

## Introduction Page

- 1 **\* Abbreviated Title:**  
Anti-Inflammatory Treatment of Schizophrenia
  - 2 **\* Full Title:**  
Anti-Inflammatory Combination Therapy for the Treatment of Schizophrenia
  - 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: VIEW4DF8709A33C06  
Name: v2\_Introduction Page

## 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.***  
Robert Buchanan
- 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:**  
Jennifer Zaranski
- 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?
William Carpenter Jr	no	no	Sub-Investigator	no
Joel Palachuvattil	no	no	Research Team Member	no
Christine Brown	no	no	Research Team Member	no
Franklin Blatt	no	no	Research Team Member	no
Alexander Duggan	no	no	Research Team Member	no
Deanna Kelly	yes	no	Sub-Investigator	no
Melissa Blake	no	no	Research Team Member	no
Christopher Kitchen	no	no	Research Team Member	no
James Gold	no	no	Sub-Investigator	no
Sarah Nisonger	no	no	Research Team Member	no
Ikwunga Wonodi	no	no	Research Team Member	no
Jacqueline Kiwanuka	yes	yes	Other	no
MacKenzie Sayer	no	no	Research Team Member	no
Elaine Weiner	no	no	Research Team Member	no
Leeka Hubzin	no	no	Research Team Member	no
Haley Demyanovich	no	no	Research Team Member	no
Matthew Glassman	no	no	Research Team Member	no
Ann Kearns	yes	yes	Research Team Member	no
Michelle Kuptzin	no	no	Research Team Member	no
Leonardo Tonelli	no	no	Sub-Investigator	no
Eric Arbach	no	no	Research Team Member	no
Robert McMahon	no	no	Statistician	no
David Gorelick	no	no	Research Team Member	no
Lynne Mathews	no	no	Research Team Member	no
Judy Liu	no	no	Research Team Member	no
Stephanie Feldman	no	no	Research Team Member	no
Charles Richardson	no	no	Research Team Member	no
Carol Simon	no	no	Research Team Member	no

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Judy Liu	no	no	Research Team Member	no
Stephanie Feldman	no	no	Research Team Member	no
Charles Richardson	no	no	Research Team Member	no
Carol Simon	no	no	Research Team Member	no

Name	Edit Submission	cc on Email	Research Role	Has SFI?
Heidi Wehring	no	no	Sub-Investigator	no
Sharon August	no	no	Research Team Member	no

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

ID: VIEW4DF85C16F280C  
Name: v2\_Research Team Information

## Resources

- \* Describe the time that the Principal Investigator will devote to conducting and completing the research:**  
The PI devotes 20% of his time to conducting and overseeing this research. This involves supervision of all staff, meeting with each research participant and review of the consent process.
- \* Describe the facilities where research procedures are conducted:**  
The study is conducted primarily at the Maryland Psychiatric Research Center (MPRC) which is located on the grounds of the Spring Grove Hospital Center. The facility includes an outpatient program and an inpatient unit which are spread across two buildings on campus. The MPRC facilities have a large range of office space which is used for patient examination, interviews and completion of research procedures.
- \* Describe the availability of medical and/or psychological resources that subjects might need as a result of anticipated consequences of the human research:**  
The MPRC has the full range of medical and psychological professionals who are able to assess and respond to any issue that may arise when a participant is at our program. This includes MDs, nurses, pharmacists and other staff who receive regular training in CPR and other standard emergency procedures. Both MPRC buildings have external defibrillators readily available.
- \* 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:**  
At the beginning of the protocol, the PI and senior research staff held a study Protocol Initiation Meeting (PIM). At this time all study aspects are reviewed and all personnel working on the project attend. This meeting details the procedures of the study. We also develop standard operating procedures for the study and assign a primary research staff member to keeping all information up to date. All personnel are told of their role on the study and we hold regular meetings with research personnel to go over study procedures and progress. In addition, all MPRC faculty and staff receive ongoing training on a variety of research issues yearly.

ID: VIEW4DF83CB97640C  
Name: v2\_Resources

## Sites Where Research Activities Will Be Conducted

- \* Is this study a:**  
☒ Multi-Site  
☐ Single Site
- \* Are you relying on an external IRB (not UM) to be the IRB of Record for this study?**  
☐ Yes ☒ No
- \* 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
DHMH-UMB Signed MOU	10/9/2013 3:17 PM	10/9/2013 3:17 PM
- \* 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
- \* Institution(s) where the research activities will be performed:**  
Maryland Psychiatric Research Center (MPRC)  
Department of Health and Mental Hygiene (DHMH) (may be applicable for any studies receiving state funding)

ID: VIEW4DF870DF2C000  
Name: v2\_Sites Where Research Activities Will Be Conducted

## UM Coordinating Center

**You indicated that UM is the Coordinating Center for this multi-site study**

- 2.1 **\* Describe the processes to ensure communication among sites.**  
Things to consider including in the communication plan:
  - all sites have the most current version of the protocol, consent document, etc.
  - all required approvals have been obtained at each site (including approval by the site's IRB of record).
  - all modifications have been communicated to sites, and approved (including approval by the site's IRB)

- of record) before the modification is implemented.
- all engaged participating sites will safeguard data as required by local information security policies.
- all local site investigators conduct the study appropriately.
- all non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

We have a full time person, Jennifer Osing who oversees, along with the PI, all the regulatory aspects of the study. For all other approved sites, Ms. Osing is in regular contact with the sites and will send any modifications to the IRBs following UMB IRB approved modifications. At our monthly meetings, we discuss and ensure that all modifications are known at each site, new protocols and consents are sent to each IRB. Once we begin any recruitment at any approved sites, we will have monthly meetings to ensure all local site investigators are conducting the study appropriately and that noncompliance with the study protocol is appropriate.

2.2 \*Describe the method for communicating to engaged participating sites including:

- reportable new information.
- problems.
- interim results.
- the closure of a study.

The PI and research team at MPRC meet monthly and will discuss any need for reportable new information or study problems to any affiliated sites. We have no plans for interim analysis of this study at this time and the closure of the study will only occur in regular contact with the local site investigators and will be done at the same time as appropriate with each IRB.

ID: VIEW4DF737D4C2806  
Name: v2\_UM Coordinating Center

## 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: VIEW4DF86705BB806  
Name: v2\_DHMH

## Funding Information

1 \* Indicate who is funding the study:

Department / Division / Internal  
Foundation

2 \* What portion of the research is being funded? (Choose all that apply)

Drug  
Staff  
Participant Compensation  
Procedures

3 Please discuss any additional information regarding funding below:

Funding for the final two study participants will come from a general internal account within the Maryland Psychiatric Research Center. Stanley Medical Research Center is the primary sponsor who has funded approximately 95% of the study.

ID: VIEW4DF85DF452406  
Name: v2\_Funding Information

## Foundation Sponsor Contact Information

You indicated that this is a Foundation funded study

1 \* Name:

The Stanley Medical Research Institute

\* Address 1:

8401 Connecticut Avenue, Suite 200

Address 2:

\* City:

Chevy Chase

\* State:

MD

\* Zip Code:  
20815

\* Country:  
USA

\* Contact Name:  
Jana C. Bowcut, MPH

\* Phone Number:  
301.571.0760 ext. 118

Grant Number 1 (if applicable):

Grant Number 2 (if applicable):

Grant Number 3 (if applicable):

Grant Number 4 (if applicable):

ID: VIEW4DF862B680000  
Name: v2\_Foundation Sponsor Information

## 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

## 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

## 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?  
*A clinical trial is a biomedical or behavioral research study of human subjects designed to answer specific questions about therapeutic interventions (drugs, treatments, or devices). Clinical trials are used to determine whether new therapeutic interventions are safe, efficacious, and effective.*  
☒ Yes ☐ No

ID: VIEW4E0280569E000  
Name: v2\_Type of Research

## 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.  
Despite adequate anti-psychotic treatment, the majority of people with schizophrenia continue to exhibit persistent positive and negative symptoms and cognitive impairments. The pharmacological treatment of these individuals is a major challenge. The only approved treatment for treatment-resistant schizophrenia is clozapine, which exhibits superior efficacy for persistent positive symptoms, but has limited effect for negative symptoms and cognitive impairments. Moreover, a significant proportion of people treated with clozapine will continue to exhibit clinically significant positive symptoms. There have been a number of alternative pharmacological approaches examined, including the use of adjunctive mood stabilizers; antipsychotic polypharmacy (e.g. the addition of a second antipsychotic to clozapine); and other psychotropic agents, but these approaches have not been shown to have robust effects. An alternative approach to the use of psychotropic agents for the treatment of persistent symptoms is the use of anti-inflammatory agents to reverse the pro-inflammatory state hypothesized to underlie the symptom and sign manifestations of the illness.  
There is extensive evidence that schizophrenia is due, in part, to disruptions of normal inflammatory responses to viral or bacterial infections or other stimuli of these

systems. The evidence includes the results of epidemiological, clinical, genetic, and neuroimaging studies. In light of the hypothesized pathophysiological role of the inflammatory system in schizophrenia, the development of an effective anti-inflammatory intervention may be of considerable therapeutic benefit. We have chosen to use combination therapy with three different classes of anti-inflammatory agents to address the potential benefit of this therapeutic approach for persistent positive symptoms and cognitive impairments. The three agents have unique anti-inflammatory mechanisms of action, which we believe offers the most robust evaluation of this therapeutic approach and maximizes the likelihood of eliciting pronounced therapeutic effects. In a hypothesis-generating framework, we will examine the efficacy of the experimental intervention for negative and depressive symptoms.

ID: VIEW4E02805CF700K  
Name: v2\_Lay Summa

## 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:

Primary Aims:

1. To determine if adjunctive anti-inflammatory combination therapy is superior to placebo for persistent positive symptoms.
2. To determine if adjunctive anti-inflammatory combination therapy is superior to placebo for depressive and negative symptoms.

Secondary Aims:

1. To determine if adjunctive anti-inflammatory combination therapy compared to placebo is associated with increased incidence of side effects.
2. To determine if adjunctive anti-inflammatory combination therapy is superior to placebo for depressive and negative symptoms.
3. To determine if adjunctive anti-inflammatory combination therapy compared to placebo is associated with an improvement in the pro-inflammatory cytokines: interleukin (IL)-1 $\beta$ , IL-6, and Tumor Necrosis Factor (TNF)- $\alpha$ .

We hypothesize adjunctive anti-inflammatory combination therapy will be associated with improvements in depressive and negative symptoms and a reduction in pro-inflammatory cytokines. We hypothesize that no elevated adverse risk will be associated with adjunctive anti-inflammatory combination therapy relative to placebo.

### 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.:

The study is a 12-week, double-blind, placebo-controlled, randomized clinical trial of the efficacy of anti-inflammatory combination therapy for the treatment of people with schizophrenia, who present with persistent positive symptoms.

There will be a 4-week evaluation phase during which baseline symptom, safety, laboratory, and neuropsychological assessments will be collected. Participants who continue to fulfill entry criteria will be entered into the 12-week Double-blind Treatment Phase.

Participants will be randomly assigned to salsalate, statin, and omega-3-fatty acid combination therapy (n=30) or placebo (n=30) using a permuted block randomization system. Treatment assignment order is random within each block, with an equal number of participants assigned to each treatment. The block sizes will vary in random sequence between 2 and 4. The salsalate target dose will be 4 gm/day, administered in two divided doses of 2 gm in the morning and 2 gm in the evening. The fluvastatin target dose will be 40 mg/day. We selected fluvastatin because it does not interfere with the metabolism of risperidone and paliperidone (two widely used antipsychotics), and it crosses the blood brain barrier. We will use a combined omega-3-fatty acid preparation of EPA and DHA in a 1gm capsule. Each 1gm capsule will contain 180.9mg of EPA and 120.6mg of DHA in doses of two capsules in the morning and two capsules in the evening (2g omega-3-fatty acid in the morning and 2g omega-3-fatty acid in the evening).

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

In general, the use of statins in schizophrenia has focused on their under-utilization in a population that is characterized by weight gain, various lipidemias, and increased cardiovascular morbidity and mortality. The only published study to date was an open-labeled evaluation of rosuvastatin on lipid levels. Rosuvastatin was effective for dyslipidemias. The effect of statins on inflammation in people with schizophrenia has not been previously examined. There are no studies of salsalate in people with schizophrenia. There have been 6 clinical trials of EPA, DHA, or their combination in people with schizophrenia.

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

Despite adequate antipsychotic treatment, the majority of people with schizophrenia continue to exhibit persistent positive and negative symptoms and cognitive impairments. The pharmacological treatment of these individuals is a major challenge. The only approved treatment for treatment-resistant schizophrenia is clozapine, which exhibits superior efficacy for persistent positive symptoms, but has limited effect for negative symptoms and cognitive impairments. Moreover, a significant proportion of people treated with clozapine will continue to exhibit clinically significant positive symptoms. There have been a number of alternative pharmacological approaches examined, including the use of adjunctive mood stabilizers; antipsychotic polypharmacy (e.g. the addition of a second antipsychotic to clozapine); and other psychotropic agents, but these approaches have not been shown to have robust effects (1). An alternative approach to the use of psychotropic agents for the treatment of persistent symptoms is the use of anti-inflammatory agents to reverse the pro-inflammatory state hypothesized to underlie the symptom and sign manifestations of the illness (2-6).

**Immune System Function in Schizophrenia:** Schizophrenia has been hypothesized to be due, in part, to disruptions of normal immune system and inflammatory responses to viral or bacterial infections or other stimuli of these systems (2-6). Epidemiological and clinical studies have provided extensive evidence that perinatal exposure to infection contributes to the etiology of schizophrenia (7). The recent reports of associations between markers of single nucleotide polymorphisms located within the major histocompatibility complex on chromosome 6p22.1 and schizophrenia (8-10) provide further support for etiological hypotheses of immune system dysfunction in schizophrenia.

There are a large number of reports that suggest that people with schizophrenia have altered cytokine levels, with one or more studies reporting elevated levels of the pro-inflammatory cytokines: IL-1 $\beta$ , IL-6, IL-12, CRP, IFN- $\gamma$ , and TNF- $\alpha$ ; and reduced levels of the anti-inflammatory cytokine: IL-10 (11). In contrast, the pro-inflammatory cytokine, IL-2, has been found to be reduced in people with schizophrenia, whereas IL-2 soluble receptor, sIL-2R, has been found to be increased in people with schizophrenia. The IL-1 receptor antagonist, IL-1RA, which inhibits the action of IL-1 $\beta$ ; and TGF- $\beta$ , which has mixed functions, may be increased in people with schizophrenia. Pro-inflammatory cytokine elevation has been found to be associated with increased signs and symptoms of the illness, including positive symptoms and cognitive impairments (12). However it is unclear whether the changes in inflammatory indices reflect a primary disturbance of the immune system or reflect secondary changes related to antipsychotic treatment, metabolic factors, cigarette consumption, or clinical status. Recent meta-analyses suggest that the control of potential confounding variables greatly reduces the number of cytokines directly implicated in the pathophysiology of the illness (1-11).

**Microglial Activation:** There are a number of factors that lead to the activation of microglia, including infections, neuronal injury, stress, and increased cytokine levels. Activated microglia produce pro-inflammatory cytokines and free radicals, including nitric oxide and superoxide (6). The chronic upregulation and production of pro-inflammatory cytokines and free radicals are hypothesized to lead to decreased neurogenesis and nerve cell repair and increased neuronal cell death (6). These microglia products may also lead to white matter abnormalities (6), which have been frequently reported in schizophrenia (13-15).

The results of post-mortem studies of microglial activation are inconclusive, with both increased and decreased microglial activation observed in the study populations (16). However, post-mortem studies may not be sensitive to transient changes in the number of microglial cells or in microglial activation (17). Two recent PET studies have documented increased microglial activation in people with schizophrenia. The two studies utilized 11C-(R)-PK111956, a peripheral benzodiazepine receptor or translocator protein (TSPO) ligand, which can be used to image activated microglial cells. In the study of van Berckel et al (18), there was

increased binding of 1 1C-(R)-PK111956 in the gray matter of people with recent-onset schizophrenia compared to those normal healthy controls. The other study was conducted in a more chronic population, but found similar results, with increased binding of 1 1C-(R)-PK111956 in the gray matter of the participants with schizophrenia, with significant group differences in the hippocampus (19).

**Anti-Inflammatory Agents for the Treatment of Schizophrenia:** The observation of increased pro-inflammatory cytokines and microglial activation in schizophrenia has raised the question of whether non-steroidal anti-inflammatory drugs (NSAIDs) may be of use in the treatment of people with schizophrenia. To date, there have been five studies that have examined the efficacy of adjunctive celecoxib and acetylsalicylic acid (aspirin), with celecoxib the most frequently used agent (20-24). Overall, the studies have found a modest benefit of these agents for positive and negative symptoms.

An interesting alternative NSAID to celecoxib and aspirin is salsalate. Salsalate (disalicylic acid) is a non-acetylated prodrug of salicylate. In comparison to aspirin and celecoxib, salsalate is a potent inhibitor of nuclear transcription factor NF- $\kappa$ B activation (25). NF- $\kappa$ B is activated by pro-inflammatory cytokines, which trigger the release of I $\kappa$ B from NF- $\kappa$ B and allows NF- $\kappa$ B to translocate into the nucleus (25-29), where it promotes the transcription of genes, whose products include pro-inflammatory cytokines, which serve, in a positive feed-forward mechanism, to further promote the activation of NF- $\kappa$ B (30). The inhibition of NF- $\kappa$ B is a major pathway for suppressing pro-inflammatory processes, including microglial activation. In addition, unlike COX-2 inhibitors and aspirin, salsalate does not irreversibly inhibit cyclooxygenases; and in comparison to aspirin, salsalate does not inhibit platelet aggregation or prolong bleeding time and, therefore, is not associated with gastric bleeding (31-35). Salsalate is also absorbed in the small intestine, which serves to further protect the gastric mucosa from injury (33,34). Salsalate has been used extensively to treat rheumatoid and other forms of arthritis and has been shown to be largely safe to use, with tinnitus, headache, abdominal pain/discomfort, and dizziness the most common side effects (36-38). Salsalate has also been used experimentally to treat people with Type 2 diabetes mellitus (25,39-41). There are no studies of salsalate in people with schizophrenia.

