Trials are separated by a 1500-ms intertrial interval (ITI). Trial types are randomized. The task length is ~45 min. Performance measures are: % omission errors (i.e. % target trials with no response), % false alarms (i.e. % no-target trials with response), reaction time (RT), and RT variability (stdev of individual-trial RTs). - The Rapid Visual Information Processing Task (RVIPT) is a sustained attention paradigm requiring the maintenance of intense rapid information processing over time. Smoking and nicotine, the latter in smokers and non-smokers, have been repeatedly shown to improve detectability and RT and prevent performance decrement over time when observed(23-28). The task consists of a stream of single digits presented at a rate of 100/min. Subjects are instructed to respond when seeing a sequence of three consecutive odd or even digits. On average, 8 targets are presented per minute. The task will be performed continuously for 2 x 15 min, separated by a break to ensure feasibility. The 2 x 15-min as opposed to 10-min task duration frequently seen in the literature is chosen to ensure a robust signal-to-noise ratio and increase demands on sustained attention. Performance measures are %Correct responses, %False alarms, RT and RT variability. - The Change Detection Task (CDT) measures short-term memory performance. Participants view an encoding array of 1 or 5 colored squares for 200 ms. After a 1000-ms delay, the square(s) reappear(s). On 50% of trials, the color of one of the squares differs, and the task is to indicate whether the sample and test array differ by pressing one of two buttons. The more items are encoded in the 4-item condition, the greater the probability that the presence or absence of a change will be accurately indicated. By subtracting 1-item trial performance, which is mostly limited by attentional lapses, from 4-item trial performance, we control for attentional aspects of performance and derive a purer index of short-term memory. The task comprises 200 trials (~10 min). After task completion, blood pressure, heart rate and subjective side effects will be measured again, and the POMS will be completed. A 5 ml blood sample will then be collected from a forearm vein, centrifuged and frozen. At completion of the experiment, samples will be analyzed for nicotine and nicotine metabolite levels, galantamine levels, and acetylcholine esterase activity. If blood pressure and heart rate are within normal range and there are no subjective symptoms, the participant is discharged, otherwise the study physician will be consulted and the participant may be asked to stay under observation for a few hours. Additional drug information: Galantamine is available as 4, 8, and 12 mg tablets. To produce capsules containing 4 mg of galantamine, 12 mg tablets will be ground up, and one third of the weight of one tablet will be packaged into one capsule. Galantamine capsules and matching placebo capsules (containing methylcellulose) will be produced by Frank Blatt, PharmD at the Maryland Psychiatric Research Center.

2 * Describe all procedures already being performed for diagnostic or treatment purposes (if not applicable to the study, enter "N/A"):

N/A

Screening is performed to check the inclusion and exclusion criteria. Significant abnormal findings will be communicated to the participant and follow-up recommended if indicated. However, because volunteers present themselves as healthy, the screening procedures are not strictly speaking diagnostic.

3 * Describe the duration of an individual participant's participation in the study:

A maximum of 4 months may elapse between the consent &screening session and the first test session, else the participant would be re-consented and re-screened. A minimum of 1 week is required between test sessions (i.e. 6 intermediate non-test days) to ensure complete wash-out. The maximum allowable time between test sessions is 2 months, but all efforts will be made to keep this interval as short as possible. Thus, the longest possible study duration for each participant is 10 months. The fastest possible study completion is 3.5 weeks.

4 * Describe the duration of the entire study:

Once fully implemented, data acquisition for the study is expected to be completed within one year.

5 * Describe any additional participant requirements:

None.

ID: VIEW4E0280585B400
Name: v2_Study Procedures

View: v2_Sample Size and Data Analysis

Sample Size and Data Analysis

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Provide the rationale and sample size calculations for the proposed target population:

Effect sizes (Cohen's d) of nicotine effects on SARAT performance were medium to large for the dose (7 mg/24 h) and population (non-smokers) to be employed here. Thus, estimating the effect size of nicotine alone as d=0.6 is conservative. We assume the effect size for galantamine by itself to be minimal. Our main interest is how much the effect of nicotine+galantamine exceeds the effect of nicotine alone + galantamine alone (i.e. the size of the nicotine x galantamine interaction). E.g., if d=0.1 for galantamine vs. placebo, d=0.6 for nicotine, and d=1.35 for nicotine+galantamine, the size of the interaction would be 1.35-(0.1+0.6)=0.65. To detect an

interaction of that size in a 2x2 within-subject ANOVA with 80% power, assuming within-subject correlation ρ=0.7, would require N=24 subjects. As long as we expect the same size by which the effect of nicotine+galantamine exceeds the added effects of either drug alone, the same N would be required regardless of the effect size of drug 2 alone.
We anticipate that ~20% of enrolled participants will fail to complete the study (loss to follow-up, loss of eligibility, or inability to tolerate a study drug or to perform the cognitive tasks at training). Thus, we expect that enrolling 30 participants will result in the desired 24 completers. In addition, we expect ~1/3 screening failures. Thus, we would like to set the recruitment ceiling at 48 volunteers.

2 * Provide the plan for data analysis. Include in the description the types of comparisons that are planned (e.g., comparison of means, comparison of proportions, regressions, analysis of variance, etc.), which is the primary comparison/analysis, and how the analyses proposed will relate to the primary purposes of the study:
All dependent variables (task performance, POMS scores) will be analyzed by 2-factor repeated-measures ANOVA assessing the interaction of nicotine effects with the presence or absence of galantamine. Significant interactions will be followed by 1-factor ANOVA and post-hoc pair-wise comparisons.

ID: VIEW4E02806052800
Name: v2_Sample Size and Data Analysis

View: v2_Sharing of Results

Sharing of Results

1 * Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subjects or others (e.g., the subject's primary care physicians) and if so, describe how it will be shared:
If significant abnormalities are identified during screening, these test results would be given to the subject, together with a recommendation regarding the appropriate type of follow-up (e.g., see family doctor or specialist).

ID: VIEW4E02808CBD800
Name: v2_Sharing of Results

View: v2_Research with Drugs or Biologics

Research with Drugs or Biologics

You indicated on the "Type of Research" page that your study involves use of unapproved drug(s)/biologic(s) or approved drug(s)/biologic(s) whose use is specified in the protocol AND/OR evaluation of food(s) or dietary supplement(s) to diagnose, cure, treat, or mitigate a disease or condition.

1 * List all drugs/biologics to be administered in this study. Be sure to list each drug/biologic with its generic name only.

	Drug Name	FDA Approved	IND Number	PI IND Holder
View	Galantamine HBr (immediate release)	yes		
View	Nicotine	yes		

2 * Attach the drug package insert or investigational drug brochure for the drugs being administered in this study:

Nicoderm	9/13/2013 3:08 PM	9/13/2013 3:08 PM
Galantamine	9/13/2013 3:08 PM	9/13/2013 3:08 PM

3 If more than one drug is administered, discuss the risk implications of drug/therapy interactions:
There is no restriction on the clinical use of galantamine in smokers. Given the wide clinical use of galantamine, it must be assumed that galantamine has been consumed by a large number of smokers. The literature contains no studies or case reports suggesting that any risks or side effects associated with the use of galantamine are increased in smokers.
The galantamine drug label includes the following statement: "A synergistic effect is expected when cholinesterase inhibitors are given concurrently with succinylcholine, other cholinesterase inhibitors, similar neuromuscular blocking agents or cholinergic agonists such as bethanechol." Bethanechol is a selective muscarinic agonist. There are no warnings about nicotinic agonists, in particular.
Several research studies have administered galantamine with nicotine to human participants, or have administered galantamine explicitly to smoking populations:
- Sacco et al. (2008, Schiz Res 103:326-7) administered acute doses of 4 mg or 8 mg of galantamine to 6 satiated and 6 abstinent smokers and 9 non-smokers with schizophrenia. No significant adverse events were associated with galantamine in any group at either dose.
- Sofuoglu et al. (2012, Psychopharm 224:413-20) administered 8 mg of galantamine/day or placebo over 4 days to 12 abstaining smokers. On day 4, 1 hr after galantamine administration, participants received in IV injection of 1 mg/70 kg of nicotine. Galantamine treatment did not change the heart rate or blood pressure response to nicotine. No adverse events of the co-administration were reported.
- Diehl et al. (2006, Int J Clin Pharmacol 44:614-22) administered skin patches releasing ~11 mg of galantamine per day for 12 weeks to 56 detoxified alcohol-dependent smokers. Compared to a placebo group (N=58), there was no difference in the number of subjects dropping out of the study, and no difference in the frequency of adverse events. There were no serious adverse events in either group. The most frequent adverse events were skin reactions to the patch in either group.
Most studies administering galantamine to different patient population that included smokers did not report adverse effects in smokers vs. non-smokers.

4 * Will you be using Investigational Drug Services?
○ Yes ◉ **No**

ID: VIEW4E0916E6E1400
Name: v2_Research with Drugs or Biologics

View: v2_Drug or Biologic Storage and Handling

Drug or Biologic Storage and Handling

4.1 * Do you have a plan regarding access controls for essential and approproate research personnel?
◉ **Yes** ○ No

4.2 * Will you have procedures for verifying physical access to the drugs(s)?
◉ **Yes** ○ No

4.3 * Will you label the drug(s) so that it is (they are) used appropriately for the study?
◉ **Yes** ○ No

4.4 * Will there be an establishment of a drug transfer process both into and out of the research site?
Yes No

4.5 * Will the storage of the drug(s) be in a secure environment and include locks on doors and controlled access?
Yes No

4.6 * Do you have a plan for only allowing trained personnel to administer the drug(s)?
Yes No

4.7 If applicable, will the storage of the drug(s) be at the appropriate temperature, with a storage and temperature log?
Yes No

ID: VIEW4E1D85CC57C00
Name: v2_Drug or Biologic Storage and Handling

View: v2_Placebos

Placebos

1 * Is this study placebo controlled?
Yes No

ID: VIEW4E0514EECCC00
Name: v2_Placebos

View: v2_Placebo Use

Placebo Use

You indicated that this study is placebo-controlled.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1.1 * Justify the use of the placebo study design and how the benefit to society outweighs the risks to the participants:
This study is using a within-subjects design. Thus, there is no placebo group, only placebo conditions (test days on which no nicotine or no galantamine is given). This study is not a treatment study; it aims for a proof of principle. Nicotine and galantamine are used as research tools to demonstrate a beneficial interaction in healthy subjects.
Question 1.3 below does not apply. Clicked "Yes" because forced to make a choice.

1.2 * Is the placebo being used in place of standard therapy?
Yes **No**

1.3 * Is the standard treatment considered effective?
Yes No

ID: VIEW4E0514D79B400
Name: v2_Placebo Use

View: v2_Psychological/Behavioral/Educational Methods and Procedures

Psychological/Behavioral/Educational Methods & Procedures

You indicated on the "Type of Research" page that your study involves a psychological/behavioral/educational method or procedure such as a survey, questionnaire, interview, or focus group.

1 * Select all behavioral methods and procedures which apply to this study:
Surveys/questionnaires
Key informant or semi-structured individual interviews
Neuropsychological or psychophysiological testing

ID: VIEW4E09416F57800
Name: v2_Psychological/Behavioral/Educational Methods and Procedures

View: v2_Surveys/Questionnaires

Surveys/Questionnaires

You indicated that this study involves surveys and/or questionnaires.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * List all questionnaires/surveys to be used in the study, including both standardized and non-standardized assessments:
Profile Of Mood States (POMS)
Concomitant Meds Forms (psychiatric and non-psychiatric medication)
Side Effects Checklist

2 * Upload a copy of all questionnaires/surveys:

Name	Created	Modified Date
Psychiatric Medication Form	9/16/2013 4:15 PM	9/27/2013 5:03 PM

Name	Created	Modified Date
Side-Effects Checklist	9/16/2013 4:15 PM	9/16/2013 4:15 PM
Non-Psychiatric Medication Form	9/16/2013 4:15 PM	9/16/2013 4:15 PM
POMS	9/16/2013 4:15 PM	9/16/2013 4:15 PM

3 * What is the total length of time that each survey is expected to take?
~ 5 min each

4 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)
Yes **No**

5 * Do any questions elicit information related to the potential for harm to self or others?
Yes **No**

5.1 If Yes, what procedures are in place to assure safety?

ID: VIEW4E09460F5EC00
Name: v2_Surveys/Questionnaires

View: v2_Interviews

Interviews

You indicated that this study involves key informant or semi-structured individual interviews.

1 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)
Yes No

2 * Upload a copy of the interview script or guide that will be used to guide the interviews:

Name	Created	Modified Date
Structured Clinical Interview for DSM	9/16/2013 4:20 PM	9/16/2013 4:20 PM

3 * What is the individual duration of each interview and what is the entire duration of the interviews?
25-60 min

4 * How will the interview responses be recorded and by whom?
The clinical research assistant on the study will record answers on assessment forms. Summarized results will be entered into a secure database.

5 * Do any questions elicit information related to the potential for harm to self or others?
Yes No

5.1 If Yes, what procedures are in place to assure safety?
If a participant were to disclose his or her intent to harm him- or herself or others, the participant will be escorted to a psychiatrist, to a social worker, or to another clinician in our outpatient psychiatric clinic for an immediate evaluation. These clinicians will then determine appropriate action and follow-up depending on the circumstances.

ID: VIEW4E0947A633C00
Name: v2_Interviews

View: v2_Testing

Testing

You indicated that this study involves neuropsychological or psychophysiological testing.

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * List all of the tests to be used in the study, including both standardized and non-standardized assessments:
Computerized attention and short-term memory tasks (SARAT, RVIPT and CDT; see Study Procedures - 1)

2 * Describe procedures related to all testing:
At the time of obtaining informed consent, an investigator will roughly describe the tasks. The tasks will be explained and practiced during the training session. During visits 3, 4, 5 and 6 (test sessions), the tasks will be briefly practiced in the morning, just after patch administration, and then performed in their full length 5 hrs after patch administration. The SARAT requires detecting stimuli presented briefly in one of four peripheral locations, preceded by central cues predicting the stimulus location with varying precision. The RVIPT requires detecting sequences of 3 consecutive odd or even digits in streams of rapidly (100/min) presented digits. The CDT requires memorizing displays of 1 or 5 colored squares (note that the figure below should show 5 squares but only shows 4) and making a judgment of whether a probe stimulus, presented 1 s later, has changed color as compared with the encoding array.

3 * Upload relevant testing materials:

Name	Created	Modified Date
Example of a SARAT task display	9/16/2013 4:44 PM	9/16/2013 4:49 PM
RVIPT display.docx	9/16/2013 4:49 PM	9/16/2013 4:49 PM
Example of CDT task display	9/16/2013 4:47 PM	9/16/2013 4:47 PM

4 * What is the individual duration of each test and what is the entire duration of all tests?
SARAT: ~45 min
RVIPT: ~30 min
CDT: ~10 min

5 * Are any of the questions likely to cause discomfort in participants or cause harm if their confidentiality were breached? (i.e., Illegal activities)
Yes **No**

6 * Do any questions elicit information related to the potential for harm to self or others?
Yes **No**

6.1 If Yes, what procedures are in place to assure safety?

ID: VIEW4E0BC1E3C2800
Name: v2_Testing

View: v2_Sample Collection/Analysis

Sample Collection/Analysis

You indicated on the "Type of Research" page that your study involves a sample (specimen) collection and/or analysis.

1 * What type of samples will be involved in this study? (Check all that apply)
Prospective (will be collected)

2 * Will genetic analysis/testing be done on any of the samples?
Yes **No**

3 * Will this study involve banking of samples (storing for future research use)?
Yes **No**

4 * What is the purpose of the sample collection and/or analysis?
(1) A urine sample collected during screening and at the beginning of each of the three test sessions will be used for a drug screen and, if female, a pregnancy test. A drug and a urine sample collected during screening will undergo standard laboratory tests to test inclusion and exclusion criteria for the study.
(2) In each of the four test sessions (visits 3, 4, 5 and 6), a 5-ml blood sample will be collected to determine blood levels of nicotine, nicotine metabolites and galantamine, and acetylcholine esterase activity at the conclusion of the study.

5 * Is there the possibility that cell lines will be developed with any of the samples?
Yes **No**

6 * Will the samples be released to anyone not listed as an investigator on the protocol?
Yes **No**

6.1 If Yes, give name(s) and affiliation(s):

7 * Will the sample material be sold or given to any third parties?
Yes **No**

7.1 If Yes, give name(s) and address(es):

ID: VIEW4E0E1A4B80000
Name: v2_Sample Collection/Analysis

View: v2_Prospective Samples

Prospective Samples

You indicated that the study involves collection of prospective samples (specimens).

1 * What type of sample will be collected? (Check all that apply)
Blood
Urine

1.1 If Other, specify:

2 For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subject's entire participation time:
(1) Around 20 ml (4 teaspoons) of venous blood will be drawn during the screening visit.
(2) In each of the four test sessions (visits 3, 4, 5 and 6), 5 ml (about 1 teaspoon) of venous blood will be drawn.
In total, 40 ml of venous blood will be drawn over the course of the study.