The omega-3-fatty acids eicosapentaenoic (EPA) and docosahexaenoic (DHA) have been shown to have anti-inflammatory properties. The major mechanism through which EPA and DHA exert their anti-inflammatory effects is through their oxygenation into resolvins or protectins, which are potent anti-inflammatory agents. There have been 6 clinical trials of EPA, DHA, or their combination in people with schizophrenia (42-48). The results have been mixed with most studies failing to show a significant separation between the omega-3-fatty acid and placebo groups. The one notable exception was the study conducted by Amminger et al, in people who met criteria for high-risk of psychotic disorder (48). A combination of EPA and DHA was found to significantly reduce the rate of conversion to full-blown psychosis.

Finally, statins are lipid-lowering drugs, which act through the inhibition of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA). However, there is emerging evidence that statins also exert anti-inflammatory effects independent of their lipid-lowering effects (49-53). In vitro studies have demonstrated that statins interfere with adhesion, migration, and infiltration of pro-inflammatory cells; and diminish TH1 immune responses and T-cell proliferation and diminish IL-6, IFN- $\gamma$ , and TNF- $\alpha$  expression and function. The mechanism underlying these anti-inflammatory may be mediated by the inhibition of HMG-CoA, which leads to decreased prenylation of signal transducers of inflammation pathways. Statins may also decrease activation of NF- $\kappa$ B through direct action or through their effects on peroxisome proliferator activated receptors (PPAR)  $\alpha$ ,  $\gamma$ , or  $\delta$ .

In general, the use of statins in schizophrenia has focused on their under-utilization in a population that is characterized by weight gain, various lipidemias, and increased cardiovascular morbidity and mortality (54,55). The only published study to date was an open-labeled evaluation of rosuvastatin on lipid levels (56). Rosuvastatin was effective for dyslipidemias. The effect of statins on inflammation in people with schizophrenia has not been previously examined.

**Significance:** In light of the hypothesized pathophysiological role of pro-inflammatory cytokines in schizophrenia, the development of an effective anti-inflammatory intervention may be of considerable therapeutic benefit. We have chosen to use combination therapy with three different classes of anti-inflammatory agents to address the potential benefit of this therapeutic approach for persistent positive symptoms and cognitive impairments. The three agents have unique anti-inflammatory mechanisms of action, which we believe offers the most robust evaluation of this therapeutic approach and maximizes the likelihood of eliciting pronounced therapeutic effects. In a hypothesis-generating framework, we will examine the efficacy of the experimental intervention for negative and depressive symptoms.

See Supporting literature for references.

ID: VIEW4E02805EA0C0  
Name: v2\_Justification, Objective, & Research Design

## 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. Buchanan RW, Kreyenbuhl J, Kelly DL, Noel JM, Boggs DL, Fischer BA, Himelhoch S, Fang B, Peterson E, Aquino PR, Keller W ; Schizophrenia Patient Outcomes Research Team (PORT). The 2009 Schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophr Bull 36(1):71-93, 2010.
  2. Buchanan RW, Carpenter WT. Concept of schizophrenia. In: Sadock BJ, Sadock VA (eds), Kaplan & Sadock's Comprehensive Textbook of Psychiatry/VI, Eighth Edition. New York: Lippincott Williams & Wilkins, 2005, pp 1329-1345.
  3. Hanson DR, Gottesman II. Theories of schizophrenia: a genetic-inflammatory-vascular synthesis. BMC Med Genet 6:7, 2005.
  4. Nawa H, Takei N. Recent progress in animal modeling of immune inflammatory processes in schizophrenia: implication of specific cytokines. Neurosci Res 56(1): 2-13, 2006.
  5. Fan X, Gof DC, Henderson DC. Inflammation and schizophrenia. Expert Rev Neurotherapeutics 7(7):789-796, 2007.
  6. Monji A, Kato T, Kanba S. Cytokines and schizophrenia: microglia hypothesis of schizophrenia. Psychiatry Clin Neurosci 63:257-265, 2009.
  7. Brown AS, Derkits EJ. Prenatal infection and schizophrenia: a review of epidemiologic and translational studies. Am J Psychiatry 167(3):261-280, 2010.
  8. International Schizophrenia Consortium, Purcell SM, Wray NR, et al. Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. Nature 460:748-752, 2009.
  9. Shi J, Levinson DF, Duan J, et al. Common variants on chromosome 6p22.1 are associated with schizophrenia. Nature 460:753-757, 2009.
  10. Stefansson H, Ophoff RA, Steinberg S, et al. Common variants conferring risk of schizophrenia. Nature 460:744-747, 2009.
  11. Miller BJ, Buckley P, Seabolt W, Mellor A, Kirkpatrick B. Meta-analysis of cytokine alterations in schizophrenia: clinical status and antipsychotic effects. Biol Psychiatry 70(7):663-671, 2011.
  12. Dickerson F, Stallings C, Origoni A, et al. C-reactive protein is associated with the severity of cognitive impairment but not of psychiatric symptoms in individuals with schizophrenia. Schizophr Res 93: 261-265, 2007.
  13. Lim KO, Hedehus M, Moseley M, de Crespigny A, Sullivan EV, Pfefferbaum A. Compromised white matter tract integrity in schizophrenia inferred from diffusion tensor imaging. Arch Gen Psychiatry 56(4):367-374, 1999.
  14. Szeszko PR, Ardekani BA, Ashtari M, Kumar S, Robinson DG, Sevy S, Gunduz-Bruce H, Malhotra AK, Kane JM, Bilder RM, Lim KO. White matter abnormalities in



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2 If available, upload your applicable literature search:

Name	Created	Modified Date
Supporting_Literature.doc	1/24/2012 5:07 PM	1/24/2012 5:07 PM

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: anti-inflammatory

Keyword 2: schizophrenia

Keyword 3: positive symptoms

ID: VIEW4E02805A7E40C  
Name: v2\_Supporting Literature

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

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:

The study is a 12-week, double-blind, placebo-controlled, randomized clinical trial of the efficacy of anti-inflammatory combination therapy for the treatment of people with schizophrenia, who present with persistent positive symptoms.

All participants will be of either gender and of any race, with an age range of 18 - 60. Participants will meet DSM-IV -TR criteria for schizophrenia or schizoaffective disorder. SCID assessment will be administered as needed to determine this criterion. Participants must be judged competent to participate in the informed consent process and provide voluntary informed consent.

For all patients, recruitment will occur as detailed in the recruitment section. Consenting and research activity will thereafter be conducted at MPRC.

Evaluation Phase: There will be a 4-week Evaluation Phase during which baseline symptoms, safety, laboratory, and neuropsychological assessments will be collected.

Treatment Phase: Participants who continue to fulfill entry criteria will be entered into the 12-week Double-blind Treatment Phase, in which participants will be randomly assigned to salsalate, fluvastatin, and omega-3-fatty acid combination therapy (n=30) or placebo (n=30) using a permuted block randomization system. Treatment assignment order is random within each block, with an equal number of participants assigned to each treatment. The block sizes will vary in random sequence between 2 and 4. The salsalate target dose will be 4 gm/day, administered in two divided doses of 2 gm in the morning and 2 gm in the evening. The fluvastatin target dose will be 40 mg/day. Participants randomized to fluvastatin will receive placebo fluvastatin in the morning and active drug in the evening. We selected fluvastatin (because it does not interfere with the metabolism of risperidone and paliperidone (two widely used antipsychotics), and it crosses the blood brain barrier. We will use a combined omega-3-fatty acid preparation of EPA and DHA in a 1gm capsule. Each 1gm capsule will contain 180.9mg of EPA and 120.6mg of DHA in doses of two capsules in the morning and two capsules in the evening (2g omega-3-fatty acid in the morning and 2g omega-3-fatty acid in the evening).

evening). We selected this dose of EP A and DHA, because these were the doses used in the Amminger et al. study ( No. 48, Summary of Supporting Literature section), which has, to date, produced the most profound results for this intervention.

Assessments: We will collect the following clinical, neuropsychological, safety, and laboratory assessments:

A. Clinical:

- 1) Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1980): A 20-item scale of psychiatric symptoms rated from 1 (not present) to 7 (very severe).
- 2) Scale for the Assessment of Negative Symptoms (SANS): A 22-item scale designed to quantify the severity of negative symptoms in schizophrenia. Items are rated from 0 (not present) to 5 (severe).
- 3) Calgary Depression Scale (CDS): the CDS total score will be used to measure depressive symptoms. The CDS was specifically designed to assess depressive symptoms in people with schizophrenia.
- 4) CGI-Severity of illness (CGI-S): the CGI-S will be used to assess global changes.
- 5) Fagerstrom Test for Nicotine Dependency (FTND): the FTND will be used to document smoking status and to measure change in smoking status during the course of treatment.
- 6) Columbia Suicide Severity Rating Scale (C-SSRS): The C-SSRS is a questionnaire used for suicide assessment at screening and during the course of treatment.

The primary evaluators will administer the BPRS, SANS, Calgary Depression Scale (CDS) and CGI-S at the beginning of the Evaluation Phase and bi-weekly thereafter. The FTND will be administered at the beginning and end of the Treatment Phase.

B. Neuropsychological Assessments: The MATRICS Consensus Cognitive Battery (MCCB) will be used to assess neuropsychological test performance. All participants will receive this portion of the assessments at MPRC.

C. Side Effects: Side Effect Checklist (SEC); the SEC is designed to assess vital signs and commonly occurring medication-related side effects. EKG and Vital Signs will also be monitored. At MPRC, the Side-Effect Checklist (SEC) and vital signs will be administered at treatment baseline and bi-weekly thereafter by a non-blind clinical pharmacist, who will not disclose the results to treatment/rating clinicians.

D. Laboratory: All patients will receive these assessments at MPRC. If laboratory abnormalities occur, repeat labs may be performed on visits where they are unscheduled in the assessment schedule. This will be determined by a study physician.

- 1) Safety: CBC; complete metabolic panel (CMP), including electrolytes, BUN, creatinine, fasting blood glucose, liver function tests, and lipid profile; U/A; pregnancy test; vital signs.
- 2) Cytokine profile: IL-1 $\beta$ , IL-1RA, IL-2, sIL-2R, IL-6, IL-10, IL-12, IL-17, CRP, IFN- $\gamma$ , TNF- $\alpha$ , and TGF- $\beta$ .

E. Other: We will collect blood for peripheral blood mononuclear cells (PBMC) cultures, which will be used to evaluate in vitro lipopolysaccharide-induced cytokine production. The use of PBMC cultures complements the collection of peripheral cytokine measures. The latter may be vulnerable to differential concentrations between the site of cytokine release and blood concentrations and the relatively short half-life of cytokines.

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

The procedures in this protocol are conducted for research purposes.

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

There will be a 4-week evaluation phase during which baseline symptom, safety, laboratory, and neuropsychological assessments will be collected. Participants who continue to fulfill entry criteria will be entered into the 12-week Double-blind Treatment Phase. Hence entire duration of participation for the participant is 16 weeks.

- 4 \* Describe the duration of the entire study:

We anticipate that the duration of this study will be three years.

- 5 \* Describe any additional participant requirements:

None

ID: VIEW4E0280585B40  
Name: v2\_Study Procedure

## 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:

Power for analyses:

Specific Aim 1: Based on similar MPRC studies of adjunctive treatments, we anticipate approximately a 10% dropout rate. In previous trials of similar length, we have found that the correlation,  $r$ , between baseline and follow-up scores is approximately  $r=0.6$ . The effect size,  $d/\sigma$ , detectable from this study can be estimated from the formula  $(d/\sigma)^2 = 2(\alpha + z\beta)^2(1-r^2)/n$ , where  $d$  is the MM-ANCOVA difference estimate at week 8,  $\sigma$  the standard deviation at week 8,  $z\beta = 0.84$  and  $\alpha = 1.96$  are the standard normal percentiles corresponding to power=0.80 and  $\alpha=0.05$  (two-sided). We would have power to detect an effect size:  $d=0.61$ .

Specific Aim 2: The correlation,  $r$ , between baseline and follow-up MCCB composite scores has now been reported in multiple clinical trials to be  $r>0.9$ . Substituting this value for  $r$  into the ANCOVA power formula given above, we should have power=0.80 to detect an effect size:  $d=0.33$  on the MCCB total score.

- 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:

Specific Aim #1: The effect of combined anti-inflammatory treatment versus placebo on persistent positive symptoms will be tested using the mixed model for repeated measures analysis of covariance (MM-ANCOVA): follow-up score = baseline score + study week + treatment x study week, where "study week" represents a set of binary indicators of whether the follow-up measurement comes from weeks 2, 4, 6, or 8; the main effect of treatment in this model is the average (across weeks 2, 4, 6, and 8) adjusted (for baseline score) difference in follow-up scores between anti-inflammatory treatment and placebo, while the treatment x week interaction tests for significant variation among follow-up weeks in the magnitude of the treatment effects. The primary outcome tested from this model will be a post hoc estimate of the treatment difference at week 8; exploratory analysis of the average treatment effect across weeks and changes in the magnitude of the treatment effect over time will also be conducted.

Specific Aim #2: The primary test for treatment effects on cognition will be performed using the MCCB composite score and the ANCOV A model follow-up composite score = baseline composite score + treatment. Exploratory analyses examining treatment effects for specific domains will be analyzed using the MM-ANCOV A model: follow-up domain T -score = baseline domain T -score + domain + treatment x domain, where the treatment x domain interaction term provides an overall test for variation in the magnitude of anti-inflammatory - placebo T -differences across domains, and the effects of anti-inflammatory treatments in specific domains can be estimated by post-hoc tests from this general model.

Secondary outcomes:

- 1) Treatment differences on clinical symptom outcomes (CDS depression, SANS negative symptom score) will be assessed with MM-ANCOV A, using models similar to that prescribed for analyses of positive symptoms.
- 2) Treatment differences on side effects will be assessed by comparing the proportion of participants in each group with either new onset or worsening compared to baseline for each of a list of specified side effects, using Fisher's exact test.
- 3) Treatment differences in changes in cytokine expression will be assessed using the Wilcoxon rank sum test to compare change scores on each cytokine measure. We anticipate many participants will have cytokine measurements below the limit of detection at one or both visits. For such participants, we will impute cytokine measurements equal to ½ the limit of detection for the assay.
- 4) Spearman rank correlations will be assessed between changes in symptoms and cognitive outcomes

ID: VIEW4E0280605280  
Name: v2\_Sample Size and Data Analysis

## 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:

Results may be shared in a variety of situations but are not routinely shared unless requested by the physician, participant or other involved in care. Most frequently results may be shared when a laboratory or medical test indicates a need for additional follow-up with the individual's primary care physician. When the PI or research staff is notified of abnormal or unusual laboratory or medical information the research team will discuss the test and possible meaning of the results with the participant and recommend that they contact their own physician. Depending on the particular issue the Medically Accountable Physician often will meet with the participant. In this type of situation we may provide the participant with a copy of the test results.

With the participant's written permission/release of information we are also able to directly provide this information to their physician if they desire. In a case where they do not have a primary care physician we will connect them with the appropriate resources.

ID: VIEW4E02808CBD80C  
Name: v2\_Sharing of Results

## 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
<a href="#">View</a> Fluvastatin	yes	116729	yes
<a href="#">View</a> Omega-3-fatty acid	no	116729	yes
<a href="#">View</a> Salsalate	yes	116729	yes

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

Fluvastatin Package Insert 10_2012	12/28/2011 2:00 PM	2/23/2015 2:18 PM
Lovaza_Package Insert.pdf	3/9/2012 3:12 PM	3/9/2012 3:12 PM
Salsalate Package Insert	12/28/2011 2:27 PM	12/28/2011 2:27 PM

- 3 If more than one drug is administered, discuss the risk implications of drug/therapy interactions:

We checked three databases to evaluate whether there was a significant risk of interactions among the three drugs we propose to study: a) Lexicomp Online Interaction database; b) Micromedex Online Interaction database; and c) FDA Medwatch. There were no reports of any interactions amongst these three agents. In addition, a recent article by Valdivielso and colleagues examined the concurrent use of omega-3-fatty acids and fluvastatin and reported no increased rate of side effects or interactions (see Additional Documents section for article reprint). Therefore, we estimate that the likelihood of drug interactions between fluvastatin, omega-3 fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)), and salsalate are minimal. There should be no interactions between fluvastatin and omega-3 fatty acids. There should be no interactions between fluvastatin and salsalate.

- 4 \*Will you be using Investigational Drug Services?

☒ Yes ☐ No

ID: VIEW4E0916E6E140C  
Name: v2\_Research with Drugs or Biologics

## Placebos

- 1 \*Is this study placebo controlled?