3 * What type of samples will be collected? (Check all that apply)
Samples obtained specifically for research purposes-obtained via a separate collection procedure done solely for the purposes of the study

3.1 If Other, specify:

4 * How are these samples labeled? For example, do they contain name, initials, dates, Social Security number, medical record number, or other unique code?
(1) The samples obtained during screening are sent to LabCorp for analysis and are labeled with name and date. The requisition accompanying the samples is labeled with name, date, date of birth, gender, ordering physician, MPRC address and account number, initials of who obtained the sample, and whether or not the sample was obtained in a fasting state. Labcorp is required to maintain the privacy of PHI under HIPAA.
(2) The samples for determination of nicotine and nicotine metabolite levels will be sent to Dr. Huestis's lab at NIDA-IRP and will be labeled by MPRC ID and study ID, date, test session number, and initials of person who drew the blood. Dr. Huestis's group cannot link MPRC IDs to other identifying data.
(3) The samples for determination of galantamine levels and acetylcholine esterase activty will be sent to Dr. Abuquerque's and Dr. Pereira's lab at the UMSOM Department of Pharmacology and Experimental Therapeutics. These samples will be labeled as detailed under (2). Dr. Albuquerque's and Dr. Pereira's group also cannot link MPRC IDs to other identifying data.

5 * Will sample(s) be made available to the research subject (or his/her medical doctor) for other testing?
○ Yes ◉ **No**

6 * If a participant withdraws from the study, will that participant have the option to get the remaining portion of their sample(s) back?
○ Yes ◉ **No**

7 * If the participant withdraws, explain how their sample(s) will be handled (For example, will sample(s) be destroyed, anonymized, etc.):
(1) The samples will be destroyed after tests for inclusion/exclusion criteria have been completed.
(2) and (3) The samples obtained for nicotine and metabolite level analysis will be frozen until the study is completed. At this point, the samples will be analyzed and then destroyed. This will be done even if the participant withdraws from the study before completion.

8 * Will the samples be destroyed after the study is over?
◉ **Yes** ○ No

8.1 If No, describe how the samples will be stored, where they will be stored, and for how long.

ID: VIEW4E0E257D60C00
Name: v2_Prospective Samples

View: v2_Clinical Trial Registration

Clinical Trial Registration

You indicated on the "Type of Research" page that your study is a clinical trial.

1 * Does the UM Clinical Trials Registry policy require registration of this trial?
◉ **Yes** ○ No

2 * Has this trial been registered?
◉ **Yes** ○ No

ID: VIEW4E093BF078C00
Name: v2_Clinical Trial Registration

View: v2_Clinical Trial Registration Information

Clinical Trial Registration Information

You indicated that this clinical trial has been registered.

1 * Was this trial registered at www.clinicaltrials.gov?
◉ **Yes** ○ No

2 If no, was this trial registered on a site other than clinicaltrials.gov?
○ Yes ○ No

2.1 If Yes, specify the name of the other site:

2.2 Provide justification for registering this trial on this site:

3 * Registration Number
NCT02420327

ID: VIEW4E093BF1D0800
Name: v2_Clinical Trial Registration Information

View: v2_Participant Selection

Participant Selection

1 * How many local potential participants (or specimens/charts) do you anticipate will be screened for this study? ***Screening includes determining potential participants' initial eligibility for and/or interest in a study.***
100

2 * How many participants (or specimens, or charts) will be enrolled/used for this study? ***A local prospective participant is considered enrolled in the study when a UM-approved Informed Consent Document (not including separate screening consent forms) is signed.***

Local - the number being enrolled at this site:
100

Worldwide - the number being enrolled total at all sites (including local enrollment):
100

3 * Gender:
Male
Female

4 * Age(s):
18 years and older (Adult)

5 * Race/Ethnicity:
All Races Included

6 * Language(s):
English

6.1 Specify Other:

7 * Are you excluding a specific population, sub-group, or class?
(•) **Yes** ( ) No

7.1 If Yes, indicate your justification for excluding a specific population, sub-group, class, etc.:
Pregnant or lactating women will be excluded because the study involves drug administration.

ID: VIEW4E0E519C1D000
Name: v2_Participant Selection

View: v2_Vulnerable Populations

Vulnerable Populations

1 * Will you be including ANY of the following Vulnerable Populations? (Select all that apply)
Students

You may not include any members of the above populations as subjects in your research unless you indicate this here.

ID: VIEW4E0E519917800
Name: v2_Vulnerable Populations

View: v2_Vulnerable Populations - Students

Vulnerable Populations - Students

You indicated that students are included in this study.

1 * Describe the types of students that are included in this study:
Any individual who meets the inclusion/exclusion criteria will be allowed to participate in the study - regardless of whether or not they have student status at any school or university.

2 * Describe how you will prevent undue influence.
No special effort is made to recruit students, nor is there any special effort to eliminate them from the eligible pool of subjects. In order to protect the confidentiality of this group as well as of all subjects in this protocol, numbers rather than names will appear on charts, files, and digital data. The code linking the names with the number will be locked with limited access. Medical records will be kept confidential, with access granted only to those medical and research professionals directly involved with the study. No information that could be linked to any single participant will be reported in publications and presentations. Confidentiality will be protected to the fullest extent permitted by law. Participation of students in the University of Maryland System in research at the MPRC will not in any way affect educational plans or social relationship with the hospital/academic opportunity. The $20/hr incentive is not coercive. The Informed Consent process will be as outlined above and will not differ from that of other volunteers.

ID: VIEW4E0E519F32000
Name: v2_Vulnerable Populations - Students

View: v2_Eligibility

Eligibility

1 * Do you have an existing Eligibility checklist(s) for this study?
( ) Yes (•) **No**

1.1 If Yes, upload here. If you need a template, you can download it by clicking **HERE**. The checklists you upload will also be available under the Documents tab of this application.

Name	Created	Modified Date

Name	Created	Modified Date
There are no items to display		

1.2 If No, create an eligibility checklist below:

List inclusion criteria (List each Inclusion Criteria individually, using the ADD button):

	Number	Criteria
View	1	Aged 21 to 55 years.
View	2	No exposure to any nicotine-containing product in the last year.
View	3	Smoked no more that 40 cigarettes, cigars or cigarillos in lifetime.
View	4	Normal or corrected to normal vision (at least 20/80).
View	5	Body weight 110-220 lbs.

List exclusion criteria (List each Exclusion Criteria individually, using the ADD button):

	Number	Criteria
View	1	Pregnant or breast-feeding.
View	2	Drug or alcohol abuse or dependence currently or in the last 2 years.
View	3	DSM Axis I mood, anxiety or psychotic disorder.
View	4	Cardiovascular or cerebrovascular disease, such as history of myocardial infarction and ischemia, heart failure, angina, stroke, severe arrhythmias, or EKG abnormalities (Wolf-Parkinson-White syndrome, Complete left bundle branch block, PR interval <120 ms or >200 ms, Prolonged QT interval (corrected) >500 ms, Cardiac arrhythmias as defined by PACs >3 per min or PVCs >1 per min).
View	5	Uncontrolled hypertension (resting systolic BP above 140 or diastolic above 90 mm Hg).
View	6	Hypotension (resting systolic BP below 90 or diastolic below 60).
View	7	Significant kidney or liver impairment.
View	8	Moderate to severe asthma.
View	9	Obstructive pulmonary disease.
View	10	Type I or II diabetes.
View	11	Use of any centrally active medications; any peripherally acting cholinergic medications; cimetidine; ketoconazole; erythromycin; quinidine, or chronic nonsteroidal anti-inflammatory drugs.
View	12	History of or current neurological illnesses, such as stroke, seizure disorders, neurodegenerative diseases, or organic brain syndrome.
View	13	Learning disability, mental retardation, or any other condition that impedes cognition.
View	14	Heart rate <55 bpm.
View	15	Current or history of gastric ulcer disease.
View	16	Any surgeries requiring full anesthesia scheduled within 2 weeks of any of the study test sessions.
View	17	Anemia
View	18	Inability to perform the Rapid Visual Information Processing Task.

After entering the inclusion and exclusion criteria above, click the Save link. CICERO will automatically generate a printable Eligibility Checklist for you to use in your research. To review the checklist, click on the resulting link below. This checklist is also available under the Documents tab of this application.

Eligibility Checklist for HP-00057097 v9-23-2013-1379946670467(0.01)

ID: VIEW4E0E5185F9000
Name: v2_Eligibility

View: v2_Recruitment

Recruitment

1 * Describe plans for recruitment, including the identification of potential participants (or acquisition of charts/records/samples) and initial interactions with them: (If this study involves the VA please list all sites at which recruitment will take place.):
Participants will be recruited from the MPRC healthy control pool. Recruitment and screening for this control pool is covered under UMB IRB Protocol HP-00045643. Subjects enrolled in this protocol have agreed to be contacted by MPRC investigators to see if they are interested in participating in on-going studies. Furthermore, participants will be recruited via online ads on Craig's List, print-ads in local newspapers (which may also appear on the paper's webpage), and by registering the study with smartphone apps such as studyscavenger.com or trialsapp.com. In these apps, volunteers interested in doing studies may register their profile and get notified when a trial appears that matches their profile, or they can browse available studies in their area.

2 * Describe measures that will be implemented to avoid participant coercion or undue influence (if not applicable to the study, enter "N/A"):
During initial contact, potential participants are asked in a non-suggestive manner whether they are interested in learning more about this study. The consent form stresses that the study is voluntary and that there will be no adverse consequences for declining to participate or for ending participation early. The person obtaining consent will also emphasize this. The $20 per hour stipend is well within norms.

3 * Who will recruit participants (or acquire charts/records/samples) for this study? (Check all that apply)
PI
Study Staff

3.1 If you are using a third party, specify Third Party Recruiters:

4 Upload any recruitment tools such as screening/telephone scripts and introductory letters (do not upload advertisements here):

Name	Created	Modified Date

Name	Created	Modified Date
Craig's List Telephone Screening	9/19/2013 2:29 PM	9/19/2013 2:29 PM

ID: VIEW4E0BCAA0A6C00
Name: v2_Recruitment

View: v2_Advertising

Advertising

1 * Will you be using advertisements to recruit potential participants?
(●) **Yes** ( ) No

ID: VIEW4E0BCCF811000
Name: v2_Advertising

View: v2_Advertising Detail

Advertising Detail

You indicated that you will be using advertisements to recruit potential participants.

1.1 * Select the mode(s) of advertising (check all that apply):
Internet
Print
Other

1.1.1 If Other, specify:
Flyers to be put up on public bulletin boards in cafes, grocery stores, etc.

1.2 * Provide exact text of all proposed advertisement(s):
Craig's List ad:
The University of Maryland Baltimore, Maryland Psychiatric Research Center (Catonsville, MD 21228) is recruiting healthy non-smokers, 21-55 years of age, for a research study. Dr. Britta Hahn is the principal investigator. The study investigates attention, and it involves 6 visits. On two visits, you would be asked to wear a low-dose nicotine patch. On two visits, you would be asked to take a low dose of galantamine, a drug widely used for treating symptoms of Alzheimer's disease. Volunteers will be paid approximately $700 for completing the study. Tel: 410-402-6888.

Smart phone recruitment apps:
"The Use of Low-Dose Galantamine to Modulate the Attentional Effects of Low-Dose Nicotine
We study the effects of a low-dose nicotine patch on attention in the presence or absence of a low dose of galantamine, an FDA-approved drug used for treating Alzheimer's disease. The study involves wearing a nicotine patch for about 7 hours on two days, and taking a capsule containing a low dose of galantamine on two days. On each of four visit, you would be performing concentration tasks on a computer for 2 hours. You would be paid ~$700 for completing the study. To be in the study, you need to be a healthy non-smokers, 21-55 years of age, and weigh 110-220 lbs. "
The text may vary slightly depending on whether the app has separate fields and pre-defined categories for, e.g., age, compensation etc.

Print ad and Flyer:
"Are You A Healthy Non-Smoker?
Research Participants are needed to test whether the effects of nicotine on attention can be enhanced by a drug called galantamine. This mechanism may become useful in the treatment of schizophrenia, Alzheimer's disease, or other conditions.
You may qualify for our research study if you are:
*A healthy non-smoker
*21-55 years of age
*Weigh 110-220lbs
Qualified candidates for the Study will make 6 visits to Maryland Psychiatric Research Center (MPRC) in Catonsville, MD. On two visits, you would be asked to wear a low-dose nicotine patch. On two visits, you would be asked to take a low dose of galantamine.
*Compensation ~$700 for the completion of study
Call today for a confidential screening or more information:
Call 410-402-6888
OR email colmstead@mprc.umaryland.edu with your contact information
Maryland Psychiatric Research Center
www.mprc.umaryland.edu"

1.3 * Upload advertisement(s) here:

Name	Created	Modified Date
Craig's List Ad	9/19/2013 2:36 PM	7/11/2016 9:04 AM
Print ad	8/28/2014 4:35 PM	7/11/2016 9:03 AM
Flyer	11/20/2014 1:55 PM	7/11/2016 9:03 AM
Print ad Stevens	8/29/2014 3:33 PM	8/29/2014 3:34 PM
Print ad McComas	8/29/2014 3:33 PM	8/29/2014 3:33 PM

ID: VIEW4E0BCE82B8C00
Name: v2_Advertising Detail

View: v2_Research Related Risks

Research Related Risks

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer box below.

1 * Individually list each research-related risk, using a separate line for each. Next to each risk, delineate the likelihood/seriousness of the risk, and the provisions for minimizing the risk:
1. Some of the questions asked, in person or by questionnaire, to asses subjective state or drug side effects may be perceived as embarrassing. This is a relatively likely, but minor risk. Risk Minimization: Research activities occur in private settings. The confidentiality of all replies will be ensured and emphasized to participants.

2. Breach of confidentiality is always a concern in research. This is a serious, but relatively unlikely risk. Risk Minimization: Participants are assigned a code number, which will be the only identifier on all research data, including specimen samples and data in electronic and hard copy form. ID codes will be maintained in a secure electronic database separate from the study data, to which only investigators will have access. All data with identifiers are maintained separately from research data. Hardcopies of all records with identifiers are stored under double-locked conditions. Demographic and medical data will be stored in the ORP Clinical Database. All databases are handled via a local area network (LAN) maintained behind a Netscreen 5XP firewall with multiple layers of protection against unauthorized intrusion. Databases are maintained on a university server and are additionally protected by a 5-tiered system involving restricted access at the desktop, directory, database, reporting and table levels. Permissions are set by the PI. Data downloaded for analysis will be identified only by subject ID code. In addition, each participant is assigned a medical records folder to store paper copies of medically relevant documents. These charts are kept in locked filing cabinets in a locked room, and access is limited to MPRC study and clinical staff. The identity of participants will not be revealed to any unauthorized person or in any vehicle of public communication. A Certificate of Confidentiality was obtained to further protect participants.
3. Participants may find the cognitive tasks they are asked to perform boring, difficult or frustrating. The occurrence of at least boredom may be common, but none of these risks are severe. Risk Minimization: Tasks are organized in blocks of up to 5 min to give participants the chance to rest between blocks. In addition, the tasks are designed to make performance neither too difficult nor too easy. Participants receive extensive training before experimental testing begins. Participants who cannot perform the tasks are excluded from the study.

Risks related to nicotine patch administration:
1. Skin irritation is one of the most common side effect of nicotine patches but is expected to be of minor severity and to dissipate spontaneously after patch removal. Risk minimization: Participants are informed of this risk in the consent form and are aware that they can end participation and ask for the patch to be removed if any side effect becomes too unpleasant.
2. Nausea is a common side effect of nicotine in non-smokers, the target population of the present study. Nausea is expected to dissipate spontaneously and rapidly (1-2 hrs) after patch removal. Risk minimization: The lowest available dose of transdermal nicotine (7mg/24hrs) will be tested. Participants are informed of this risk in the consent form and are aware that they can end participation and ask for the patch to be removed if any side effect becomes too unpleasant. Nausea is actively assessed on an hourly basis, but unsolicited self-reports are encouraged.
3. Vomiting is expected to be rare given the small dose. Risk minimization: Nausea is assessed hourly and participants are asked to report nausea. The patch will be removed if nausea becomes too unpleasant, which is likely to prevent most occurrences of vomiting.
4. Palpitations and diaphoresis may occur but are not expected to cause severe discomfort. Risk minimization: Subjects' blood pressure, heart rate and subjective state will be monitored at regular intervals. The patch will be removed immediately if resting blood pressure >160/100 or heart-rate >120 x 2 or if side effects subjectively become too unpleasant for the participant.
5. Headache: A recent study in non-smoking subjects with and without schizophrenia administering 14mg/24hrs of transdermal nicotine as the present protocol reported headache in 14 out of 60 participants. This is thus a relatively likely but minor risk. By administering a smaller dose, fewer occurrences are expected in the present study. Risk Minimization: Participants are informed of this risk in the consent form and are aware that they can end participation and ask for the patch to be removed if any side effect becomes too unpleasant.
6. Abdominal pain and dry mouth are expected to be rare, but may cause significant discomfort. Risk Minimization: Participants are informed of this risk in the consent form and are aware that they can end participation and ask for the patch to be removed if any side effect becomes too unpleasant.
7. Restlessness, sleepiness, dizziness or temporary mood changes may occur but are expected to be mild. Risk Minimization: Participants are informed of this risk in the consent form and are aware that they can end participation and ask for the patch to be removed if any side effect becomes too unpleasant.
8. Boredom during the long pre-test absorption period is likely to occur. Risk Minimization: Participants will be provided with reading material and movies.
General risk minimization procedures: Only individuals who meet certain medical history criteria will be admitted into the study. Subjects' blood pressure, heart rate and subjective state will be monitored at regular intervals. The patch will be removed immediately if requested by the participant, if the participant feels too unwell or vomits, or if blood pressure or heart-rate exceeds the specified threshold. The blind will be broken immediately and a medical doctor consulted if any severe or unexpected adverse events occur.