☒ Yes ☐ No

ID: VIEW4E0514EECCC00  
Name: v2\_Placebos

## 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:  
The placebo being used in this study is not being used in place of standard therapy . The study medication or placebo will be used as an adjunct to ongoing antipsychotic medication treatment.
- 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

## 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: VIEW4E09416F57801  
Name: v2\_Psychological/Behavioral/Educational Methods and Procedures

## 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:  
Fagerstrom Test of Nicotine Dependence  
Clinical Global Impression
- 2 \*Upload a copy of all questionnaires/surveys:
- | Name                                   | Created           | Modified Date     |
|--|-------------------|-------------------|
| Fagerstrom Test of Nicotine Dependence | 1/10/2012 2:14 PM | 1/10/2012 2:14 PM |
| Clinical Global Impression             | 1/10/2012 2:10 PM | 1/10/2012 2:10 PM |
- 3 \*What is the total length of time that each survey is expected to take?  
Approximately 15 minutes
- 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/Questionnaire

## 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       |
|---|---------------------|---------------------|
| Columbia Suicide Severity Rating Scale_Since Last Visit | 3/15/2013 11:27 AM  | 3/15/2013 11:27 AM  |
| Columbia Suicide Severity Rating Scale_Baseline         | 3/15/2013 11:26 AM  | 3/15/2013 11:26 AM  |
| Calgary Depression Scale                                | 12/29/2011 12:11 PM | 12/29/2011 12:11 PM |
| SCID Summary Sheet                                      | 12/29/2011 12:06 PM | 12/29/2011 12:06 PM |
| Scale for the Assessment of Negative Symptoms           | 12/29/2011 12:06 PM | 12/29/2011 12:06 PM |
| Brief Psychiatric Rating Scale (BPRS)                   | 12/29/2011 11:50 AM | 12/29/2011 12:02 PM |

- 3 \* What is the individual duration of each interview and what is the entire duration of the interviews?  
Approximately 30 - 90 minutes
- 4 \* How will the interview responses be recorded and by whom?  
The data are recorded on assessment forms (attached above). This information is then 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 information is solicited from a participant, which suggests that there is a potential for harm to self or others, then the research assistant will notify a member of the treatment team, who will conduct a thorough evaluation of the participant.

ID: VIEW4E0947A633C0  
Name: v2\_Interviews

## 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:  
MATRICS Consensus Cognitive Battery (MCCB)
- 2 \* Describe procedures related to all testing:  
MCCB: Cognitive function will be assessed in all participants using a test battery chosen from the National Institute of Health (NIMH) Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Project [Green, 2004]. The MCCB tests were chosen by a panel of experts on cognition in schizophrenia, and the MCCB is specifically designed to assess treatment-related changes in cognition in patients with schizophrenia. The MCCB assesses cognitive functions in the following domains using the following tests:  
Speed of Processing: Symbol-Coding, Trail Making A.  
Attention/Vigilance: Continuous Performance Test -- Identical Pairs (CPT-IP) (computer test)  
Working Memory: University of Maryland -- Letter-Number Span, Wechsler Memory Scale (WMS) - III Spatial Span.  
Verbal Learning: Hopkins Verbal Learning Test (HVLT) -- Revised.  
Visual Learning: Brief Visuospatial Memory Test (BVM) -- Revised.  
Reasoning and Problem Solving: Neuropsychological Assessment Battery (NAB) -- Mazes.
- 3 \* Upload relevant testing materials:
- | Name  | Created          | Modified Date    |
|---|------------------|------------------|
| Matrics Battery - Symbol Coding                             | 1/9/2012 3:12 PM | 1/9/2012 3:38 PM |
| Matrics Battery - Hopkins Verbal Learning Test              | 1/9/2012 3:15 PM | 1/9/2012 3:19 PM |
| Matrics Battery - MSCEIT Section D and H                    | 1/9/2012 3:16 PM | 1/9/2012 3:18 PM |
| Matrics Battery - WMS Spatial Span                          | 1/9/2012 3:17 PM | 1/9/2012 3:17 PM |
| Matrics Battery - University of Maryland Letter Number Span | 1/9/2012 3:17 PM | 1/9/2012 3:17 PM |
| Matrics Battery - Mazes                                     | 1/9/2012 3:16 PM | 1/9/2012 3:16 PM |
| Matrics Battery - Category Fluency                          | 1/9/2012 3:12 PM | 1/9/2012 3:12 PM |
| Matrics Battery - BVM                                       | 1/9/2012 3:11 PM | 1/9/2012 3:11 PM |
| Matrics battery - Trailmaking A                             | 1/9/2012 3:11 PM | 1/9/2012 3:11 PM |
- 4 \* What is the individual duration of each test and what is the entire duration of all tests?  
Approximately an hour.
- 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: VIEW4E0BC1E3C280  
Name: v2\_Testing

## 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?  
 Samples will be collected to determine study eligibility , for safety assessments, cytokine assays and peripheral blood mononuclear cultures. Samples collected for cell culture assays will be stored in Dr . Leonardo H. Tonelli's laboratory at UMB, Medical School Teaching Facility Building, 685 W Baltimore Street, Room 958
- 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):  
 Clinical samples will be sent for processing to LabCorp where all our clinical specimens are processed.
- 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: VIEW4E0E1A4B8000x  
 Name: v2\_Sample Collection/Analysis

## 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:  
 Approximately 4 teaspoons of blood will be drawn during screening, at the beginning of the treatment phase, and at the end of the treatment phase for a study total of 12 teaspoons of blood.
- 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?  
 The samples contain the participant's name and date of birth.
- 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.):  
 If a participant withdraws consent, then the samples will be destroyed. If they withdraw from the study, then the samples will be kept until the end of the study , analyzed with other similar samples, then destroyed.
- 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: VIEW4E0E257D60C0x  
 Name: v2\_Prospective Sample

## 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: VIEW4E093BF078C06  
Name: v2\_Clinical Trial Registration

## Clinical Trial Registration Information

You indicated that this clinical trial has been registered.

- 1 \* Was this trial registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)?  
☒ Yes ☐ No
- 2 If no, was this trial registered on a site other than [clinicaltrials.gov](http://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  
NCT01514682

ID: VIEW4E093BF1D0806  
Name: v2\_Clinical Trial Registration Information

## 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.**  
80
- 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:  
70  
  
Worldwide - the number being enrolled total at all sites (including local enrollment):  
70
- 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.:  
Women who are pregnant or nursing will be excluded because of the unknown risks of the study drugs on the fetus or newborn infant.

ID: VIEW4E0E519C1D006  
Name: v2\_Participant Selection

## Vulnerable Populations

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



None of the above

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

ID: VIEW4E0E519917801  
Name: v2\_Mlnerable Populations

## 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
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		
<a href="#">View</a>	1	Participant is 18-60 years old
<a href="#">View</a>	2	Participant's meets DSM-IV-TR criteria for schizophrenia or schizoaf fective disorder
<a href="#">View</a>	3	Participant's BPRS total score is 45 or more on the 18 item version (scale: 1-7); or Clinical Global Impression (CGI) severity of illness item score is 4 (moderate) or more
<a href="#">View</a>	4	Participant's BPRS positive symptom item total score is 8 or more, and a score of 4 or more on at least one individual item
<a href="#">View</a>	5	Participant is clinically stable
<a href="#">View</a>	6	Participant has received treatment with the same antipsychotic for at least 60 days, and a constant therapeutic dose for at least 30 days prior to study entry

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

Number Criteria		
<a href="#">View</a>	1	Participant meets DSM-IV-TR criteria for alcohol or substance dependence (except nicotine) within the last 6 months or DSM-IV-TR criteria for alcohol or substance abuse (except nicotine) within the last month
<a href="#">View</a>	2	Participant with a current infection or an organic brain disorder or medical condition, whose pathology or treatment could alter the presentation or treatment of schizophrenia
<a href="#">View</a>	3	Participant with a current infection, organic brain disorder or medical condition, that significantly increases the risk associated with the proposed treatment protocol
<a href="#">View</a>	4	Participant with a history of: aspirin allergy , pre-existing tinnitus, tuberculosis, HIV , or hepatitis C; or autoimmune disease
<a href="#">View</a>	5	Participant who is currently treated with a statin; warfarin, dipyradimole, or other anti-coagulants.
<a href="#">View</a>	6	Participant is currently treated with an omega-3-fatty acid preparation and cannot discontinue their use of the preparation for the duration of the study
<a href="#">View</a>	7	Female participant who is pregnant or breastfeeding
<a href="#">View</a>	8	Female participant who is sexually active and not using any form of birth control such as oral contraceptives or IUDs
<a href="#">View</a>	10	Participant with current/active peptic ulcer disease or gastritis; anemia or thrombocytopenia (platelet count $\leq 120$ )
<a href="#">View</a>	11	Participant who is currently treated with a medication that can increase the risk of myopathy and rhabdomyolysis such as Fluconazole, Ketoconazole, Erythromycin, daptomycin, colchicine or immunosuppresants that alter statin levels.

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-00051603\_26 v3-16-2016-1458139588816(0.01)

ID: VIEW4E0E5185F9001  
Name: v2\_Eligibility

## Recruitment

- 1 \* Describe plans for recruitment, including the identification of potential participants (or acquisition of charts/records/samples) and initial interactions with them:

Potential MPRC and community participants will be identified primarily through chart review or nomination by their primary clinicians who are aware of study entry criteria and demands, and have been asked to identify clinically stable patients who may be interested in research participation. MPRC and community participants may also be self or peer referred for this study .

Additionally, we seek to include interested individuals who are on probation or conditional release, and who are patients at the mental health clinics where we conduct recruitment activity. The protocol for recruitment of patients with schizophrenia will apply to patients with schizophrenia and who are also on probation or conditional release. We would only seek to recruit patients on conditional release or probation who do NOT receive their care at MPRC in order to eliminate any possible perception of coercion based on the provision of psychiatric care.

Further, it should be re-iterated that research assistants who will interact with patients in this study are all specially trained to work with persons with serious mental illnesses. MPRC Research staf f will first consult the participant's psychiatrist or NP for permission to begin the consent process. This arrangement will help avoid approaching people who may be in crisis or may not be able to comprehend the study procedures, risks, and benefits.

- 2 \* Describe measures that will be implemented to avoid participant coercion or undue influence (if not applicable to the study, enter "N/A"):

All participants will be provided a complete description of the proposed study . This will include the purpose of the study , procedures, risks, a copy of the study schedule, and alternatives to participation. Should the participant express interest in the study , investigators will discuss the Informed Consent documentation form with the participant, and the participant will be given a copy of the form for further perusal. A non-investigator clinician member of the treatment team will ascertain whether the prospective participant is able to participate in the informed consent process (see Final Section Additional Documents: Evaluation to Sign Consent Form). If the participant is able to participate in the informed consent process and agrees to participate in the study , then agreement to participate will be documented on the Informed Consent form. All participants will receive a copy of the signed consent form. If the participant is not able to participate in the informed consent process, then they will not be entered into the study . All discussions with potential participants will take place in private behind closed doors.

Compensation for participants' time is offered but is standard for this type of study and thus is not coercive.

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

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
There are no items to display		

ID: VIEW4E0BCAA0A6C0C  
Name: v2\_Recruitment

## Advertising

- 1 \* Will you be using advertisements to recruit potential participants?

☒ Yes ☐ No

ID: VIEW4E0BCCF81000  
Name: v2\_Advertising

## 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):

Print

- 1.1.1 If Other, specify:

- 1.2 \* Provide exact text of all proposed advertisement(s):

Do you have schizophrenia or schizoaffective disorder?

You may be eligible for a research study .

Participants will be paid for time and travel. Studies take place in the Baltimore area and are strictly confidential. There is no cost for participation or study-related tests. Must be 18 or older.

Please help share this information about these studies.

Call for a confidential screening:

Alexander Duggan 410-402-7205

- 1.3 \* Upload advertisement(s) here:

Name	Created	Modified Date
MPRC Flyer	4/24/2013 2:01 PM	6/2/2016 2:40 PM

ID: VIEW4E0BCE82B8C0C  
Name: v2\_Advertising Detail

## 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:

Salsalate:

1- Tinnitus. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect. If the participant is unable to tolerate the drug at the target dose of 4 grams per day then 500 mg reductions will be made in a stepwise fashion until the tinnitus remits or a minimum dose of 2 grams per day is reached.

2 - Headache. Not likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect.

3 - Dizziness. Not likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect.

4 - Nausea, dyspepsia, and the remote possibility of GI bleeding. Not likely and possibly serious. These are less common side effects and occur infrequently in individuals taking the drug for only 6 weeks. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with specific questions included to address these side effects. If a participant develops GI bleeding the drug will be stopped immediately .

5 - Pregnancy risks. Somewhat likely and serious. There is some evidence with medications similar to Salsalate that an unborn child may have trouble with the heart forming correctly. If a woman is pregnant or planning on becoming pregnant she cannot participate in this study .

Fluvastatin:

1 - Headache. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect.

2 - Dyspepsia. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect.

3 - Myalgia. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect. If the participant is unable to tolerate the medication then the dose will be reduced to 20mg. If the participant is still not able to tolerate the drug, then they will be discontinued from the study .

4 - Abdominal pain and nausea. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with specific questions included to address these two side effects.

5 - Memory loss and confusion. Not likely and possibly serious. There are reports of patients taking statins reporting memory loss and confusion. However, the effects have generally not been serious and the patients' symptoms were reversed by stopping the statin. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with specific questions included to address these two side effects.

6 - Increased glucose levels. Not likely and possibly serious. Increases in blood sugar levels (hyperglycemia) have been reported with statin use. The FDA is also aware of studies showing that patients being treated with statins may have a small increased risk of increased blood sugar levels and of being diagnosed with type 2 diabetes mellitus. Participants with uncontrolled type 1 or type 2 diabetes mellitus will be excluded from the study . In addition, we will obtain baseline and end of study fasting glucose levels, and a non-fasting glucose level at week 6 of the double-blind phase. If the non-fasting glucose level is greater than 200 mg/dL, then, if applicable, their adherence to hypoglycemic and diabetic dietary restrictions will be assessed. If there glucose level can be returned to normal, then they will be allowed to stay in the study. However, if there is not a problem with their adherence to their diabetes treatment regimen, or if the glucose elevation represents a new sign, then they will be withdrawn from the study .

7 - Hepatotoxicity. Not likely and possibly serious. This is a less common side effect and occurs infrequently; "Initial post-marketing surveillance studies of the statins revealed an elevation in hepatic transaminase to values greater than three times the upper limit of normal, with an incidence as great as 1%. The incidence appeared to be dose related. However, in the placebo-controlled outcome trials in which 10- to 40-mg doses of simvastatin, lovastatin, fluvastatin, atorvastatin, pravastatin, or rosuvastatin were used, the incidence of 3-fold elevations in hepatic transaminases was 1-3% in the active drug treatment groups and 1.1% in placebo patients (Law et al., 2006; Ridker et al., 2008). No cases of liver failure occurred in these trials. Although serious hepatotoxicity is rare, 30 cases of liver failure associated with statin use were reported to the FDA between 1987 and 2000, a rate of about one case per million person-years of use (Law et al., 2006)." (Burton et al. 2011). The FDA has recently concluded that serious liver injury with statins is rare and unpredictable in individual patients, and that routine periodic monitoring of liver enzymes does not appear to be effective in detecting or preventing this rare side effect. However, on a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects. If participants exhibit signs or symptoms of hepatitis then laboratory tests evaluating liver function will be ordered and the medications will be stopped immediately .

8 - Myopathy. Not likely possible serious. This is a less common side effect. "The major adverse effect associated with statin use is myopathy (Wilke et al., 2007). Between 1987 and 2001, the FDA recorded 42 deaths from rhabdomyolysis induced by statins. This is a rate of one death per million prescriptions (30-day supply). In the statin trials described earlier (under "Hepatotoxicity"), rhabdomyolysis occurred in eight active drug recipients versus five placebo subjects. Among active drug recipients, 0.17% had CK values exceeding 10 times the upper limit of normal; among placebo-treated subjects, the incidence was 0.13%. Only 13 out of 55 drug-treated subjects and 4 out of 43 placebo subjects with greater than 10-fold elevations of CK reported any muscle symptoms (Law et al., 2006). Concomitant use of drugs that diminish statin catabolism or interfere with hepatic uptake is associated with myopathy and rhabdomyolysis in 50-60% of all cases (Law and Rudnicka, 2006; Thompson et al., 2003). These medications including gemfibrozil (38%), cyclosporine (4%), digoxin (5%), warfarin (4%), macrolide antibiotics (3%), mibefradil (2%), and azole antifungals (1%) (Thompson et al., 2003) will be excluded." (Burton et al. 2011) On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects. If participants exhibit signs or symptoms of myopathy, then laboratory tests evaluating creatinine protein kinase (CPK; a marker of muscle breakdown) will be ordered. If CPK is not markedly elevated (i.e., 3x normal), then the medication will be continued and CPK will be monitored on a weekly basis. If CPK is elevated, then the medications will be stopped immediately .

9 - Pregnancy risks. Somewhat likely and serious. Fats circulating in the body are important for the proper development of an unborn child. Fluvastatin lowers the fats circulating in the blood and may adversely affect the normal development of an unborn child. Women who are pregnant or planning on becoming pregnant will not be able to participate in this study .

Omega-3-fatty acids:

1 - Dyspepsia. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects.

2 - Eructation. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects.

3 - Taste Perversion. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects.

4 - Increased Bleeding Time. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects.