Risks related to galantamine administration:
1. Nausea and vomiting are among the most common side effects of galantamine and would cause significant discomfort, but they are expected to be rare with the two isolated low test doses of 4 mg. A study administering a single dose of 4 mg of galantamine to healthy subjects (Zhao et al. 2002, J Clin Pharmacol 42:1002-10) reported that the incidence rates of adverse events at this dose were comparable to those with placebo. Risk minimization: Galantamine will be administered with food, and investigators will ensure adequate fluid intake. Both actions have been shown to reduce the likelihood of gastrointestinal side effects.
2. Loss of appetite is also among the most common side effects of galantamine but would be considered of low seriousness given the two isolated administrations of galantamine. Furthermore, loss of appetite is expected to be rare at the test dose of 4 mg, based on Zhao et al.'s findings (see above). Risk minimization: Galantamine will be administered with food, and investigators will ensure adequate fluid intake. Both actions have been shown to reduce the likelihood of gastrointestinal side effects.
3. Diarrhea can be a side effect of galantamine when used clinically. Diarrhea would be associated with moderate discomfort but is expected to be rare at the test dose of 4 mg (Zhao et al.). Risk minimization: Galantamine will be administered with food, and investigators will ensure adequate fluid intake. Both actions have been shown to reduce the likelihood of gastrointestinal side effects.
4. Abdominal pain would be associated with moderate levels of discomfort but is expected to be rare. Risk minimization: Galantamine will be administered with food, and investigators will ensure adequate fluid intake.
5. Dyspepsia would be associated with moderate levels of discomfort but is expected to be rare. Risk minimization: Galantamine will be administered with food, and investigators will ensure adequate fluid intake.
6. Upper and lower GI bleeding is reported on the drug label and would be a serious risk, but it is not expected with the two isolated doses of 4 mg.
7. Dehydration would be a serious risk, but it is very unlikely given the two low isolated dose administrations. Risk minimization: Investigators will ensure adequate fluid intake. The reason for its importance will be stressed to the participant.
8. Fatigue and drowsiness would be risks of low seriousness, and they are unlikely given the low test dose. Risk minimization: Subjective side effects are assessed at regular intervals.
9. Postural hypotension and dizziness would be risks of moderate seriousness, but they are unlikely given the test dose. Risk minimization: Blood pressure and subjective side effects are assessed at regular intervals, and the participant has the opportunity to lie down if necessary. Volunteers with pre-existing hypotension are excluded from the study.
10. Fainting is listed on the drug label, but the drug label also cites data showing that the risk of syncope is 0.7% with placebo (2/286) and 0.4% with twice daily 4 mg of galantamine (3/692); see p. 3 of the attached drug label. Thus, fainting is not expected in relation with our test dose of galantamine.
11. Bradycardia would be a relatively serious risk, but it is unlikely given the test dose of galantamine. Even in clinical trials with clinical doses of galantamine, conducted in elderly subjects, the incidence of bradycardia was as low as 1.2%. Risk minimization: Volunteers with a resting heart rate <55 bpm at screening are excluded from the study. Participants with resting heart rate <55 just before the patch would have been administered or just before the capsule would have been administered will not be allowed to continue with the study session.
12. Headache is sometimes observed with the clinical use of galantamine (7.6%, vs. 5.4% with placebo). It would be associated with moderate discomfort and is considered unlikely given the low test dose. Risk minimiziation: none.
13. Rhinitis would be of low seriousness and is considered unlikely to occur as a result of an isolated dose of 4 mg of galantamine. Risk minimization: none.
14. Depression would be a serious risk but is considered very unlikely with two isolated administrations of 4 mg of galantamine. Risk minimization: Volunteers with a pre-existing psychotic, mood, or anxiety disorder will not be enrolled into the study.
15. Anemia would be a serious risk but is considered very unlikely with two isolated administrations of 4 mg of galantamine. Risk minimization: A complete blood count will be performed during screening. Participants with pre-existing anemia or other significant pathology will not be enrolled into the study.
16. Anorexia is listed on the drug label as having occurred in clinical trials with galantamine, but it is not expected with two isolated doses of 4 mg of galantamine each.
17. Insomnia after a test day involving galantamine is a risk of relatively low seriousness and likelihood given the test dose. Risk minimization: none.
18. Hematuria is infrequently observed with clinical doses of galantamine given chronically, and it is not expected with two isolated administrations of 4 mg of galantamine.

19. Tremor is listed on the drug label as having occurred in clinical trials with galantamine, but it is not expected with two isolated doses of 4 mg of galantamine each.
General risk minimization for galantamine side effects: Participants have to have a minimum body weight of 110 lbs, to reduce the risk of disproportionately high blood concentrations in some participants. Subjects' blood pressure, heart rate and subjective state will be monitored at regular intervals. The blind will be broken immediately and a medical doctor consulted if any severe or unexpected adverse events occur. The test dose of galantamine (4 mg) is very low as compared with the clinical dose of 16-24 mg/day.

Interaction of galantamine and nicotine: There are no known effects of nicotine on the metabolism of galantamine and vice versa. Galantamine has been safely co-administered with nicotine in experimental settings and clinically when prescribed to smokers.

Risks related to blood draws:
1. Skin irritation is expected to be rare and of minor severity. Risk Minimization: Blood draws will only be performed by experienced medical or nursing staff.
2. Pain/discomfort is expected to be common but of minor severity. Risk Minimization: Blood draws will only be performed by experienced medical or nursing staff.
3. Weakness or light-headedness is expected to be rare and to dissipate quickly. Risk Minimization: Blood draws will only be performed by experienced medical or nursing staff. Participants will be asked to lie down if experiencing the onset of these symptoms.
4. Syncope is expected to be very rare but is of significant severity if it occurs. Risk Minimization: Blood draws will only be performed by experienced medical or nursing staff. Participants will be asked to lie down if experiencing weakness or light-headedness.
5. Bleeding is expected to be common but of minor severity. Risk Minimization: Blood draws will only be performed by experienced medical or nursing staff.
6. Swelling at the draw site is expected to be rare and of minor severity. Risk Minimization: Blood draws will only be performed by experienced medical or nursing staff.

ID: VIEW4E1B52509F000
Name: v2_Research Related Risks

View: v2_Potential Benefits and Alternatives

Potential Benefits and Alternatives

If you uploaded a separate research protocol document in the 'Research Protocol' page, cite the applicable section and page numbers from that document in the answer boxes below.

1 * Describe the potential direct benefit(s) to participants:
There are no benefits to study participants. This is not a treatment study.

2 * Describe the importance of the knowledge expected to result from the study:
The cognitive-enhancing effects of nAChR agonists have widely been accepted to be of therapeutic potential for a variety of disease states marked by cognitive dysfunction, such as schizophrenia, AD, and ADHD. Over the last two decades, drug development efforts have been invested into more selective nAChR agonists, aiming for more pronounced benefits with reduced side effects. However, effects have tended to be of small magnitude and uncertain clinical significance. Many compounds failed clinical trials due to limited efficacy. Thus, cognitive-enhancing effects harvested from nAChR agonists to date have not lived up to their expected potential. The current project aims at enabling more successful nAChR drug development strategies by evaluating a potential strategy of raising the effect size ceiling. Thus, the knowledge derived from the present study has the potential to result in novel nAChR ligand therapies able to induce clinically significant cognitive benefits, and in more effective treatments of cognitive deficits seen in chronic disease states such as schizophrenia, AD, MCI, schizophrenia and ADHD.

3 * Describe how the potential risks to participants are reasonable in relationship to the potential benefits:
The risks related to the acute administrations of nicotine and galantamine at the low doses proposed, to blood draws, cognitive testing, and handling of private information, will be minimized as outlined above. We consider these risks to be low in comparison with the scientific and potential clinical merits to be gained.

4 * Describe the alternatives to participation in this study. If there are no alternatives, state that participation is voluntary and the alternative is not to participate. For intervention studies, describe appropriate alternative clinical procedures or courses of treatment available to subjects.
Participation in this study is voluntary, and the alternative is not to participate.

ID: VIEW4E1B5251B0400
Name: v2_Potential Benefits and Alternatives

View: v2_Withdrawal of Participants

Withdrawal of Participants

If the questions below are not applicable to the research (i.e., chart review), enter "N/A".

1 * Describe anticipated circumstances under which subjects will be withdrawn from the research without their agreement:
Participants may be withdrawn if they display adverse effects of any study intervention that would make their continued participation in the study unsafe, if they cannot or do not follow instructions (for example, not ingest caffeine or alcohol on study days, or perform the cognitive tasks), of if study staff is unable to schedule all study sessions within the allowed time period (such as when subjects stop responding to calls or there are scheduling problems).

2 * Describe procedures for orderly termination:
Participants are informed that their study participation is terminated, and they are paid for their time up to this time point.

3 * Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection:
The study does not have any follow-up. Withdrawal would end any procedures associated with the study. If participants withdraw or are withdrawn due to side effects of the study drugs, they will be asked to stay on at the Research Center for continued monitoring until the study physician considers it safe for them to leave.

ID: VIEW4E1B52531F800
Name: v2_Withdrawal of Participants

View: v2_Privacy of Participants

Privacy of Participants

If the study does not involve interaction with participants, answer "N/A" to the questions below.

1 * Describe how you will ensure the privacy of potential participants throughout the study ***(privacy refers to persons and their interest in controlling access to themselves):***
Participants will be afforded privacy during all research interactions by using research staff offices or other private rooms. Consenting, screening, completing questionnaires and any medical procedures will all take place behind closed doors.

2 * Describe the location where potential participants will receive research information and detail the specific actions the study team will take to ensure adequate privacy areas:
Potential participants will be approached by phone, or on MPRC premises if they happen to be there for another study. In the latter case, a study associate will take the participant to a private room before describing the study and inquiring about their interest. For the Informed consent process, the investigator meets with the volunteer in a closed room at MPRC.

3 * Describe potential environmental stressors that may be associated with the research:
No environmental stressors are anticipated for the study. Research activities take place in quiet rooms behind closed doors.

ID: VIEW4E1B525B87C00
Name: v2_Privacy of Participants

View: v2_Confidentiality of Data

Confidentiality of Data

1 * Will stored research data contain identifiers or be able to be linked to and identify individual participants (either directly or through a code/research ID)?
Yes

2 * Where will research data be kept (address electronic and paper data as applicable)? (If this is a VA study please list specific sites that data will be kept.)
All paper records are kept under double lock conditions. Hard copies of research data are labeled by subject code number only and are stored in folders in locked filing cabinets. Research records containing the participant's name, such as consent forms, inclusion/exclusion checklists etc., are stored in locked cabinets in a locked room, separate from files containing research data.
Data from computer tests, identified only by participant number, are backed up in a restricted-access folder on an MPRC data drive. Grouped study data are contained within files on this same drive. Medical data will be stored in the ORP Clinical Database.
Blood samples obtained for analysis of nicotine and nicotine metabolite levels are labeled only with a subject and study ID number and stored in a locked MPRC freezer until study completion, at which point they will be shipped to Dr. Marilyn Huestis' Chemistry and Drug Metabolism Section at NIDA.

3 * How will such data be secured?
- All databases are handled via a local area network (LAN) maintained behind a Netscreen 5XP firewall with multiple layers of protection against unauthorized intrusion. Databases are maintained on the center's server and are additionally protected by a 5-tiered system involving restricted access at the desktop, directory, database, reporting and table levels. All databases are maintained and monitored by a professional data manager. Data downloaded from either database will be identified only by participant number.
- Records containing subject names (such as payment records and HIPAA and consent forms) are kept in locked filing cabinets in a locked room.
- All research data are labeled by MPRC number and study number only. Research folders are stored in a locked cabinet. These data are also entered onto password protected secured servers. Access to these data drive is always via password protected computers.
- Blood samples will be secured by being labeled with the study and MPRC subject number, but never with subject names.

4 * Who will have access to research data?
Access to research data is limited to the Principal Investigator, research sub-investigators and team members listed on this protocol. The study nurse will have access to medical screening information.
Additionally, members of Dr. Marilyn Huestis' Chemistry and Drug Metabolism Section at NIDA will have access to blood samples for nicotine and nicotine metabolite level analysis. These samples are labeled by MPRC subject ID and study ID only, and members of Dr. Huestis' team are unable to link these ID numbers to any personal subject identifiers. All individuals who will be reviewing or receiving identifiable study data are on this protocol.
Regulatory personnel from authorized entities will also have access to research data.

5 * Will study data or test results be recorded in the participant's medical records?
○ Yes ◉ **No**

6 * Will any data be destroyed? ***(Please note that data for FDA regulated research and VA research cannot be deleted)***
○ Yes ◉ **No**

6.1 If Yes, what data (e.g., all data, some recordings, interview notes), when and how?

7 Do you plan to obtain a Certificate of Confidentiality?
◉ **Yes** ○ No

7.1 If Yes, upload your Certificate of Confidentiality. If you have not yet obtained the Certificate, please note that once it is obtained, you will need to submit an amendment to attach the document, make any needed changes to the submission and make needed changes to the Informed Consent Document.

Name	Created	Modified Date
Certificate of Confidentiality	6/23/2014 4:25 PM	6/23/2014 4:25 PM

8 * Discuss any other potential confidentiality issues related to this study:
None.

ID: VIEW4E1B5265E0400
Name: v2_Confidentiality of Data

View: v2_Monitoring Plan Selection

Monitoring Plan Selection

1 * Type of data safety monitoring plan for the study:
Data Safety Monitoring by a Committee

ID: VIEW4E1B00E30D400
Name: v2_Monitoring Plan Selection

View: v2_Monitoring Plan - Committee

Monitoring Plan - Committee

You indicated that the monitoring will be done by a Committee.

1 * Will the Committee be Internal or External?
Internal DSMB

2 * What data will be reviewed?
Adverse Events
Enrollment Numbers

2.1 If Other, specify:

3 * What will be the frequency of the review?
Annually

3.1 If Other, specify:

4 * Safety monitoring results will be reported to:
IRB

4.1 If Other, specify:

ID: VIEW4E1B025761800
Name: v2_Monitoring Plan - Committee

View: v2_Monitoring Plan - Internal DSMB

Monitoring Plan - Internal DSMB

You indicated that the monitoring committee will be an internal DSMB.

1 * List Internal DSMB Members:

	Name
View	Robert McMahon, Ph.D.
View	Julie Kreyenbuhl, Pharm.D.
View	Glenda Housel, M.D.
View	Scott Aaronson, M.D.
View	Clayton Brown, Ph.D.
View	Charles Richardson, M.D.

2 * Confirm that no financial or other conflicts of interest exists for the above individuals.
(●) **Yes** ( ) No

3 * Will there be an interim efficacy analysis?
( ) Yes (●) **No**

3.1 If Yes, when?

4 * Briefly describe the DSM review process itself. Will it be an open or closed review to the investigator? Blinded/unblinded data? How will confidentiality of individual participant data be maintained?
The standing MPRC Data and Safety Monitoring Board (DSMB) will oversee this greater than minimal risk protocol.
The Principle Investigator is invited to meetings at which the protocol is discussed. Because identifying information is not kept with study data, data can be safely reviewed without disclosure of private information. Data is presented in aggregate and participants' names or identifying information is not used in discussions.
The DSMB will: 1) review the proposed protocol and consent forms; 2) evaluate recruitment and rate of enrollment in relation to study targets; 3) monitor the occurrence of reportable events and early withdrawals or terminations; 4) review the study data management system; 5) establish stop rules for the study as a whole. All serious adverse events (SAEs) will be reported to the DSMB, PI, and the University of Maryland School of Medicine IRB. The PI will receive all SAE reports within 24 hours of their occurrence and forward them appropriately. The PI and DSMB will determine whether possible protocol modifications are required to minimize the further occurrence of such events. The DSMB plan will be submitted for IRB(s) review and approval following the first meeting of that committee, as will subsequent reports.

5 * What are the criteria defined in the protocol to be used for decision making regarding continuation, modification, or termination of study?
Early study termination of the study will be considered in the event of a subject death, seizure, or other unexpected serious adverse event determined to be possibly, probably or definitely related to study drug. Modifications such as changes in recruitment goals or study timeline will be based on enrollment milestones and will be reported to the DSMB and the IRB. Otherwise, the research will continue as projected.