Myopathy and rhabdomyolysis:

There is a small chance that participants treated with the combination of a statin and certain concomitant medications (Fluconazole, Ketoconazole, Cimetidine, Omeprazole, Ranitidine, Colchicine, Daptomycin, Erythromycin, Glyburide, Immunosuppressants, i.e. Cyclosporine, Phenytoin, Gemfibrozil, or Fenofibrate) may have an increased risk of myopathy and rhabdomyolysis. Therefore, if a participant is on any of these concomitant medications we will assess them weekly with the side effect checklist assessment for commonly occurring drug side effects. If participants exhibit signs or symptoms of myopathy or rhabdomyolysis, then laboratory tests evaluating creatinine protein kinase (CPK; a marker of muscle breakdown) will be ordered. If CPK is not markedly elevated (i.e., 3x normal), then the study medications will be continued and CPK will be monitored on a weekly basis. If CPK is elevated, then the study medications will be stopped immediately .

ID: VIEW4E1B52509F00L  
Name: v2\_Research Related Risk.

## 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:**  
Participants may or may not experience a temporary improvement in some aspects of cognitive impairments and negative symptoms associated with schizophrenia. The treatments used in this study do not have proven efficacy.
- 2 **\* Describe the importance of the knowledge expected to result from the study:**  
Treatment for persistent positive symptoms and cognitive impairments in people with severe mental illness is a serious public health and mental issue. Testing new and promising medications may yield significant findings for a population that has a high rate of disability. Moreover, there are no empirically validated interventions, who present with these aspects of the illness, to help this patient population despite the considerable health, financial, social and psychological costs imposed by their disorder. The present research will test new medications for this population. The benefits of studying a potentially effective means of treating such an impaired population are substantial. The data may be of considerable value in developing new methods of treatment, which would benefit other people with schizophrenia in the future.
- 3 **\* Describe how the potential risks to participants are reasonable in relationship to the potential benefits:**  
The benefits of the knowledge gained in the field of treatment for schizophrenia far outweigh the potential study risks associated with study participation.
- 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 is voluntary and the alternative is not to participate.

ID: VIEW4E1B5251B0401  
Name: v2\_Potential Benefits and Alternatives

## 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:**  
The Principal Investigator of the research study can remove a subject from the research study without their agreement. Possible reasons for removal include failure to follow instructions of the research staff or if the Principal Investigator decides that the research study is no longer in the subject's best interest. The sponsor can also end the research study early.
- 2 **\* Describe procedures for orderly termination:**  
Should a participant require early termination from the study, all medications will be discontinued immediately. There are no safety issues if study medications are discontinued abruptly.
- 3 **\* Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection:**  
If a subject withdraws from the study, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

ID: VIEW4E1B52531F801  
Name: v2\_Withdrawal 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*):**  
With respect to confidentiality and privacy, the welfare of the participant is safeguarded by responsible, systematically controlled procedures for the collection of information for research purposes.  
  
Participants at the MPRC will be afforded privacy during all research interactions by using private rooms with doors closed. Only the participant and limited study personnel will be present during the exam/procedures, unless the participant requests otherwise.
- 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:**  
All consent discussions and research assessments with participants or potential participants will be conducted in private, behind closed doors.
- 3 **\* Describe potential environmental stressors that may be associated with the research:**  
There are no unusual environmental stressors associated with this study. Research activities take place in comfortable, quiet rooms behind closed doors.

ID: VIEW4E1B525B87C01  
Name: v2\_Privacy of Participant

## 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)?**  
At the MPRC, research data (hard copies in folders) will be stored in locked file cabinets in locked rooms. Computerized data entry will be password protected. All the research data will be identified only by research ID numbers.

Coded samples collected for cell culture assays will be stored in Dr. Leonardo H. Tonelli's laboratory at UMB, Medical School Teaching Facility Building, 685 W Baltimore Street, Room 958.

- 3 **\*How will such data be secured?**  
Hard copies of research data will be stored in locked file cabinets in rooms with restricted access, that will be locked as needed. Computerized data entry will be password protected and be identified only by research ID numbers. Electronic files at the MPRC are handled via a local area network (LAN) maintained behind a Netscreen 5XP firewall with multiple layers of protection against unauthorized intrusion. MPRC Databases are maintained on the center's server, are regularly backed up, and are additionally protected by a 5-tiered system involving restricted access at the desktop, directory, database, reporting and table levels.
- 4 **\*Who will have access to research data?**  
Only the PI, his research staff, and regulatory officials will have access to the research data with identifiers. When research team members are no longer on the research team, their access to the data will be removed.
- 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 |
|-------------------------------|---------|---------------|
| There are no items to display |         |               |
- 8 **\*Discuss any other potential confidentiality issues related to this study:**  
All information recorded for research purposes, including computer input data, is identified by code number rather than by name, and subsequent published or presented material related to the project will not be traceable to specific individuals. However, code number and participant name can be linked via an internal database system, which is protected by a two-step password system. Following completion of data collection, subject files are maintained in a secure area in retrievable form for future subject-requested clinical use. Research data will be kept in a locked file in a locked office.

ID: VIEW4E1B5265E040  
Name: v2\_Confidentiality of Dat

## Monitoring Plan Selection

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

ID: VIEW4E1B00E30D40  
Name: v2\_Monitoring Plan Selectio

## 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  
Laboratory Tests  
Medical Compliance  
Procedure Reports  
Outcomes (Primary, Secondary)  
Preliminary Analyses
- 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  
Sponsor
- 4.1 If Other, specify:

# Monitoring Plan - Internal DSMB

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

## 1 \* List Internal DSMB Members:

Name
<a href="#">View Robert McMahon, Ph.D.</a>
<a href="#">View Glenda Housel, M.D.</a>
<a href="#">View Clayton Brown, Ph.D.</a>
<a href="#">View Charles Richardson, M.D.</a>
<a href="#">View Julie Kreyenbuhl, Pharm.D., Ph.D.</a>
<a href="#">View Scott Aaronson, M.D.</a>

## 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?

Data and Safety Monitoring Board. The MPRC has established a Data and Safety Monitoring Board (DSMB), which is comprised of two psychiatrists, a statistician, a pharmacist, and a community representative. The psychiatrists are experts in the clinical treatment of people with schizophrenia. None of the DSMB members reviewing this study will be investigators on the proposed project; however, Dr. McMahon serves as a non-voting member of the DSMB to assist in the monitoring of all MPRC trials. The DSMB will be charged with the following responsibilities:

- 1) to establish a regular meeting schedule;
- 2) to review the proposed protocol;
- 3) to review the proposed consent form prior to IRB submission;
- 4) to monitor study progress and the occurrence of side effects/adverse events, and serious adverse events throughout the course of the study; and
- 5) to review with Dr. McMahon, the statistician for the project, the study data management system.

The DSMB will review reports on protocol progress, side effects and adverse events twice a year. In addition, all serious adverse events (SAEs) will be reported to the DSMB, P.I., the University of Maryland School of Medicine IRB, and the appropriate NIH program of ficer. The P.I. will receive all SAE reports within 24 hours of their occurrence. The DSMB, University of Maryland School of Medicine IRB, and NIH program officer will receive the reports within 48 hours. If the incidence of any side effect/adverse event is 25% or more or any SAE occurs in excess in either treatment group, then the DSMB will notify the P.I. The P.I. and DSMB will determine whether possible protocol modifications are required to minimize the further occurrence of such events.

SAEs will be defined as any adverse experience that is unexpected or: i) results in death; ii) results in persistent or significant disability/incapacity; iii) results in or prolongs an existing inpatient hospitalization (even if the hospitalization is a precautionary measure for observation); iv) is a congenital anomaly/birth defect in of fspring of subjects taking the product regardless of time to diagnosis; v) is cancer; vi) is the result of an overdose, whether accidental or intentional; or vii) is a suicide attempt (but not suicidal ideation).

Initial Meeting for New Protocols: When required by a funding institution, an IRB or other governing body, new protocols will be reviewed by the DSMB prior to study enrollment. Safety precautions, procedures for recording and reporting AEs and SAEs, and the monitoring proposal will be discussed. The purpose of the DSMB initial review of the study is to learn directly from the study investigators the goals of the study and its rationale. Additionally, the study investigators will present any specific issues they would like the DSMB to consider while monitoring the data. The DSMB may propose hypothetical scenarios that may be encountered while monitoring the study, and ask the study investigators how they would hope the DSMB would react to it and why. Once the study begins, the DSMB is less able to interact with the study investigators without disclosing interim results.

Annual Meeting for Ongoing Protocols: Once a protocol has been initially reviewed by the DSMB, the study data will be presented to the DSMB on an annual basis, or more frequently as mandated by IRBs, FDA, or Pharmaceutical companies. Adverse events, serious adverse events, study withdrawals or terminations, and the rate of recruitment will be evaluated. If a study is progressing as outlined in the protocol, with no AEs, SAEs and few withdrawals or terminations, and rate of recruitment is consistently sufficient, a report will be sent to the DSMB Committee to meet annual review requirements in lieu of the P.I. presenting the material in person. After review of this report however, the DSMB may request to meet with the P.I. at the next scheduled quarterly meeting to address any additional questions they have regarding the protocol.

After reviewing a protocol, the DSMB Committee may make recommendations concerning the continuation, modification, or termination of the trial. The primary goal of each committee member is to evaluate the safety, study conduct, and scientific validity and integrity of the trial.

If required by the IRB, FDA, or Sponsor, or if precipitated by an event, the principal study investigator will prepare an interim protocol summary addressing specific concerns he or she has about the protocol for the DSMB Committee. The summary and all relevant documentation will be sent to the DSMB members. Only on an as needed basis, the study statistician will prepare a study data (unblinded) report and forward to the MPRC DSMB Coordinator to send to the DSMB members as well. These reports will contain the most up-to-date data permitted by the timeframe necessary for the statistician to prepare and review the analyses. The study statistician's report with the unblinded data, will usually contain his or her assessment of the progress of the trial, including recommendations on whether it should be terminated or modified. Only the DSMB members will receive copies of the unblinded data report. The DSMB will meet regularly to monitor the cumulative safety data during the period when participants are receiving study therapy. The meetings will occur on a quarterly basis and the members will meet in person or by teleconference. The DSMB will monitor the study according to the guidelines specified in the study protocol, unless it is determined that a modification is in the best interest of the study and its participants.



The DSMB Chair will set the meeting agenda, which may include Open and Closed Sessions. The DSMB members, the study statistician and the principle study investigator will attend the Open Session, at which data concerning study conduct and aggregate safety data are discussed. Closed Sessions will be on an as-needed basis. If indicated because of AEs, SAEs, multiple withdrawals or early terminations, the DSMB members and the study statistician will attend a Closed Session. Any safety and efficacy data analyzed by the treatment arm will be discussed only in a Closed Session. It is critical that information presented in the Closed Session not be revealed to the study investigators, except as explicitly authorized by the DSMB. The study investigators will remain blinded to the interim data because knowledge of emerging trends between treatment arms may influence subject enrollment, management and evaluation, thus compromising the study.

**Communication of DSMB Recommendations:** At the conclusion of each DSMB meeting, the Board will provide a verbal report to the principal study investigator indicating areas of concern regarding performance and safety. The DSMB must not communicate any information that could lead to the unblinding of investigators or suggest interim treatment-specific results. Soon thereafter, the DSMB Chair will provide the principal study investigator with a written summary of the Board's recommendations. In addition to the minutes, the DSMB Chair will include a memorandum to the principal study investigator documenting (a) the date of the review, (b) that all relevant interim safety and efficacy data were reviewed, (c) recommendations concerning the study execution or modifications to the study protocol, and (d) the anticipated date of the next review. The principal study investigator will promptly forward a copy of this memorandum to the University of Maryland IRB and each additional IRB that oversees the approval of the study. This is in pursuant to the NIH's Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Supported Multicenter Clinical Trials (release date: June 11, 1999, <http://grants.nih.gov/grants/guide/notice-files/not99-107.html>).

If the DSMB recommends an amendment to the protocol, it must be approved by the appropriate IRB. If as a result of interim data monitoring the DSMB determines that a trial (a) has answered the primary study question, (b) will not be able to reach a firm conclusion, (c) is not being conducted according to high scientific or ethical standards, or (d) poses an unreasonable or unnecessary risk to study participants, the DSMB will recommend to the principle investigator that the study protocol be terminated, temporarily suspended or amended, as appropriate. This recommendation will be conveyed to and discussed with the principal study investigator before any action is taken. It will be important to ensure that the principal study investigator understands the DSMB's rationale. In addition, prior to a public announcement of a trial's early termination, a plan should be developed and implemented for notifying the study investigators, the IRBs and the study participants.

**Records.** Participant records are confidential. When scientific data are published, no information that could identify an individual is used. The names of research participants are never reported. All records are kept in locked cabinets or rooms and are only available to approved members of the research team.

## 5 \*What are the criteria defined in the protocol to be used for decision making regarding continuation, modification, or termination of study?

**Symptom re-emergence.** The course of schizophrenia includes periods when symptoms become worse. This occurs in standard clinical treatment, and may continue to occur during research participation. Some research protocols may be associated with an increased risk of symptom re-emergence, for instance an experimental drug that turns out to be ineffective, or if the participant is in a drug-free or placebo period. Participants in drug studies are closely monitored for increased symptoms and side effects. When clinically necessary the protocol is interrupted and an individual is put back on non-experimental medication. We have also developed a procedure to assess worsening objectively (see below):

**Objective Criteria for Termination of Protocol:**

Any of the following conditions will result in protocol termination.

- a. The subject is judged to be entering a clinically significant exacerbation of his/her illness by their treating clinician.
- b. Either of the following:
  1. Relative to the baseline Brief Psychiatric Research Scale (BPRS) item scores, an increase of 3 points or more OR an increase from 5 to 7 on any one of the following BPRS items: somatic concern, conceptual disorganization, hostility, suspiciousness, hallucinatory behavior, or unusual thought content.
  2. An increase of 2 or more on the Clinical Global Impression – global severity rating.
- c. Complete cessation of eating and drinking for a period exceeding 24 hours.

Serious Adverse Events are reported immediately to the IRB, to the DHMH IRB, to the Inpatient Program/Chief, to the MPRC Head and to the SGHC Clinical Director. Where appropriate, a report is also sent to the FDA. A serious adverse event (SAE) is any adverse experience that:

- Results in death.
- Results in persistent or significant disability/incapacity.
- Results in or prolongs an existing inpatient hospitalization (even if the hospitalization is a precautionary measure for observation).
- Is a congenital anomaly/birth defect in offspring of subjects taking the product regardless of time to diagnosis.
- Is cancer.
- Is the result of an overdose, whether accidental or intentional.
- Is a suicide attempt (not suicidal ideation only)
- For outpatient participants: Is an admission to an inpatient facility.
- For inpatient participants:
  1. Is the participant being placed in locked door seclusion for a period exceeding 2 hours?
  2. Is the participant being placed in physical restraints?
  3. Is an elopement from the facility defined as an unauthorized absence exceeding 12 hours or documentation as elopement in the clinical chart?

ID: VIEW4E1B0261D940  
Name: v2\_Monitoring Plan - Internal DSM

## 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:  
 None

ID: VIEW4E1B5D964180f  
 Name: v2\_Research Related Cost

## 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:
- | Name                          | Created | Modified Date |
|-------------------------------|---------|---------------|
| There are no items to display |         |               |
- 1.2.2

ID: VIEW4E1B629EEC00f  
 Name: v2\_Compensation for Research-Related Inj

## Payment to Participants

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

ID: VIEW4E1C52A5D780f  
 Name: v2\_Payment to Participan

## 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)  
 Time and effort
- 1.1 If Other, specify:
- 2 \* What is the total dollar value of the payments over the duration of the study? **Total payment(s) for participation in resear ch of \$600 or more is required to be reported on an IRS Form 1099.**  
 \$345
- 3 \* Describe the timing and distrubution plan for the payment (schedule, means, etc.)?  
 Participants will be paid \$45 for the initial evaluation and \$25/visit for additional visits. Participants will receive the total amount of \$345 upon completion of the study . Should a participant terminate early from the study , they will be paid for the visits completed.
- 4 \* Method(s) of payment to be Used:  
 Check
- 4.1 If Other, specify:

## 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: VIEW4E1B0A214400  
Name: v2\_HIPAA

## 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  
Social Security numbers
- 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).*  
This research would not practicably be done without access to and use of PHI because such access allows for efficient screening of individuals. A review of PHI in chart records will increase the likelihood that only those individuals that meet certain study-specific criteria are suggested to clinical care givers as potential study participants. Using this approach, individuals who are ineligible based on readily discernible eligibility criteria are never approached about this study.  
  
The actual SSN in its entirety is requested of an individual the first time they enroll in a study. The SSN is requested of the study participant so that the University may be compliant with IRS reporting requirements for aggregate payments exceeding \$600. Such an aggregate is possible if a participant completes several University of Maryland studies in a given year. The SSN information is stored for about 5 years following the participant's last study payment. Thereafter this information is destroyed using secure shredding. Forms with SSN information are stored with locked cabinets which are accessible to approved staff individuals.
- 3 \* What is the source(s) of the PHI?  
Clinical chart, participants, and treatment providers. Dates on research assessments.
- 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).  
The Protected Health Information will not be reused.
- 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")  
Requesting waiver/alteration of authorization (includes waiver of authorization for recruitment only)
- 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: VIEW4E1B0A24AA401  
Name: v2\_Protected Health Information

## Waiver/Alteration of Authorization

You indicated that a waiver/alteration of authorization is requested.

- 1 \* Provide rationale for how the research presents no more than minimal risk to the privacy of individuals:  
Only the PI and the research staff will have access to a participant's private information. All research records will have an ID number on them and not a participant's name. All study records related to a participant will be kept in locked file cabinets in a locked office.
- 2 \* Describe the plan to ensure the protection of PHI collected during this study from improper use and disclosure:  
PHI for this study will be protected at all times. All source documentation for the study is kept in a locked cabinet in a locked room. Data for the study is entered onto a password protected secured server. No publication of data will disclose information that could be linked to a single participant.
- 3 \* Describe the plan to destroy the PHI collected during this study at the earliest opportunity consistent with the conduct of the research. If there is a need to retain PHI, provide a justification:  
PHI is stored for about 5 years following the participant's last study payment. Thereafter this information is destroyed using secure shredding. Forms with PHI are stored with locked cabinets which are accessible to approved staff individuals.
- 4 \* Why could the research not practicably be done without access to and use of this PHI?  
This research would not practicably be done without access to and use of PHI because such access allows for efficient screening of individuals. A review of PHI in chart records will increase the likelihood that only those individuals that meet certain study-specific criteria are suggested to clinical care givers as potential study participants. Using this approach, individuals who are ineligible based on readily discernible eligibility criteria are never approached about this study.  
A waiver of HIPAA authorization is justified for this study because the use of the PHI involves no more than minimal risk to the privacy of the potential participants.

- 5 \* **Why could the research not practicably be done without the waiver or alteration?**  
This research could not practicably be done without the waiver because it would be difficult to obtain consent for access of chart records from each potentially eligible individual.
- 6 \* **Will the subjects' PHI be disclosed to (or shared with) any individuals or entities outside of UM?**  
☒ Yes ☐ No
- 6.1 **If Yes, describe the individuals or entities outside of UM to whom PHI will be disclosed.**  
Clinical samples will be sent for processing to LabCorp where all our clinical specimens are processed.

ID: VIEW4E1B0A289640  
Name: v2\_Waiver/Alteration of Authorization

## 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:**  
Potential participants will be identified through chart review or nomination by the treatment team. No participant will be approached for recruitment without approval of a primary clinician, who will determine suitability of the person for the protocol. A chart review will be completed for all nominated potential participants to reduce the likelihood that participants will be found ineligible after participating in more extensive assessment. The study interviewer will verify with the primary clinician that a potential participant is sufficiently stabilized to consider participation and has capacity to provide consent. This is done prior to the study interviewer approaching a potential participant. The study interviewer will be introduced to the potential participant and provide a brief overview of the project.
- Research staff members are trained to recognize symptoms of severe mental illness and cognitive impairment that could undermine an individual's ability to provide informed consent. Interested participants will be provided study information and an informed consent form that contains all pertinent details of participation. As some potential participants will have poor reading skills, the consent form will be read aloud in tandem with their own silent reading of the document. Our research staff are carefully trained on obtaining consent from and interacting with people with seriously mentally illness and supervised by senior staff members. The individual securing consent will review any points about which the participant is unclear, and the participant will be invited to ask questions as needed. All participants who express willingness to provide consent will be queried about each paragraph of the agreement in order to insure that they have adequate understanding of what they are agreeing to. Research staff are trained in strategies for interacting with people with severe mental illness, including speaking slowly and clearly, stopping to summarize frequently, and providing time for questions.
- After reading the consent, and before obtaining a signature, a brief questionnaire, the Evaluation to Sign Consent (ESC), is administered to verify that the subject is competent to provide consent and has demonstrated comprehension of the consent document. The recruiter will also make a clinical judgment and not recruit participants who appear unable to grasp key aspects of the procedure. This approach, which requires a proactive demonstration on the part of the participant that they understand what is being requested, has been used extensively at our sites. Per IRB regulations, a copy of the signed consent form is given to the participant, a copy is placed in the participant's medical record, and the original is kept in the laboratory. Research assistants obtaining informed consent will be experienced clinicians. They will receive detailed and standardized training as to how to obtain informed consent from people with severe mental illness. They will be observed obtaining informed consent from a potential participant by senior staff prior to being allowed to recruit on their own. Prior to signing the consent form, participants will be informed that participation in the study is contingent upon their meeting diagnostic criteria as determined in the clinical interview. All discussions with potential study participants will take place in a private room behind closed doors.
- 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:**  
Our research staff who are carefully trained in obtaining consent from and interacting with people with severe mental illness and are supervised by senior staff members.
- 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 study interviewer will be introduced to the potential subject and provide a brief overview of the project in a private room behind closed doors.
- 7 \* **Describe the provisions for assessing participant understanding:**  
All participants who express willingness to provide consent will be queried about each paragraph of the agreement in order to insure that they have adequate understanding of what they are agreeing to. Research staff are trained in strategies for interacting with people with severe mental illness, including speaking slowly and clearly, stopping to summarize frequently, and providing time for questions. After reading the consent, and before obtaining a signature, a brief questionnaire, the Evaluation to Sign Consent (ESC) is administered to verify that the participant is competent to provide consent and has demonstrated comprehension of the consent document. The recruiter will also make a clinical judgment and not recruit participants who appear unable to grasp key aspects of the procedure. This approach, which requires a proactive demonstration on the part of the participant that they understand what is being requested, has been used extensively at our sites.
- 8 \* **Describe the consideration for ongoing consent:**  
The study is short in duration and all participants will be seen at least bi-weekly once treatment commences. Their continuing consent will be assessed verbally at

## Consent and HIPAA Authorization Forms - Draft

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

Name	Created	Modified Date
UMB Consent	1/13/2012 12:10 PM	11/30/2016 4:19 PM

**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:

UMB HIPAA Form	3/15/2013 12:50 PM	5/16/2014 8:23 PM
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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: VIEW4E1C7712D3006  
Name: v2\_Consent Forms - Dra

## 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:

**MPRC Outpatient**

If this information is incorrect, please notify the HRPO of fice.

### 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: VIEW4E1AF91AB240L  
Name: v2\_Organization Review Requirements (other than IF

## 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. **Yes**
- 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?
- If the answer to this question is wrong, an IBC submission is not required, use the Jump To menu or your browser's <<Back button and return to the IBC RSC review requirements page to change your answer .
- 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: VIEW4E1AF91ED4C0L  
Name: v2\_Institutional Biosafety Committee Review Requi

## 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                                      | Workspace | SmartForm |
|---|-----------|-----------|
| IBC: Anti-Inflammatory Treatment of Schizophrenia (HP-00051603) |           |           |
- 2 **Required Department and Specialty Reviews**- Based on the PI's organization (department, division, etc.) of 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 |
|----------------------|---------------|
| MPRC Outpatient      | Complete      |

ID: VIEW4E1C8D9AE400L  
Name: v2\_Summary of Required Reviews (other than IF

## Additional Documents

- 1 Upload all additional documents here:
- | Name | Created | Modified Date |
|------|---------|---------------|
|------|---------|---------------|

Assessment Schedule_v1 1.6.14	10/9/2013 4:45 PM	11/6/2014 3:32 PM
LAB_GlucoseFS.doc	10/9/2013 4:34 PM	10/9/2013 4:34 PM
TotalCytokines.doc	6/28/2013 1:47 PM	6/28/2013 1:47 PM
MedAccount_Salsalate.doc	6/28/2013 12:50 PM	6/28/2013 12:50 PM
MedAccount_Omega3.doc	6/28/2013 12:50 PM	6/28/2013 12:50 PM
MedAccount_Fluvastatin.doc	6/28/2013 12:50 PM	6/28/2013 12:50 PM
Physical Exam form	6/28/2013 12:48 PM	6/28/2013 12:48 PM
Full Study Protocol	4/24/2013 1:56 PM	4/24/2013 1:56 PM
Side Effect Checklist	4/24/2013 1:55 PM	4/24/2013 1:55 PM
FDA_IND approval letter 2012.pdf	3/15/2013 12:04 PM	3/15/2013 12:04 PM
DSMB Minutes	3/15/2013 12:02 PM	3/15/2013 12:02 PM

Name	Created	Modified Date
ConCom medication Form	4/5/2012 3:09 PM	4/5/2012 3:09 PM
EKG Results Form	4/5/2012 3:08 PM	4/5/2012 3:08 PM
LABS Forms	4/5/2012 3:07 PM	4/5/2012 3:07 PM
Medical History Form	4/5/2012 3:07 PM	4/5/2012 3:07 PM
Non Psych Con Medications Form	4/5/2012 3:06 PM	4/5/2012 3:06 PM
Vital Signs Form	4/5/2012 3:05 PM	4/5/2012 3:05 PM
Pregnancy Test Form	4/5/2012 3:04 PM	4/5/2012 3:04 PM
Urine Toxicology	4/5/2012 3:03 PM	4/5/2012 3:03 PM
Demographics Form 2	4/5/2012 2:23 PM	4/5/2012 2:23 PM
Demographics Form 1	4/5/2012 2:23 PM	4/5/2012 2:23 PM
Valdivielso et al_Cardiovascular Diabetology_1_2009.pdf	3/9/2012 4:06 PM	3/9/2012 4:06 PM
Evaluation to Sign Consent Form	12/27/2011 11:40 AM	12/27/2011 11:40 AM

ID: VIEW4E0962513A00  
Name: v2\_Additional Document

## 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
MPRC Outpatient	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: Anti-Inflammatory Treatment of Schizophrenia (HP-00051603)

[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: VIEW4E1B10C50000  
Name: v2\_Final Page of Application

## Add a Team Member

- \*Select Team Member:**  
William Carpenter Jr
- Research Role:**  
Sub-Investigator
- \*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
- \*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:

William T. Carpenter, Jr., MD, is a Professor of the University of Maryland School of Medicine, Department of Psychiatry and past Director (1977-2013) of the Maryland Psychiatric Research Center. Dr. Carpenter's major professional interest has been severe mental illness, especially schizophrenia, including phenomenology of the psychoses, the etiology, pathophysiology, anatomy, and treatment of schizophrenia.

## Add a Team Member

1 \* Select Team Member:

Joel Palachuvattil

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:

Joel Palachuvattil, MS, has over ten years of experience in data management. He is currently a database engineer at MPRC, with previous database development and administration experience in the areas of human subjects research, nutrition research, and education.

## Add a Team Member

1 \* Select Team Member:

Christine Brown

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:

Christine Brown- Degree In Mental Health Counseling with 40 years of experience working with the CMI population in both inpatient and outpatient settings. I started working at MPRC (ORP) in 2007, recruiting new patients for the ORP and for research studies.

## 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, Pharm D. is a pharmacist with 30 + years in the field. Presently working as the Chief Pharmacist at International Nutrition Inc. Licensed to dispense all classes of medication as well as extensive patient counseling.

## Add a Team Member

- 1 \*Select Team Member:  
 Alexander Duggan
- 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
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☐ 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:  
 Alexander Duggan with BA in psychology joined the MPRC in April 2012 as a research recruiter . His primary role with the Outpatient Research Program has been recruiting for clinical research trials.

## Add a Team Member

- 1 \*Select Team Member:  
 Deanna Kelly
- 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
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☐ 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:  
 Deanna L. Kelly, PharmD., BCPP is a clinical investigator with a long history of clinical research in people with severe mental illness and substance abuse research. She has received grant funding from NIMH, NIDA and several foundations and served as PI on numerous studies of people with severe mental illness and substance abuse. She serves on the DHMH IRB and NIMH DSMB. She is knowledgeable about the study sites, culture and society of participants and personnel related to the protocol.

## Add a Team Member

- 1 \*Select Team Member:  
 Melissa Blake
- 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:

Melissa Blake, MSW, LGSW-has approximately 13 years of experience working with the chronic mentally ill population. Also has over 8 years of experience in assisting with research protocols with this population.

## Add a Team Member

- 1 \*Select Team Member:

Christopher Kitchen

- 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:

Chris Kitchen - M.A. with more than 5 years experience working with substance abuse and mental illness populations at the National Institute on Drug Abuse.

## Add a Team Member

- 1 \*Select Team Member:

James Gold

- 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:

James M. Gold, PhD; Clinical Psychologist over 25 years of experience as a clinical investigator with a focus on the application of cognitive neuroscience approaches to understanding the cognitive and motivational impairments of schizophrenia. Serves as PI on multiple UMB research protocols; supervises conduct of cognitive and neurophysiological measures under those protocols in his laboratory , as well as in collaboration with other investigators using cognitive endpoints in their studies..

## Add a Team Member

- 1 \*Select Team Member:

Sarah Nisonger

- 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.  
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☐ 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:  
 Sarah Nisonger – MS, LGPC with six years experience working in clinical and research settings, with both the general population and individuals with severe mental illness.

## Add a Team Member

- 1 \*Select Team Member:  
 Ikwunga Wonodi
- 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.  
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☐ 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:  
 Ikwunga Wonodi, M.D., with extensive clinical and research experience, graduated medical school 24 years ago and has over 13yrs experience working in clinical research settings.

## Add a Team Member

- 1 \*Select Team Member:  
 Jacqueline Kiwanuka
- 2 Research Role:  
 Other
- 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.  
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☒ 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:  
 Jacqueline Kiwanuka, MBA. Lab Manager and overall project coordinator . Ms.  
 Kiwanuka is the manager of Dr . Gold's laboratory. She takes lead responsibility for the IRB, regulatory , and compliance monitoring efforts needed to support his projects.

## Add a Team Member

- 1 \*Select Team Member:  
 MacKenzie Sayer
- 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.  
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☐ 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:  
MacKenzie Sayer is a new Research Associate recently hired by MPRC to work on research protocols. MacKenzie has recently graduated from Virginia Tech University with a BS in psychology. Her primary research responsibilities will include running research protocols to include completing research assessments, and consenting participants.

## Add a Team Member

- 1 \*Select Team Member:  
Elaine Weiner
- 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.  
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- 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:  
Elaine Weiner MD – Assistant Professor of Psychiatry . Board certified in Psychiatry. Completed a psychiatry research residency at University of Maryland School of Medicine and has been Medical Director at the Outpatient Research Program of the MPRC since 1993. In addition to her clinical and administrative duties, she facilitates the implementation of a variety of clinical research protocol and has her own research interest in smoking cessation in people with schizophrenia.

## Add a Team Member

- 1 \*Select Team Member:  
Leeka Hubzin
- 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.  
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- 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:  
Leeka Hubzin, MS in Clinical Psychology , has been working as a clinical research assistant at the MPRC since 2009. Her primary role is assessment, coordination and recruitment of research participants.

## Add a Team Member

- 1 **\*Select Team Member:**  
Haley Demyanovich
- 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.**  
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☐ 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:**  
Haley Demyanovich, BA joined the MPRC in October 2013 as a Clinical Research Assistant. Her primary role with the Treatment Research Program is coordinating clinical research trials.

## Add a Team Member

- 1 **\*Select Team Member:**  
Matthew Glassman
- 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
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☐ 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:**  
Matthew Glassman—M.S. w/ 3+ years of research experience working with the Treatment Research and Neuro-Imaging Research Programs at MPRC and the National Institute on Drug Abuse.

## Add a Team Member

- 1 **\*Select Team Member:**  
Ann Kearns
- 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:**  
Ann Kearns- Has worked in a variety of psychiatric settings over the past 18years. She has 12 years of experience at the Maryland Psychiatric Research Center , performing a variety of research activities, and regulatory compliance work.

## Add a Team Member

- 1 \*Select Team Member:  
Michelle Kuptzin
- 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
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☐ 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:  
Michelle Kuptzin, MS, OTR/L is an Occupational Therapist at the Spring Grove Hospital Center/Inpatient Research Program.

## Add a Team Member

- 1 \*Select Team Member:  
Leonardo Tonelli
- 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:  
Leonardo H Tonelli, Ph.D. is an Assistant Professor and the head of the Laboratory of Behavioral Neuroimmunology (LBNI) at the Mood and Anxiety Program (MAP), Department of Psychiatry, University of Maryland School of Medicine. He received his PhD degree in Neurobiology from University of Cordoba, Argentina. He Joined the Department of Psychiatry in 2005 and established an independent research program.

## Add a Team Member

- 1 \*Select Team Member:  
Eric Arbach
- 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.  
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- 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:  
Eric Arbach, MSW, LCSW-C, with 14 years of clinical experience working with the seriously mentally ill population and assisting in research protocols.

## Add a Team Member

- 1 \*Select Team Member:  
Robert McMahon
- 2 Research Role:  
Statistician
- 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 McMahon is a PhD Biostatistician and Professor of Psychiatry , who has worked at the Maryland Psychiatric Research Center (MPRC) as Director of Biostatistics and Data Management, collaborating with MPRC investigators in a wide variety of clinical research into the neuropsychology , neurophysiology , genetics and treatment of schizophrenia and other mental disorders.

## Add a Team Member

- 1 \*Select Team Member:  
David Gorelick
- 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:  
David A. Gorelick, MD, PhD is board certified in Psychiatry and Addiction Medicine. Dr. Gorelick has more than 30 years experience in clinical research involving people with substance abuse and/or severe mental illness, and has served as Principal Investigator for numerous controlled clinical trials. He is familiar with human research regulations, having served for 10 years as chair of the NIDA IRB, and is knowledgeable about the study sites, culture and society of the participants and personnel related to this protocol.

## Add a Team Member

- 1 \*Select Team Member:  
Lynne Mathews
- 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:  
Lynne Mathews, MSW, LCSW-C with 15 years of clinical and research experience working with the seriously mentally ill population.

## Add a Team Member

- 1 \*Select Team Member:  
Judy Liu
- 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
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☐ 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:  
Judy Liu, RN, MS with extensive clinical, research, therapy, teaching and management experience in research center , mental health clinic, hospital and school. Has been working at Maryland Psychiatric Research Center for 15 years.