ID: VIEW4E1B0261D9400
Name: v2_Monitoring Plan - Internal DSMB

View: v2_Research Related Costs

Research-Related Costs

1 * Is the study's financial supporter (e.g., commercial sponsor, federal or state grant or contract, private foundation, physician-sponsor) covering any research-related costs?
Yes

1.1 If Yes, check all that apply:
Research-Related Services (personnel costs, tests, supplies, exams, x-rays, or consultations required in the study)
Investigational or Study Drug
Investigational Procedure(s)

1.2 If No, who is responsible for payment?

2 * Who is responsible for the uncovered research-related costs?
There will be no uncovered research-related costs

2.1 If Other, specify:

3 If the participant is responsible for any research-related costs, identify and estimate the dollar amount:

ID: VIEW4E1B5D9641800
Name: v2_Research Related Costs

View: v2_Compensation for Research-Related Injury

Compensation for Research-Related Injury

1 * Is this study under a master agreement that includes a provision requiring the sponsor to provide compensation to participants for research-related injury?
○ Yes ◉ **No**

1.1 If Yes, please provide the date and title of the agreement and upload the portion of the contract language relevant to compensation for research-related injury:

Name	Created	Modified Date
There are no items to display		

1.2 If No (the study is not under a master agreement), is there proposed contract language concerning payment to participants for treatment in the event of a research-related injury?
○ Yes ◉ **No**

1.2.1 If Yes, indicate the status of the contract review/approval with the ORD and upload the proposed language relevant to compensation for research-related injury:

1.2.2

Name	Created	Modified Date
There are no items to display		

ID: VIEW4E1B629EEC000
Name: v2_Compensation for Research-Related Injury

View: v2_Payment to Participants

Payment to Participants

1 * Will participants receive payment (money, gift certificates, coupons, etc.) for their participation in this research?
◉ **Yes** ○ No

ID: VIEW4E1C52A5D7800
Name: v2_Payment to Participants

View: v2_Payment Detail

Payment Detail

You indicated that participants will receive payment (money, gift certificates, coupons, etc.) for their participation in this research.

1 * Payment to participants will be for: (check all that apply)
Other

1.1 If Other, specify:
Time spent on study

2 * What is the total dollar value of the payments over the duration of the study? ***Total payment(s) for participation in research of $600***

or more is required to be reported on an IRS Form 1099.
$740

3 * Describe the timing and distrubution plan for the payment (schedule, means, etc.)?
Participants will be paid $20 per hour of study participation (including screening). This includes periods of time between drug administration and testing, when participants are not actively performing any study procedures. Based on an estimated total consent and screening time of 3 hours and study time of 34 hours (training session: 2 hours; test sessions: 8 hours x 4), total compensation for study time will be approximately $740 per participant. Participants withdrawing from the study will receive payment for the portion of the study completed. For participants who end up spending more time on the study, for example if screening takes longer than expected, total study compensation will be higher. Participants will be paid for the entire study when they complete it, decide they no longer want to participate, or are withdrawn. Participants who terminate participation before completing the study will be paid for the time they invested. Payment can be processed after individual study visits if so requested by the participant.

4 * Method(s) of payment to be Used:
Check

4.1 If Other, specify:

ID: VIEW4E1C54A6ACC00
Name: v2_Payment Detail

View: v2_HIPAA

HIPAA (Health Insurance Portability and Accountability Act)

1 * HIPAA applies to the University of Maryland School of Medicine, the University of Maryland School of Dentistry and the VA. Are you affiliated with, or will be accessing data from, any of these places? (•) **Yes** ( ) No

2 If Yes, will the study view, access, share, collect, use, or analyze health information that is individually identifiable under HIPAA?
(•) **Yes** ( ) No

ID: VIEW4E1B0A2114400
Name: v2_HIPAA

View: v2_Protected Health Information

Protected Health Information (PHI)

You indicated that HIPAA applies and the study will view, access, share, collect, use, or analyze health information that is individually identifiable.

1 * Which PHI elements will be used or disclosed in this study? (Check all that apply)
Name
Address (if more specific than Zip Code)
Dates
Telephone numbers
Email addresses

2 * Why is the PHI necessary for this research?
If SSNs are going to be used, describe the specific use and type of SSN to be used (real, scrambled, last 4 digits).
The name and address is needed to issue and mail the check. Date of birth is needed to verify the age inclusion criterion. Telephone number and e-mail address are for scheduling study appointments.

3 * What is the source(s) of the PHI?
The participant (driver's licence for name and age). In rare cases, the participant's physician may be contacted, with the participant's written permission, to verify or clarify health information relevant to testing the study inclusion/exclusion criteria. The participant may also be asked if they would obtain this information from their physician to share with the study team

4 * Provide written assurance that Protected Health Information will not be reused. (Note: this refers to re-use on another study or for a purpose which has not been approved, not to the re-use of screening data during the current study).
Protected Health Information will not be reused for any other study, or for any purpose which has not been approved.

5 * How will permission to allow the use/disclosure of the individual's protected health information (PHI) be obtained? (Choose all that apply:)
Obtain written authorization *(upload authorization form at the end of the application under "Consent and HIPAA Authorization Forms")*

5.1 If you are using a limited data set (LDS), please attach the Data Use Agreement (DUA):

Name	Created	Modified Date
There are no items to display		

ID: VIEW4E1B0A24AA400
Name: v2_Protected Health Information

View: v2_Informed Consent Process

Informed Consent Process

If the study does not involve interaction with participants or a waiver of consent is being requested , answer "N/A" to the questions below.

1 * Indicate the type(s) of consent that will be involved in this study: (check all that apply)

Written Consent Form

2 * Describe the Informed Consent process in detail:
Written informed consent will be obtained from each subject at entry into the study. Informed consent is obtained by the following process: The subject reviews the study consent form and HIPAA form. The investigator first reviews the HIPAA "Authorization To Obtain, Use And Disclose Protected Health Information For Research". If this authorization is signed, the investigator then reviews the consent with the candidate and encourages and answers any questions. Once a participant verbally demonstrates understanding and agrees to the process, they are invited to sign and date the consent form, and the investigator co-signs. All participants are given a copy of the consent form for their records, and a second copy is stored with other protocol consents in a master enrollment study binder. Once the signed consent has been obtained, the investigator will note the participant's study enrollment in a secure database.
The consent form informs participants that up to two repeat or additional testing sessions may be required (e.g. fire alarm during testing period, vital signs out of range prior to drug administration on a test day); therefore, this document will be considered as the consent should a participant be recalled.

3 * Confirm that the consent process will explain the following:
- The activities involve research.
- The procedures to be performed.
- That participation is voluntary.
- The name and contact information for the investigator.

(●) **Yes** ( ) No

4 * Describe who will obtain Informed Consent:
The Principal Investigator, or the clinical research assistant running the study will obtain Informed Consent.

5 * If obtaining consent from a legally authorized representative (LAR), describe how you will confirm that the individual is the LAR and can provide legally effective informed consent. *(Answer "N/A" if not obtaining consent from LARs)*
N/A

6 * Describe the setting for consent:
The consent setting is sitting at a table in a room with the door shut for participant privacy.

7 * Describe the provisions for assessing participant understanding:
Volunteers are encouraged to ask questions throughout the consent process and are required to verbally demonstrate comprehension. If necessary, the consent documents will be reviewed several times to ensure comprehension.

8 * Describe the consideration for ongoing consent:
Participants who are actively involved in the study are re-consented if there is a significant change in the consent form, such as if there is a change in study procedures. Participants will also be re-consented if a period of more than 4 months has elapsed between the informed consent/screening session and the first test session.

ID: VIEW4E1C661D0AC00
Name: v2_Informed Consent Process

View: v2_Consent Forms - Draft

Consent and HIPAA Authorization Forms - Draft

1 Upload all of your Consent Forms for approval. Use only Microsoft Word.

Name	Created	Modified Date
Consent form	9/26/2013 3:10 PM	4/25/2016 8:58 AM

IMPORTANT NOTE: the above list of consent forms (if any) are DRAFT versions. Under no circumstances should copies of these be distributed to patients/study subjects. If/when this research submission is approved by the IRB, approved consent forms will be available for download and use from the "Documents" tab of the Submission's workspace (click Exit and then look for the Documents tab - approved submissions only)

2 Upload any HIPAA authorization forms here:

HIPAA form	9/23/2013 4:55 PM	9/27/2013 5:06 PM

Please refer to HRPO's website for specific instructions for preparing informed consent documents and to access current templates:
http://hrpo.umaryland.edu/researchers/consents.html

ID: VIEW4E1C7712D3000
Name: v2_Consent Forms - Draft

View: v2_Organization Review Requirements (other than IRB)

Organization Review Requirements (other than IRB)

Answer the following questions to determine additional organizational review requirements:

1 **Department/Division Review** - All research submissions are required to undergo department/division/institutional review prior to IRB review. The following entity is listed as the required department/division/institutional review:

Maryland Psych Research Ctr

If this information is incorrect, please notify the HRPO office.

2 **RSC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Radiation Safety Committee may be required.

* 2.1 Does the research involve the use of ionizing radiation? ○ Yes ◉ **No**

2.2 Does the research involve the sampling of radioactive human materials for subsequent use or analysis in a laboratory?

3 **IBC Review Criteria** - select 'Yes' if the answer is 'Yes' for any of the following questions. Review by the Institutional Biosafety Committee may be required.

* 3.1 Does the research involve human gene transfer? ◉ **Yes** ○ No
-OR-
Does the research specifically apply to human studies in which induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, and such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected? This type of research is often referred to as recombinant vaccine trials.