## Add a Team Member

- 1 \*Select Team Member:  
Stephanie Feldman
- 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:  
Stephanie Feldman- MSW with extensive clinical and research experience. Has worked in many different settings over the past 30 years and has been involved in issues related to mental health advocacy .

## Add a Team Member

- 1 \*Select Team Member:  
Charles Richardson
- 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:  
Charles Richardson, MD is the lead clinician for the Treatment Research Program at the Spring Grove Hospital Center. He supervises the overall clinical program and directs the execution of research protocols, while contributing to protocol development and analysis. He has been working at Spring Grove since 1989.

## Add a Team Member

- 1 \* Select Team Member:  
Carol Simon
- 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:  
Carol Simon, LPN Clinical, Research nurse, teaching and management experience in Research Center and Community Health Clinic. Has been working at Maryland Psychiatric Research Center for 16 years.

## Add a Team Member

- 1 \* Select Team Member:  
Heidi Wehring
- 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:  
Heidi Wehring Investigator/ PharmD has conducted and participated in many research studies and pharmacy related programs. Knowledgeable about the MD mental health system, psychiatric pharmacy and design and conduct of clinical studies.

## Add a Team Member

- 1 \* Select Team Member:  
Sharon August
- 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:

Sharon August, MA in Clinical Psychology, has been at MPRC since 2002, as a clinical research assistant involved in recruitment, coordination, and evaluation of research participants in behavior neuropsychological studies as well as cognitive assessments in clinical trials. She provides training and supervision in neuropsychological assessment at MPRC.

Name	Edit Submission	cc on Email	Research Role	Has SFI?
Heidi Wehring	no	no	Sub-Investigator	no
Sharon August	no	no	Research Team Member	no

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

ID: VIEW4DF85C16F280C  
Name: v2\_Research Team Information

## Resources

- \* Describe the time that the Principal Investigator will devote to conducting and completing the research:**  
The PI devotes 20% of his time to conducting and overseeing this research. This involves supervision of all staff, meeting with each research participant and review of the consent process.
- \* Describe the facilities where research procedures are conducted:**  
The study is conducted primarily at the Maryland Psychiatric Research Center (MPRC) which is located on the grounds of the Spring Grove Hospital Center. The facility includes an outpatient program and an inpatient unit which are spread across two buildings on campus. The MPRC facilities have a large range of office space which is used for patient examination, interviews and completion of research procedures.
- \* Describe the availability of medical and/or psychological resources that subjects might need as a result of anticipated consequences of the human research:**  
The MPRC has the full range of medical and psychological professionals who are able to assess and respond to any issue that may arise when a participant is at our program. This includes MDs, nurses, pharmacists and other staff who receive regular training in CPR and other standard emergency procedures. Both MPRC buildings have external defibrillators readily available.
- \* 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:**  
At the beginning of the protocol, the PI and senior research staff held a study Protocol Initiation Meeting (PIM). At this time all study aspects are reviewed and all personnel working on the project attend. This meeting details the procedures of the study. We also develop standard operating procedures for the study and assign a primary research staff member to keeping all information up to date. All personnel are told of their role on the study and we hold regular meetings with research personnel to go over study procedures and progress. In addition, all MPRC faculty and staff receive ongoing training on a variety of research issues yearly.

ID: VIEW4DF83CB97640C  
Name: v2\_Resources

## Sites Where Research Activities Will Be Conducted

- \* Is this study a:**  
☒ Multi-Site  
☐ Single Site
- \* Are you relying on an external IRB (not UM) to be the IRB of Record for this study?**  
☐ Yes ☒ No
- \* 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
DHMH-UMB Signed MOU	10/9/2013 3:17 PM	10/9/2013 3:17 PM
- \* 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
- \* Institution(s) where the research activities will be performed:**  
Maryland Psychiatric Research Center (MPRC)  
Department of Health and Mental Hygiene (DHMH) (may be applicable for any studies receiving state funding)

ID: VIEW4DF870DF2C000  
Name: v2\_Sites Where Research Activities Will Be Conducted

## UM Coordinating Center

**You indicated that UM is the Coordinating Center for this multi-site study**

- 2.1 \* Describe the processes to ensure communication among sites.**  
Things to consider including in the communication plan:
  - all sites have the most current version of the protocol, consent document, etc.
  - all required approvals have been obtained at each site (including approval by the site's IRB of record).
  - all modifications have been communicated to sites, and approved (including approval by the site's IRB)

- of record) before the modification is implemented.
- All engaged participating sites will safeguard data as required by local information security policies.
- All local site investigators conduct the study appropriately.
- All non-compliance with the study protocol or applicable requirements will be reported in accordance with local policy.

We have a full time person, Jennifer Oasing who oversees, along with the PI, all the regulatory aspects of the study. For all other approved sites, Ms. Oasing is in regular contact with the sites and will send any modifications to the IRBs following UMB IRB approved modifications. At our monthly meetings, we discuss and ensure that all modifications are known at each site, new protocols and consents are sent to each IRB. Once we begin any recruitment at any approved sites, we will have monthly meetings to ensure all local site investigators are conducting the study appropriately and that noncompliance with the study protocol is appropriate.

2.2 \*Describe the method for communicating to engaged participating sites including:

- reportable new information.
- problems.
- interim results.
- the closure of a study.

The PI and research team at MPRC meet monthly and will discuss any need for reportable new information or study problems to any affiliated sites. We have no plans for interim analysis of this study at this time and the closure of the study will only occur in regular contact with the local site investigators and will be done at the same time as appropriate with each IRB.

ID: VIEW4DF737D4C2806  
Name: v2\_UM Coordinating Center

## 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: VIEW4DF86705BB806  
Name: v2\_DHMH

## Funding Information

1 \* Indicate who is funding the study:

Department / Division / Internal  
Foundation

2 \* What portion of the research is being funded? (Choose all that apply)

Drug  
Staff  
Participant Compensation  
Procedures

3 Please discuss any additional information regarding funding below:

Funding for the final two study participants will come from a general internal account within the Maryland Psychiatric Research Center. Stanley Medical Research Center is the primary sponsor who has funded approximately 95% of the study.

ID: VIEW4DF85DF452406  
Name: v2\_Funding Information

## Foundation Sponsor Contact Information

You indicated that this is a Foundation funded study

1 \* Name:

The Stanley Medical Research Institute

\* Address 1:

8401 Connecticut Avenue, Suite 200

Address 2:

\* City:

Chevy Chase

\* State:

MD

\* Zip Code:  
20815

\* Country:  
USA

\* Contact Name:  
Jana C. Bowcut, MPH

\* Phone Number:  
301.571.0760 ext. 118

Grant Number 1 (if applicable):

Grant Number 2 (if applicable):

Grant Number 3 (if applicable):

Grant Number 4 (if applicable):

ID: VIEW4DF862B680000  
Name: v2\_Foundation Sponsor Information

## 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

## 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

## 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?  
*A clinical trial is a biomedical or behavioral research study of human subjects designed to answer specific questions about therapeutic interventions (drugs, treatments, or devices). Clinical trials are used to determine whether new therapeutic interventions are safe, efficacious, and effective.*  
☒ Yes ☐ No

ID: VIEW4E0280569E000  
Name: v2\_Type of Research

## 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.  
Despite adequate anti-psychotic treatment, the majority of people with schizophrenia continue to exhibit persistent positive and negative symptoms and cognitive impairments. The pharmacological treatment of these individuals is a major challenge. The only approved treatment for treatment-resistant schizophrenia is clozapine, which exhibits superior efficacy for persistent positive symptoms, but has limited effect for negative symptoms and cognitive impairments. Moreover, a significant proportion of people treated with clozapine will continue to exhibit clinically significant positive symptoms. There have been a number of alternative pharmacological approaches examined, including the use of adjunctive mood stabilizers; antipsychotic polypharmacy (e.g. the addition of a second antipsychotic to clozapine); and other psychotropic agents, but these approaches have not been shown to have robust effects. An alternative approach to the use of psychotropic agents for the treatment of persistent symptoms is the use of anti-inflammatory agents to reverse the pro-inflammatory state hypothesized to underlie the symptom and sign manifestations of the illness.  
There is extensive evidence that schizophrenia is due, in part, to disruptions of normal inflammatory responses to viral or bacterial infections or other stimuli of these

Specific Aim #2: The primary test for treatment effects on cognition will be performed using the MCCB composite score and the ANCOV A model follow-up composite score = baseline composite score + treatment. Exploratory analyses examining treatment effects for specific domains will be analyzed using the MM-ANCOV A model: follow-up domain T -score = baseline domain T -score + domain + treatment x domain, where the treatment x domain interaction term provides an overall test for variation in the magnitude of anti-inflammatory - placebo T -differences across domains, and the effects of anti-inflammatory treatments in specific domains can be estimated by post-hoc tests from this general model.

Secondary outcomes:

- 1) Treatment differences on clinical symptom outcomes (CDS depression, SANS negative symptom score) will be assessed with MM-ANCOV A, using models similar to that prescribed for analyses of positive symptoms.
- 2) Treatment differences on side effects will be assessed by comparing the proportion of participants in each group with either new onset or worsening compared to baseline for each of a list of specified side effects, using Fisher's exact test.
- 3) Treatment differences in changes in cytokine expression will be assessed using the Wilcoxon rank sum test to compare change scores on each cytokine measure. We anticipate many participants will have cytokine measurements below the limit of detection at one or both visits. For such participants, we will impute cytokine measurements equal to ½ the limit of detection for the assay.
- 4) Spearman rank correlations will be assessed between changes in symptoms and cognitive outcomes

ID: VIEW4E0280605280  
Name: v2\_Sample Size and Data Analysis

## 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:**

Results may be shared in a variety of situations but are not routinely shared unless requested by the physician, participant or other involved in care. Most frequently results may be shared when a laboratory or medical test indicates a need for additional follow-up with the individual's primary care physician. When the PI or research staff is notified of abnormal or unusual laboratory or medical information the research team will discuss the test and possible meaning of the results with the participant and recommend that they contact their own physician. Depending on the particular issue the Medically Accountable Physician often will meet with the participant. In this type of situation we may provide the participant with a copy of the test results.

With the participant's written permission/release of information we are also able to directly provide this information to their physician if they desire. In a case where they do not have a primary care physician we will connect them with the appropriate resources.

ID: VIEW4E02808CBD80C  
Name: v2\_Sharing of Results

## 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
<a href="#">View</a> Fluvastatin	yes	116729	yes
<a href="#">View</a> Omega-3-fatty acid	no	116729	yes
<a href="#">View</a> Salsalate	yes	116729	yes

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

Fluvastatin Package Insert 10_2012	12/28/2011 2:00 PM	2/23/2015 2:18 PM
Lovaza_Package Insert.pdf	3/9/2012 3:12 PM	3/9/2012 3:12 PM
Salsalate Package Insert	12/28/2011 2:27 PM	12/28/2011 2:27 PM

- 3 **If more than one drug is administered, discuss the risk implications of drug/therapy interactions:**

We checked three databases to evaluate whether there was a significant risk of interactions among the three drugs we propose to study: a) Lexicomp Online Interaction database; b) Micromedex Online Interaction database; and c) FDA Medwatch. There were no reports of any interactions amongst these three agents. In addition, a recent article by Valdivielso and colleagues examined the concurrent use of omega-3-fatty acids and fluvastatin and reported no increased rate of side effects or interactions (see Additional Documents section for article reprint). Therefore, we estimate that the likelihood of drug interactions between fluvastatin, omega-3 fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)), and salsalate are minimal. There should be no interactions between fluvastatin and omega-3 fatty acids. There should be no interactions between fluvastatin and salsalate.

- 4 **\* Will you be using Investigational Drug Services?**

☒ Yes ☐ No

ID: VIEW4E0916E6E140C  
Name: v2\_Research with Drugs or Biologics

## Placebos

- 1 **\* Is this study placebo controlled?**

☒ Yes ☐ No

ID: VIEW4E0514EECCC00  
Name: v2\_Placebos

## 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:  
The placebo being used in this study is not being used in place of standard therapy . The study medication or placebo will be used as an adjunct to ongoing antipsychotic medication treatment.
- 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

## 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: VIEW4E09416F57801  
Name: v2\_Psychological/Behavioral/Educational Methods and Procedures

## 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:  
Fagerstrom Test of Nicotine Dependence  
Clinical Global Impression
- 2 \*Upload a copy of all questionnaires/surveys:
- | Name                                   | Created           | Modified Date     |
|--|-------------------|-------------------|
| Fagerstrom Test of Nicotine Dependence | 1/10/2012 2:14 PM | 1/10/2012 2:14 PM |
| Clinical Global Impression             | 1/10/2012 2:10 PM | 1/10/2012 2:10 PM |
- 3 \*What is the total length of time that each survey is expected to take?  
Approximately 15 minutes
- 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/Questionnaire

## 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       |
|---|---------------------|---------------------|
| Columbia Suicide Severity Rating Scale_Since Last Visit | 3/15/2013 11:27 AM  | 3/15/2013 11:27 AM  |
| Columbia Suicide Severity Rating Scale_Baseline         | 3/15/2013 11:26 AM  | 3/15/2013 11:26 AM  |
| Calgary Depression Scale                                | 12/29/2011 12:11 PM | 12/29/2011 12:11 PM |
| SCID Summary Sheet                                      | 12/29/2011 12:06 PM | 12/29/2011 12:06 PM |
| Scale for the Assessment of Negative Symptoms           | 12/29/2011 12:06 PM | 12/29/2011 12:06 PM |
| Brief Psychiatric Rating Scale (BPRS)                   | 12/29/2011 11:50 AM | 12/29/2011 12:02 PM |

- 3 \* What is the individual duration of each interview and what is the entire duration of the interviews?  
Approximately 30 - 90 minutes
- 4 \* How will the interview responses be recorded and by whom?  
The data are recorded on assessment forms (attached above). This information is then 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 information is solicited from a participant, which suggests that there is a potential for harm to self or others, then the research assistant will notify a member of the treatment team, who will conduct a thorough evaluation of the participant.

ID: VIEW4E0947A633C0X  
Name: v2\_Interviews

## 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:  
MATRICS Consensus Cognitive Battery (MCCB)
- 2 \* Describe procedures related to all testing:  
MCCB: Cognitive function will be assessed in all participants using a test battery chosen from the National Institute of Health (NIMH) Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Project [Green, 2004]. The MCCB tests were chosen by a panel of experts on cognition in schizophrenia, and the MCCB is specifically designed to assess treatment-related changes in cognition in patients with schizophrenia. The MCCB assesses cognitive functions in the following domains using the following tests:  
Speed of Processing: Symbol-Coding, Trail Making A.  
Attention/Vigilance: Continuous Performance Test -- Identical Pairs (CPT-IP) (computer test)  
Working Memory: University of Maryland -- Letter-Number Span, Wechsler Memory Scale (WMS) - III Spatial Span.  
Verbal Learning: Hopkins Verbal Learning Test (HVLT) -- Revised.  
Visual Learning: Brief Visuospatial Memory Test (BVMPT) -- Revised.  
Reasoning and Problem Solving: Neuropsychological Assessment Battery (NAB) -- Mazes.
- 3 \* Upload relevant testing materials:
- | Name  | Created          | Modified Date    |
|---|------------------|------------------|
| Matrics Battery - Symbol Coding                             | 1/9/2012 3:12 PM | 1/9/2012 3:38 PM |
| Matrics Battery - Hopkins Verbal Learning Test              | 1/9/2012 3:15 PM | 1/9/2012 3:19 PM |
| Matrics Battery - MSCEIT Section D and H                    | 1/9/2012 3:16 PM | 1/9/2012 3:18 PM |
| Matrics Battery - WMS Spatial Span                          | 1/9/2012 3:17 PM | 1/9/2012 3:17 PM |
| Matrics Battery - University of Maryland Letter Number Span | 1/9/2012 3:17 PM | 1/9/2012 3:17 PM |
| Matrics Battery - Mazes                                     | 1/9/2012 3:16 PM | 1/9/2012 3:16 PM |
| Matrics Battery - Category Fluency                          | 1/9/2012 3:12 PM | 1/9/2012 3:12 PM |
| Matrics Battery - BVMPT                                     | 1/9/2012 3:11 PM | 1/9/2012 3:11 PM |
| Matrics battery - Trailmaking A                             | 1/9/2012 3:11 PM | 1/9/2012 3:11 PM |
- 4 \* What is the individual duration of each test and what is the entire duration of all tests?  
Approximately an hour.
- 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: VIEW4E0BC1E3C280X  
Name: v2\_Testing

## 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?  
 Samples will be collected to determine study eligibility , for safety assessments, cytokine assays and peripheral blood mononuclear cultures. Samples collected for cell culture assays will be stored in Dr . Leonardo H. Tonelli's laboratory at UMB, Medical School Teaching Facility Building, 685 W Baltimore Street, Room 958
- 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):  
 Clinical samples will be sent for processing to LabCorp where all our clinical specimens are processed.
- 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: VIEW4E0E1A4B8000x  
 Name: v2\_Sample Collection/Analysis

## 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:  
 Approximately 4 teaspoons of blood will be drawn during screening, at the beginning of the treatment phase, and at the end of the treatment phase for a study total of 12 teaspoons of blood.
- 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?  
 The samples contain the participant's name and date of birth.
- 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.):  
 If a participant withdraws consent, then the samples will be destroyed. If they withdraw from the study, then the samples will be kept until the end of the study , analyzed with other similar samples, then destroyed.
- 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: VIEW4E0E257D60C0x  
 Name: v2\_Prospective Sample

## 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: VIEW4E093BF078C0K  
Name: v2\_Clinical Trial Registration

## Clinical Trial Registration Information

You indicated that this clinical trial has been registered.