3.2 Does the research involve the exposure of human subjects to pathogenic microorganisms, or the exposure of research staff to human subjects or samples known or reasonably expected to carry infectious disease(s)?

3.3 Does the research involve the sampling of materials from persons with no known infectious disease and where the only risk to study staff is occupational exposure to bloodborne pathogens as defined by the OSHA Bloodborne Pathogen Standard?

4 **Cancer Center Criteria** - Answer the following to determine if review by the Cancer Center (Hematology-Oncology) may be required.

* Does the protocol involve in any way studies related to the prevention, treatment, diagnosis, or imaging of neoplastic diseases? ○ Yes ◉ **No**

5 **General Clinical Research Center Review Criteria** - the GCRC offers free and/or cost shared resources for patient-oriented research. Click Here for more information.

Answer the following to determine if review by the GCRC may be required.

* Will the General Clinical Research Center (GCRC) facility or resources be used to conduct this activity? ○ Yes ◉ **No**

6 **VA Review Criteria** - Answer the following questions to determine if review by the VAMHCS R&D Committee may be required.

* 6.1 - Will the research be conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments)? ○ Yes ◉ **No**
* 6.2 - Will the research utilize VA resources (e.g., equipment, funds, medical records, databases, tissues, etc.)? ○ Yes ◉ **No**
* 6.3 - Will the research be conducted on VA property, including space leased to and used by VA? ○ Yes ◉ **No**

PLEASE NOTE that the research may be funded by VA, by other sponsors, or may be unfunded.

ID: VIEW4E1AF91AB2400
Name: v2_Organization Review Requirements (other than IRB)

View: v2_Institutional Biosafety Committee Review Required

Institutional Biosafety Committee Review Required

1 **NOTE**: based on your answers to questions on a previous page (see below) review by the Institutional Biosafety Committee (IBC) is required. This will involve extra steps on your (study team) part. Clicking the Continue button will result in the system creating a blank IBC Submission form for you. You will be required to fill out and submit this IBC form before you will be able to submit the Protocol form. The IBC Submission workspace and form can be reached by clicking the appropriate button on the left hand side of the Protocol submission's workspace (web page) after exiting the Protocol form.

2 **Question** - answered on IBC RSC review requirements page:
3.1 Does the research involve human gene transfer? - OR - Does the research specifically apply to human studies in which induction or enhancement of an immune response to a vector-encoded microbial immunogen is the major goal, and such an immune response has been demonstrated in model systems, and the persistence of the vector-encoded immunogen is not expected? This type of research is often referred to as recombinant vaccine trials.
3.2 Does the research involve: a) the exposure of human subjects to pathogenic microorganisms, or b) the potential exposure of UMB research staff to infectious materials through the sampling or processing of materials from patients with known infectious disease or from environmental surfaces?
3.3 Does the research involve the sampling of materials from persons with no known infectious disease and where the only risk to study staff is occupational exposure to bloodborne pathogens as defined by the OSHA Bloodborne Pathogen Standard? **Yes**

If the answer to this question is wrong, an IBC submission is not required, use the Jump To menu or your browser's <

3 * **Confirm** - you have read the above information and understand that in addition to the IRB Protocol form, you will fill out and submit the IBC Submission form :

(•) **Yes** ( ) No

ID: VIEW4E1AF91ED4C00
Name: v2_Institutional Biosafety Committee Review Required

View: v2_Summary of Required Reviews (other than IRB)

Summary of Required Reviews (other than IRB)

1 **Additional Committee Reviews** - Based on your responses to the previous questions, you have identified the following additional reviews. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's webpage.

Name of Related Submission		
IBC: Galantamine potentiation of nicotine (HP-00057097)	Workspace	SmartForm

2 **Required Department and Specialty Reviews** - Based on the PI's organization (department, division, etc.) affiliation and answers to previous questions (use of Cancer Center, etc.), the organizations listed below are required to review this application. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	Review Status
Maryland Psych Research Ctr	Complete

ID: VIEW4E1C8D9AE4000
Name: v2_Summary of Required Reviews (other than IRB)

View: v2_Additional Documents

Additional Documents

1 Upload all additional documents here:

Name	Created	Modified Date
Training Certificates Schloesser	11/20/2014 1:50 PM	11/20/2014 1:50 PM
DSMB Minutes 2014	6/23/2014 4:29 PM	6/23/2014 4:29 PM

ID: VIEW4E0962513A000
Name: v2_Additional Documents

View: v2_Final Page of Application

Final Page of Application

You have reached the final page of this application. It is recommended that you click on the "Hide/Show Errors" link on the upper or lower breadcrumb row of this page. The "Hide/Show Errors" will do a search of your application, and highlight areas that are required or need to be completed prior to submitting.

By submitting this application, you are electronically routing the protocol for departmental scientific review and all other necessary reviews. According to information you have provided, this application will be routed to the following Departments for review prior to being forwarded to the IRB for review. These reviews are conducted online and no additional forms or steps by the study team are required.

Name of Organization	Review Status
Maryland Psych Research Ctr	Complete

Required Safety Committee Reviews - In addition to the IRB, the following committees must review this submission. Each additional committee has a separate online form that the study team will be required to fill out. All committee applications (IRB plus those listed here) must be completed properly before the 'package' of applications can be submitted. The team may complete these additional forms in any order or at any time prior to submission of the IRB Application. To complete or view these additional committees' forms, click on the links below or exit this application and click on the appropriate button on left side of this submission's Workspace.

Name of Related Submission		
IBC: Galantamine potentiation of nicotine (HP-00057097)	Workspace	SmartForm

You may check the progress of your application at any time by returning to the Workspace of this submission. A detailed history, including notes, dates, and times of events, is provided to you for this purpose.

If a reviewer returns the application to you, you must address their concerns and resubmit the protocol for review to all designated departments. After all departments have reviewed the application, it will automatically be sent to the IRB for review. Changes made to the submission after its approval must be submitted as modifications.

Investigator Attestation
By submitting this application, I, the Principal Investigator (PI), certify that the information provided in this application is complete and correct. Research will be conducted according to the submission as described, only by the approved principal investigator and study team members.

In addition, I agree to the responsibilities of a PI, including:

- Obtaining informed consent (if applicable) from all subjects as outlined in the submission.
- Reporting new information to the IRB per the requirements of the Investigator Manual.
- Obtaining renewal of the protocol prior to the expiration of the approval period or halt all study activities upon study expiration.
- Accepting ultimate responsibility for the protection of the rights and welfare of human subjects, conduct of the study and the ethical performance of the project.
- Ensuring performance of all research activities by qualified personnel according to the IRB approved submission.
- Ensuring that research personnel have or will receive appropriate training.
- Ensuring no changes will be made in the research until approved by the IRB (except when necessary to eliminate apparent immediate hazards to subjects).

Click the "Finish" button and then click "Submit Application" in the submission Workspace.

ID: VIEW4E1B10C500000
Name: v2_Final Page of Application

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Franklin Blatt

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
Yes **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
Yes **No**

5 * Does this study team member have a financial interest related to this research?
Yes **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Franklin Blatt, PharmD, is a pharmacist at the Maryland Psychiatric Research Center.

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Marie Yuille

2 Research Role:
Research Team Member

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
Yes **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
Yes **No**

5 * Does this study team member have a financial interest related to this research?
Yes **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:
Marie Yuille is an undergraduate student of psychology in her senior year. She has been involved in research projects as part of her course work. She will work under close supervision of other study staff.

View: IRB - Add a Team Member

Add a Team Member

1 * Select Team Member:
Robert Buchanan

2 Research Role:
Sub-Investigator

3 * Edit Rights - Should this person be allowed full edit rights to the submission, including: editing the online forms and the ability to execute activities? Note - a person with edit rights will automatically be added to the CC list and will receive all emails regarding this protocol, even if the answer to #4 below is No.
Yes **No**

4 * CC on Email Correspondence - Should this person be copied on all emails sent by the HRPO office to the PI/POC? Study team members with edit rights will automatically receive all emails:
Yes **No**

5 * Does this study team member have a financial interest related to this research?

Yes **No**

6 * Briefly describe experience conducting research and knowledge of the local study sites, culture, and society:

Robert W. Buchanan, M.D. is a Psychiatrist with over 25 years of experience as a clinical investigator with a focus on descriptive studies of the phenomenology of schizophrenia; the conduct of structural and biochemical neuroimaging studies; and the conduct of clinical trials, which range from proof of concept Phase 1B and 2a studies to Phase 4 post-marketing studies. I have served as P.I. on multiple UMB research protocols, as well as worked in collaboration with other investigators in the conduct of descriptive, neuroimaging, and clinical trials. I am very familiar and knowledgeable about the study sites, culture and society related to working on this protocol.