- 1 \* Was this trial registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)?  
☒ Yes ☐ No
- 2 If no, was this trial registered on a site other than [clinicaltrials.gov](http://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  
NCT01514682

ID: VIEW4E093BF1D080K  
Name: v2\_Clinical Trial Registration Information

## 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.**  
80
- 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:  
70  
  
Worldwide - the number being enrolled total at all sites (including local enrollment):  
70
- 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.:  
Women who are pregnant or nursing will be excluded because of the unknown risks of the study drugs on the fetus or newborn infant.

ID: VIEW4E0E519C1D00K  
Name: v2\_Participant Selection

## Vulnerable Populations

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

None of the above

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

ID: VIEW4E0E519917801  
Name: v2\_Mlnerable Populations

## 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
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		
<a href="#">View</a>	1	Participant is 18-60 years old
<a href="#">View</a>	2	Participant's meets DSM-IV-TR criteria for schizophrenia or schizoaf fective disorder
<a href="#">View</a>	3	Participant's BPRS total score is 45 or more on the 18 item version (scale: 1-7); or Clinical Global Impression (CGI) severity of illness item score is 4 (moderate) or more
<a href="#">View</a>	4	Participant's BPRS positive symptom item total score is 8 or more, and a score of 4 or more on at least one individual item
<a href="#">View</a>	5	Participant is clinically stable
<a href="#">View</a>	6	Participant has received treatment with the same antipsychotic for at least 60 days, and a constant therapeutic dose for at least 30 days prior to study entry

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

Number Criteria		
<a href="#">View</a>	1	Participant meets DSM-IV-TR criteria for alcohol or substance dependence (except nicotine) within the last 6 months or DSM-IV-TR criteria for alcohol or substance abuse (except nicotine) within the last month
<a href="#">View</a>	2	Participant with a current infection or an organic brain disorder or medical condition, whose pathology or treatment could alter the presentation or treatment of schizophrenia
<a href="#">View</a>	3	Participant with a current infection, organic brain disorder or medical condition, that significantly increases the risk associated with the proposed treatment protocol
<a href="#">View</a>	4	Participant with a history of: aspirin allergy , pre-existing tinnitus, tuberculosis, HIV , or hepatitis C; or autoimmune disease
<a href="#">View</a>	5	Participant who is currently treated with a statin; warfarin, dipyradimole, or other anti-coagulants.
<a href="#">View</a>	6	Participant is currently treated with an omega-3-fatty acid preparation and cannot discontinue their use of the preparation for the duration of the study
<a href="#">View</a>	7	Female participant who is pregnant or breastfeeding
<a href="#">View</a>	8	Female participant who is sexually active and not using any form of birth control such as oral contraceptives or IUDs
<a href="#">View</a>	10	Participant with current/active peptic ulcer disease or gastritis; anemia or thrombocytopenia (platelet count $\leq 120$ )
<a href="#">View</a>	11	Participant who is currently treated with a medication that can increase the risk of myopathy and rhabdomyolysis such as Fluconazole, Ketoconazole, Erythromycin, daptomycin, colchicine or immunosuppresants that alter statin levels.

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-00051603\_26 v3-16-2016-1458139588816(0.01)

ID: VIEW4E0E5185F9001  
Name: v2\_Eligibility

## Recruitment

- 1 \* Describe plans for recruitment, including the identification of potential participants (or acquisition of charts/records/samples) and initial interactions with them:

Potential MPRC and community participants will be identified primarily through chart review or nomination by their primary clinicians who are aware of study entry criteria and demands, and have been asked to identify clinically stable patients who may be interested in research participation. MPRC and community participants may also be self or peer referred for this study .

Additionally, we seek to include interested individuals who are on probation or conditional release, and who are patients at the mental health clinics where we conduct recruitment activity. The protocol for recruitment of patients with schizophrenia will apply to patients with schizophrenia and who are also on probation or conditional release. We would only seek to recruit patients on conditional release or probation who do NOT receive their care at MPRC in order to eliminate any possible perception of coercion based on the provision of psychiatric care.

Further, it should be re-iterated that research assistants who will interact with patients in this study are all specially trained to work with persons with serious mental illnesses. MPRC Research staf f will first consult the participant's psychiatrist or NP for permission to begin the consent process. This arrangement will help avoid approaching people who may be in crisis or may not be able to comprehend the study procedures, risks, and benefits.

- 2 \* Describe measures that will be implemented to avoid participant coercion or undue influence (if not applicable to the study, enter "N/A"):

All participants will be provided a complete description of the proposed study . This will include the purpose of the study , procedures, risks, a copy of the study schedule, and alternatives to participation. Should the participant express interest in the study , investigators will discuss the Informed Consent documentation form with the participant, and the participant will be given a copy of the form for further perusal. A non-investigator clinician member of the treatment team will ascertain whether the prospective participant is able to participate in the informed consent process (see Final Section Additional Documents: Evaluation to Sign Consent Form). If the participant is able to participate in the informed consent process and agrees to participate in the study , then agreement to participate will be documented on the Informed Consent form. All participants will receive a copy of the signed consent form. If the participant is not able to participate in the informed consent process, then they will not be entered into the study . All discussions with potential participants will take place in private behind closed doors.

Compensation for participants' time is offered but is standard for this type of study and thus is not coercive.

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

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
There are no items to display		

ID: VIEW4E0BCAA0A6C0C  
Name: v2\_Recruitment

## Advertising

- 1 \* Will you be using advertisements to recruit potential participants?

☒ Yes ☐ No

ID: VIEW4E0BCCF81000  
Name: v2\_Advertising

## 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):

Print

- 1.1.1 If Other, specify:

- 1.2 \* Provide exact text of all proposed advertisement(s):

Do you have schizophrenia or schizoaffective disorder?

You may be eligible for a research study .

Participants will be paid for time and travel. Studies take place in the Baltimore area and are strictly confidential. There is no cost for participation or study-related tests. Must be 18 or older.

Please help share this information about these studies.

Call for a confidential screening:

Alexander Duggan 410-402-7205

- 1.3 \* Upload advertisement(s) here:

Name	Created	Modified Date
MPRC Flyer	4/24/2013 2:01 PM	6/2/2016 2:40 PM

ID: VIEW4E0BCE82B8C0C  
Name: v2\_Advertising Detail

## 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:

Salsalate:

1- Tinnitus. Somewhat likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect. If the participant is unable to tolerate the drug at the target dose of 4 grams per day then 500 mg reductions will be made in a stepwise fashion until the tinnitus remits or a minimum dose of 2 grams per day is reached.

2 - Headache. Not likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect.

3 - Dizziness. Not likely and not serious. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with a specific question included to address this side effect.

4 - Nausea, dyspepsia, and the remote possibility of GI bleeding. Not likely and possibly serious. These are less common side effects and occur infrequently in individuals taking the drug for only 6 weeks. On a weekly basis, participants will undergo side effect checklist assessment of commonly occurring drug side effects, with specific questions included to address these side effects. If a participant develops GI bleeding the drug will be stopped immediately .

- 3 **\*How will such data be secured?**  
Hard copies of research data will be stored in locked file cabinets in rooms with restricted access, that will be locked as needed. Computerized data entry will be password protected and be identified only by research ID numbers. Electronic files at the MPRC are handled via a local area network (LAN) maintained behind a Netscreen 5XP firewall with multiple layers of protection against unauthorized intrusion. MPRC Databases are maintained on the center's server, are regularly backed up, and are additionally protected by a 5-tiered system involving restricted access at the desktop, directory, database, reporting and table levels.
- 4 **\*Who will have access to research data?**  
Only the PI, his research staff, and regulatory officials will have access to the research data with identifiers. When research team members are no longer on the research team, their access to the data will be removed.
- 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 |
|-------------------------------|---------|---------------|
| There are no items to display |         |               |
- 8 **\*Discuss any other potential confidentiality issues related to this study:**  
All information recorded for research purposes, including computer input data, is identified by code number rather than by name, and subsequent published or presented material related to the project will not be traceable to specific individuals. However, code number and participant name can be linked via an internal database system, which is protected by a two-step password system. Following completion of data collection, subject files are maintained in a secure area in retrievable form for future subject-requested clinical use. Research data will be kept in a locked file in a locked office.

ID: VIEW4E1B5265E040  
Name: v2\_Confidentiality of Dat

## Monitoring Plan Selection

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

ID: VIEW4E1B00E30D40  
Name: v2\_Monitoring Plan Selectio

## 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  
Laboratory Tests  
Medical Compliance  
Procedure Reports  
Outcomes (Primary, Secondary)  
Preliminary Analyses
- 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  
Sponsor
- 4.1 If Other, specify:



# Monitoring Plan - Internal DSMB

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

## 1 \* List Internal DSMB Members:

Name
<a href="#">View Robert McMahon, Ph.D.</a>
<a href="#">View Glenda Housel, M.D.</a>
<a href="#">View Clayton Brown, Ph.D.</a>
<a href="#">View Charles Richardson, M.D.</a>
<a href="#">View Julie Kreyenbuhl, Pharm.D., Ph.D.</a>
<a href="#">View Scott Aaronson, M.D.</a>

## 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?

Data and Safety Monitoring Board. The MPRC has established a Data and Safety Monitoring Board (DSMB), which is comprised of two psychiatrists, a statistician, a pharmacist, and a community representative. The psychiatrists are experts in the clinical treatment of people with schizophrenia. None of the DSMB members reviewing this study will be investigators on the proposed project; however, Dr. McMahon serves as a non-voting member of the DSMB to assist in the monitoring of all MPRC trials. The DSMB will be charged with the following responsibilities:

- 1) to establish a regular meeting schedule;
- 2) to review the proposed protocol;
- 3) to review the proposed consent form prior to IRB submission;
- 4) to monitor study progress and the occurrence of side effects/adverse events, and serious adverse events throughout the course of the study; and
- 5) to review with Dr. McMahon, the statistician for the project, the study data management system.

The DSMB will review reports on protocol progress, side effects and adverse events twice a year. In addition, all serious adverse events (SAEs) will be reported to the DSMB, P.I., the University of Maryland School of Medicine IRB, and the appropriate NIH program of ficer. The P.I. will receive all SAE reports within 24 hours of their occurrence. The DSMB, University of Maryland School of Medicine IRB, and NIH program of ficer will receive the reports within 48 hours. If the incidence of any side effect/adverse event is 25% or more or any SAE occurs in excess in either treatment group, then the DSMB will notify the P.I. The P.I. and DSMB will determine whether possible protocol modifications are required to minimize the further occurrence of such events.

SAEs will be defined as any adverse experience that is unexpected or: i) results in death; ii) results in persistent or significant disability/incapacity; iii) results in or prolongs an existing inpatient hospitalization (even if the hospitalization is a precautionary measure for observation); iv) is a congenital anomaly/birth defect in of fspring of subjects taking the product regardless of time to diagnosis; v) is cancer; vi) is the result of an overdose, whether accidental or intentional; or vii) is a suicide attempt (but not suicidal ideation).

Initial Meeting for New Protocols: When required by a funding institution, an IRB or other governing body, new protocols will be reviewed by the DSMB prior to study enrollment. Safety precautions, procedures for recording and reporting AEs and SAEs, and the monitoring proposal will be discussed. The purpose of the DSMB initial review of the study is to learn directly from the study investigators the goals of the study and its rationale. Additionally, the study investigators will present any specific issues they would like the DSMB to consider while monitoring the data. The DSMB may propose hypothetical scenarios that may be encountered while monitoring the study, and ask the study investigators how they would hope the DSMB would react to it and why. Once the study begins, the DSMB is less able to interact with the study investigators without disclosing interim results.

Annual Meeting for Ongoing Protocols: Once a protocol has been initially reviewed by the DSMB, the study data will be presented to the DSMB on an annual basis, or more frequently as mandated by IRBs, FDA, or Pharmaceutical companies. Adverse events, serious adverse events, study withdrawals or terminations, and the rate of recruitment will be evaluated. If a study is progressing as outlined in the protocol, with no AEs, SAEs and few withdrawals or terminations, and rate of recruitment is consistently sufficient, a report will be sent to the DSMB Committee to meet annual review requirements in lieu of the P.I. presenting the material in person. After review of this report however, the DSMB may request to meet with the P.I. at the next scheduled quarterly meeting to address any additional questions they have regarding the protocol.

After reviewing a protocol, the DSMB Committee may make recommendations concerning the continuation, modification, or termination of the trial. The primary goal of each committee member is to evaluate the safety, study conduct, and scientific validity and integrity of the trial.

If required by the IRB, FDA, or Sponsor, or if precipitated by an event, the principal study investigator will prepare an interim protocol summary addressing specific concerns he or she has about the protocol for the DSMB Committee. The summary and all relevant documentation will be sent to the DSMB members. Only on an as needed basis, the study statistician will prepare a study data (unblinded) report and forward to the MPRC DSMB Coordinator to send to the DSMB members as well. These reports will contain the most up-to-date data permitted by the timeframe necessary for the statistician to prepare and review the analyses. The study statistician's report with the unblinded data, will usually contain his or her assessment of the progress of the trial, including recommendations on whether it should be terminated or modified. Only the DSMB members will receive copies of the unblinded data report. The DSMB will meet regularly to monitor the cumulative safety data during the period when participants are receiving study therapy. The meetings will occur on a quarterly basis and the members will meet in person or by teleconference. The DSMB will monitor the study according to the guidelines specified in the study protocol, unless it is determined that a modification is in the best interest of the study and its participants.

- 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:  
None

ID: VIEW4E1B5D964180f  
Name: v2\_Research Related Cost

## 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:
- | Name                          | Created | Modified Date |
|-------------------------------|---------|---------------|
| There are no items to display |         |               |

ID: VIEW4E1B629EEC00f  
Name: v2\_Compensation for Research-Related Inj

## Payment to Participants

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

ID: VIEW4E1C52A5D780f  
Name: v2\_Payment to Participan

## 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)  
Time and effort
- 1.1 If Other, specify:
- 2 \* What is the total dollar value of the payments over the duration of the study? **Total payment(s) for participation in resear ch of \$600 or more is required to be reported on an IRS Form 1099.**  
\$345
- 3 \* Describe the timing and distrubution plan for the payment (schedule, means, etc.)?  
Participants will be paid \$45 for the initial evaluation and \$25/visit for additional visits. Participants will receive the total amount of \$345 upon completion of the study .  
Should a participant terminate early from the study , they will be paid for the visits completed.
- 4 \* Method(s) of payment to be Used:  
Check
- 4.1 If Other, specify:

## 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: VIEW4E1B0A214400  
Name: v2\_HIPAA

## 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  
Social Security numbers
- 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).*  
This research would not practicably be done without access to and use of PHI because such access allows for efficient screening of individuals. A review of PHI in chart records will increase the likelihood that only those individuals that meet certain study-specific criteria are suggested to clinical care givers as potential study participants. Using this approach, individuals who are ineligible based on readily discernible eligibility criteria are never approached about this study.  
  
The actual SSN in its entirety is requested of an individual the first time they enroll in a study. The SSN is requested of the study participant so that the University may be compliant with IRS reporting requirements for aggregate payments exceeding \$600. Such an aggregate is possible if a participant completes several University of Maryland studies in a given year. The SSN information is stored for about 5 years following the participant's last study payment. Thereafter this information is destroyed using secure shredding. Forms with SSN information are stored with locked cabinets which are accessible to approved staff individuals.
- 3 \* What is the source(s) of the PHI?  
Clinical chart, participants, and treatment providers. Dates on research assessments.
- 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).  
The Protected Health Information will not be reused.
- 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")  
Requesting waiver/alteration of authorization (includes waiver of authorization for recruitment only)
- 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: VIEW4E1B0A24AA40C  
Name: v2\_Protected Health Information

## Waiver/Alteration of Authorization

You indicated that a waiver/alteration of authorization is requested.

- 1 \* Provide rationale for how the research presents no more than minimal risk to the privacy of individuals:  
Only the PI and the research staff will have access to a participant's private information. All research records will have an ID number on them and not a participant's name. All study records related to a participant will be kept in locked file cabinets in a locked office.
- 2 \* Describe the plan to ensure the protection of PHI collected during this study from improper use and disclosure:  
PHI for this study will be protected at all times. All source documentation for the study is kept in a locked cabinet in a locked room. Data for the study is entered onto a password protected secured server. No publication of data will disclose information that could be linked to a single participant.
- 3 \* Describe the plan to destroy the PHI collected during this study at the earliest opportunity consistent with the conduct of the research. If there is a need to retain PHI, provide a justification:  
PHI is stored for about 5 years following the participant's last study payment. Thereafter this information is destroyed using secure shredding. Forms with PHI are stored with locked cabinets which are accessible to approved staff individuals.
- 4 \* Why could the research not practicably be done without access to and use of this PHI?  
This research would not practicably be done without access to and use of PHI because such access allows for efficient screening of individuals. A review of PHI in chart records will increase the likelihood that only those individuals that meet certain study-specific criteria are suggested to clinical care givers as potential study participants. Using this approach, individuals who are ineligible based on readily discernible eligibility criteria are never approached about this study.  
A waiver of HIPAA authorization is justified for this study because the use of the PHI involves no more than minimal risk to the privacy of the potential participants.

- 5 \* **Why could the research not practicably be done without the waiver or alteration?**  
This research could not practicably be done without the waiver because it would be difficult to obtain consent for access of chart records from each potentially eligible individual.
- 6 \* **Will the subjects' PHI be disclosed to (or shared with) any individuals or entities outside of UM?**  
☒ Yes ☐ No
- 6.1 **If Yes, describe the individuals or entities outside of UM to whom PHI will be disclosed.**  
Clinical samples will be sent for processing to LabCorp where all our clinical specimens are processed.

ID: VIEW4E1B0A289640  
Name: v2\_Waiver/Alteration of Authorization

## 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:**  
Potential participants will be identified through chart review or nomination by the treatment team. No participant will be approached for recruitment without approval of a primary clinician, who will determine suitability of the person for the protocol. A chart review will be completed for all nominated potential participants to reduce the likelihood that participants will be found ineligible after participating in more extensive assessment. The study interviewer will verify with the primary clinician that a potential participant is sufficiently stabilized to consider participation and has capacity to provide consent. This is done prior to the study interviewer approaching a potential participant. The study interviewer will be introduced to the potential participant and provide a brief overview of the project.
- Research staff members are trained to recognize symptoms of severe mental illness and cognitive impairment that could undermine an individual's ability to provide informed consent. Interested participants will be provided study information and an informed consent form that contains all pertinent details of participation. As some potential participants will have poor reading skills, the consent form will be read aloud in tandem with their own silent reading of the document. Our research staff are carefully trained on obtaining consent from and interacting with people with seriously mentally illness and supervised by senior staff members. The individual securing consent will review any points about which the participant is unclear, and the participant will be invited to ask questions as needed. All participants who express willingness to provide consent will be queried about each paragraph of the agreement in order to insure that they have adequate understanding of what they are agreeing to. Research staff are trained in strategies for interacting with people with severe mental illness, including speaking slowly and clearly, stopping to summarize frequently, and providing time for questions.
- After reading the consent, and before obtaining a signature, a brief questionnaire, the Evaluation to Sign Consent (ESC), is administered to verify that the subject is competent to provide consent and has demonstrated comprehension of the consent document. The recruiter will also make a clinical judgment and not recruit participants who appear unable to grasp key aspects of the procedure. This approach, which requires a proactive demonstration on the part of the participant that they understand what is being requested, has been used extensively at our sites. Per IRB regulations, a copy of the signed consent form is given to the participant, a copy is placed in the participant's medical record, and the original is kept in the laboratory. Research assistants obtaining informed consent will be experienced clinicians. They will receive detailed and standardized training as to how to obtain informed consent from people with severe mental illness. They will be observed obtaining informed consent from a potential participant by senior staff prior to being allowed to recruit on their own. Prior to signing the consent form, participants will be informed that participation in the study is contingent upon their meeting diagnostic criteria as determined in the clinical interview. All discussions with potential study participants will take place in a private room behind closed doors.
- 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:**  
Our research staff who are carefully trained in obtaining consent from and interacting with people with severe mental illness and are supervised by senior staff members.
- 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 study interviewer will be introduced to the potential subject and provide a brief overview of the project in a private room behind closed doors.
- 7 \* **Describe the provisions for assessing participant understanding:**  
All participants who express willingness to provide consent will be queried about each paragraph of the agreement in order to insure that they have adequate understanding of what they are agreeing to. Research staff are trained in strategies for interacting with people with severe mental illness, including speaking slowly and clearly, stopping to summarize frequently, and providing time for questions. After reading the consent, and before obtaining a signature, a brief questionnaire, the Evaluation to Sign Consent (ESC) is administered to verify that the participant is competent to provide consent and has demonstrated comprehension of the consent document. The recruiter will also make a clinical judgment and not recruit participants who appear unable to grasp key aspects of the procedure. This approach, which requires a proactive demonstration on the part of the participant that they understand what is being requested, has been used extensively at our sites.
- 8 \* **Describe the consideration for ongoing consent:**  
The study is short in duration and all participants will be seen at least bi-weekly once treatment commences. Their continuing consent will be assessed verbally at

## Consent and HIPAA Authorization Forms - Draft

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

Name	Created	Modified Date
UMB Consent	1/13/2012 12:10 PM	11/30/2016 4:19 PM

**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:

UMB HIPAA Form	3/15/2013 12:50 PM	5/16/2014 8:23 PM
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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: VIEW4E1C7712D3006  
Name: v2\_Consent Forms - Dra

## 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:

**MPRC Outpatient**

If this information is incorrect, please notify the HRPO of fice.

### 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: VIEW4E1AF91AB240L  
Name: v2\_Organization Review Requirements (other than IF

## 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. **Yes**
- 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?
- If the answer to this question is wrong, an IBC submission is not required, use the Jump To menu or your browser's <<Back button and return to the IBC RSC review requirements page to change your answer .
- 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: VIEW4E1AF91ED4C0L  
Name: v2\_Institutional Biosafety Committee Review Requi

## 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                                      | Workspace | SmartForm |
|---|-----------|-----------|
| IBC: Anti-Inflammatory Treatment of Schizophrenia (HP-00051603) |           |           |
- 2 **Required Department and Specialty Reviews**- Based on the PI's organization (department, division, etc.) of 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 |
|----------------------|---------------|
| MPRC Outpatient      | Complete      |

ID: VIEW4E1C8D9AE400L  
Name: v2\_Summary of Required Reviews (other than IF

## Additional Documents

- 1 Upload all additional documents here:
- | Name                             | Created            | Modified Date      |
|----------------------------------|--------------------|--------------------|
| Assessment Schedule_v1 1.6.14    | 10/9/2013 4:45 PM  | 11/6/2014 3:32 PM  |
| LAB_GlucoseFS.doc                | 10/9/2013 4:34 PM  | 10/9/2013 4:34 PM  |
| TotalCytokines.doc               | 6/28/2013 1:47 PM  | 6/28/2013 1:47 PM  |
| MedAccount_Salsalate.doc         | 6/28/2013 12:50 PM | 6/28/2013 12:50 PM |
| MedAccount_Omega3.doc            | 6/28/2013 12:50 PM | 6/28/2013 12:50 PM |
| MedAccount_Fluvastatin.doc       | 6/28/2013 12:50 PM | 6/28/2013 12:50 PM |
| Physical Exam form               | 6/28/2013 12:48 PM | 6/28/2013 12:48 PM |
| Full Study Protocol              | 4/24/2013 1:56 PM  | 4/24/2013 1:56 PM  |
| Side Effect Checklist            | 4/24/2013 1:55 PM  | 4/24/2013 1:55 PM  |
| FDA_IND approval letter 2012.pdf | 3/15/2013 12:04 PM | 3/15/2013 12:04 PM |
| DSMB Minutes                     | 3/15/2013 12:02 PM | 3/15/2013 12:02 PM |



Name	Created	Modified Date
ConCom medication Form	4/5/2012 3:09 PM	4/5/2012 3:09 PM
EKG Results Form	4/5/2012 3:08 PM	4/5/2012 3:08 PM
LABS Forms	4/5/2012 3:07 PM	4/5/2012 3:07 PM
Medical History Form	4/5/2012 3:07 PM	4/5/2012 3:07 PM
Non Psych Con Medications Form	4/5/2012 3:06 PM	4/5/2012 3:06 PM
Vital Signs Form	4/5/2012 3:05 PM	4/5/2012 3:05 PM
Pregnancy Test Form	4/5/2012 3:04 PM	4/5/2012 3:04 PM
Urine Toxicology	4/5/2012 3:03 PM	4/5/2012 3:03 PM
Demographics Form 2	4/5/2012 2:23 PM	4/5/2012 2:23 PM
Demographics Form 1	4/5/2012 2:23 PM	4/5/2012 2:23 PM
Valdivielso et al_Cardiovascular Diabetology_1_2009.pdf	3/9/2012 4:06 PM	3/9/2012 4:06 PM
Evaluation to Sign Consent Form	12/27/2011 11:40 AM	12/27/2011 11:40 AM

ID: VIEW4E0962513A00  
Name: v2\_Additional Document

## 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
MPRC Outpatient	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: Anti-Inflammatory Treatment of Schizophrenia (HP-00051603)

[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: VIEW4E1B10C50000  
Name: v2\_Final Page of Application

## Add a Team Member

- \*Select Team Member:**  
William Carpenter Jr
- Research Role:**  
Sub-Investigator
- \*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
- \*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:

William T. Carpenter, Jr., MD, is a Professor of the University of Maryland School of Medicine, Department of Psychiatry and past Director (1977-2013) of the Maryland Psychiatric Research Center. Dr. Carpenter's major professional interest has been severe mental illness, especially schizophrenia, including phenomenology of the psychoses, the etiology, pathophysiology, anatomy, and treatment of schizophrenia.

## Add a Team Member

1 \* Select Team Member:

Joel Palachuvattil

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:

Joel Palachuvattil, MS, has over ten years of experience in data management. He is currently a database engineer at MPRC, with previous database development and administration experience in the areas of human subjects research, nutrition research, and education.

## Add a Team Member

1 \* Select Team Member:

Christine Brown

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:

Christine Brown- Degree In Mental Health Counseling with 40 years of experience working with the CMI population in both inpatient and outpatient settings. I started working at MPRC (ORP) in 2007, recruiting new patients for the ORP and for research studies.

## 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, Pharm D. is a pharmacist with 30 + years in the field. Presently working as the Chief Pharmacist at International Nutrition Inc. Licensed to dispense all classes of medication as well as extensive patient counseling.

## Add a Team Member

- 1 \*Select Team Member:  
Alexander Duggan
- 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:  
Alexander Duggan with BA in psychology joined the MPRC in April 2012 as a research recruiter . His primary role with the Outpatient Research Program has been recruiting for clinical research trials.

## Add a Team Member

- 1 \*Select Team Member:  
Deanna Kelly
- 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:  
Deanna L. Kelly, PharmD., BCPP is a clinical investigator with a long history of clinical research in people with severe mental illness and substance abuse research. She has received grant funding from NIMH, NIDA and several foundations and served as PI on numerous studies of people with severe mental illness and substance abuse. She serves on the DHMH IRB and NIMH DSMB. She is knowledgeable about the study sites, culture and society of participants and personnel related to the protocol.

## Add a Team Member

- 1 \*Select Team Member:  
Melissa Blake
- 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:

Melissa Blake, MSW, LGSW-has approximately 13 years of experience working with the chronic mentally ill population. Also has over 8 years of experience in assisting with research protocols with this population.

## Add a Team Member

- 1 \*Select Team Member:

Christopher Kitchen

- 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:

Chris Kitchen - M.A. with more than 5 years experience working with substance abuse and mental illness populations at the National Institute on Drug Abuse.

## Add a Team Member

- 1 \*Select Team Member:

James Gold

- 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:

James M. Gold, PhD; Clinical Psychologist over 25 years of experience as a clinical investigator with a focus on the application of cognitive neuroscience approaches to understanding the cognitive and motivational impairments of schizophrenia. Serves as PI on multiple UMB research protocols; supervises conduct of cognitive and neurophysiological measures under those protocols in his laboratory , as well as in collaboration with other investigators using cognitive endpoints in their studies..

## Add a Team Member

- 1 \*Select Team Member:

Sarah Nisonger

- 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:  
 Sarah Nisonger – MS, LGPC with six years experience working in clinical and research settings, with both the general population and individuals with severe mental illness.

## Add a Team Member

- 1 \*Select Team Member:  
 Ikwunga Wonodi
- 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:  
 Ikwunga Wonodi, M.D., with extensive clinical and research experience, graduated medical school 24 years ago and has over 13yrs experience working in clinical research settings.

## Add a Team Member

- 1 \*Select Team Member:  
 Jacqueline Kiwanuka
- 2 Research Role:  
 Other
- 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:  
 Jacqueline Kiwanuka, MBA. Lab Manager and overall project coordinator . Ms.  
 Kiwanuka is the manager of Dr . Gold's laboratory. She takes lead responsibility for the IRB, regulatory , and compliance monitoring efforts needed to support his projects.

## Add a Team Member

- 1 \*Select Team Member:  
 MacKenzie Sayer
- 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:  
MacKenzie Sayer is a new Research Associate recently hired by MPRC to work on research protocols. MacKenzie has recently graduated from Virginia Tech University with a BS in psychology. Her primary research responsibilities will include running research protocols to include completing research assessments, and consenting participants.

## Add a Team Member

- 1 \*Select Team Member:  
Elaine Weiner
- 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:  
Elaine Weiner MD – Assistant Professor of Psychiatry . Board certified in Psychiatry. Completed a psychiatry research residency at University of Maryland School of Medicine and has been Medical Director at the Outpatient Research Program of the MPRC since 1993. In addition to her clinical and administrative duties, she facilitates the implementation of a variety of clinical research protocol and has her own research interest in smoking cessation in people with schizophrenia.

## Add a Team Member

- 1 \*Select Team Member:  
Leeka Hubzin
- 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:  
Leeka Hubzin, MS in Clinical Psychology , has been working as a clinical research assistant at the MPRC since 2009. Her primary role is assessment, coordination and recruitment of research participants.

## Add a Team Member

- 1 **\*Select Team Member:**  
Haley Demyanovich
- 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:**  
Haley Demyanovich, BA joined the MPRC in October 2013 as a Clinical Research Assistant. Her primary role with the Treatment Research Program is coordinating clinical research trials.

## Add a Team Member

- 1 **\*Select Team Member:**  
Matthew Glassman
- 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:**  
Matthew Glassman—M.S. w/ 3+ years of research experience working with the Treatment Research and Neuro-Imaging Research Programs at MPRC and the National Institute on Drug Abuse.

## Add a Team Member

- 1 **\*Select Team Member:**  
Ann Kearns
- 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:**  
Ann Kearns- Has worked in a variety of psychiatric settings over the past 18years. She has 12 years of experience at the Maryland Psychiatric Research Center , performing a variety of research activities, and regulatory compliance work.

## Add a Team Member

- 1 \*Select Team Member:  
Michelle Kuptzin
- 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:  
Michelle Kuptzin, MS, OTR/L is an Occupational Therapist at the Spring Grove Hospital Center/Inpatient Research Program.

## Add a Team Member

- 1 \*Select Team Member:  
Leonardo Tonelli
- 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.  
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☐ 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:  
Leonardo H Tonelli, Ph.D. is an Assistant Professor and the head of the Laboratory of Behavioral Neuroimmunology (LBNI) at the Mood and Anxiety Program (MAP), Department of Psychiatry, University of Maryland School of Medicine. He received his PhD degree in Neurobiology from University of Cordoba, Argentina. He Joined the Department of Psychiatry in 2005 and established an independent research program.

## Add a Team Member

- 1 \*Select Team Member:  
Eric Arbach
- 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.  
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- 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:  
Eric Arbach, MSW, LCSW-C, with 14 years of clinical experience working with the seriously mentally ill population and assisting in research protocols.



## Add a Team Member

- 1 \*Select Team Member:  
Robert McMahon
- 2 Research Role:  
Statistician
- 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.  
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- 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 McMahon is a PhD Biostatistician and Professor of Psychiatry , who has worked at the Maryland Psychiatric Research Center (MPRC) as Director of Biostatistics and Data Management, collaborating with MPRC investigators in a wide variety of clinical research into the neuropsychology , neurophysiology , genetics and treatment of schizophrenia and other mental disorders.

## Add a Team Member

- 1 \*Select Team Member:  
David Gorelick
- 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.  
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- 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:  
David A. Gorelick, MD, PhD is board certified in Psychiatry and Addiction Medicine. Dr. Gorelick has more than 30 years experience in clinical research involving people with substance abuse and/or severe mental illness, and has served as Principal Investigator for numerous controlled clinical trials. He is familiar with human research regulations, having served for 10 years as chair of the NIDA IRB, and is knowledgeable about the study sites, culture and society of the participants and personnel related to this protocol.

## Add a Team Member

- 1 \*Select Team Member:  
Lynne Mathews
- 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.  
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☐ 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:  
Lynne Mathews, MSW, LCSW-C with 15 years of clinical and research experience working with the seriously mentally ill population.

## Add a Team Member

- 1 \*Select Team Member:  
Judy Liu
- 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.  
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- 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:  
Judy Liu, RN, MS with extensive clinical, research, therapy, teaching and management experience in research center , mental health clinic, hospital and school. Has been working at Maryland Psychiatric Research Center for 15 years.

## Add a Team Member

- 1 \*Select Team Member:  
Stephanie Feldman
- 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.  
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- 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:  
Stephanie Feldman- MSW with extensive clinical and research experience. Has worked in many different settings over the past 30 years and has been involved in issues related to mental health advocacy .

## Add a Team Member

- 1 \*Select Team Member:  
Charles Richardson
- 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.  
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- 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:  
Charles Richardson, MD is the lead clinician for the Treatment Research Program at the Spring Grove Hospital Center. He supervises the overall clinical program and directs the execution of research protocols, while contributing to protocol development and analysis. He has been working at Spring Grove since 1989.

## Add a Team Member

- 1 \* Select Team Member:  
Carol Simon
- 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:  
Carol Simon, LPN Clinical, Research nurse, teaching and management experience in Research Center and Community Health Clinic. Has been working at Maryland Psychiatric Research Center for 16 years.

## Add a Team Member

- 1 \* Select Team Member:  
Heidi Wehring
- 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:  
Heidi Wehring Investigator/ PharmD has conducted and participated in many research studies and pharmacy related programs. Knowledgeable about the MD mental health system, psychiatric pharmacy and design and conduct of clinical studies.

## Add a Team Member

- 1 \* Select Team Member:  
Sharon August
- 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.  
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☐ 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:

Sharon August, MA in Clinical Psychology, has been at MPRC since 2002, as a clinical research assistant involved in recruitment, coordination, and evaluation of research participants in behavior neuropsychological studies as well as cognitive assessments in clinical trials. She provides training and supervision in neuropsychological assessment at MPRC.