Draft MAPS Study Outline and Synopsis * November 19, 2009

***Study Title*:** Placebo-Controlled, Double-Blind study of the safety and efficacy of smoked cannabis in 30 veterans with PTSD

***Study description**:* This study will enroll 30 veterans diagnosed with PTSD with CAPS scores of 50 or higher into a placebo-controlled, double-blind study of self-administered smoked cannabis for the treatment of PTSD symptoms. Study duration will be nine weeks. Participants will be randomly assigned to receive 2 grams per day of placebo, 6% THC or 12% THC cannabis. The study will consist of an hour-long baseline assessment of PTSD symptoms, one 30 minute introductory session to prepare subjects for the use of marijuana, self-administration of cannabis for six weeks, a 60-minute assessment of PTSD symptoms at six weeks, followed by a three week medication cessation period after the cannabis use has stopped, and a third 60-minute assessment of PTSD symptoms at nine weeks after the study of the study. Participants who received placebo cannabis can enroll in a second open-label segment following identical study procedures.

***Investigator**s*: Sue Sisley, MD

***Subjects**:* 30 veterans diagnosed with PTSD of at least six months duration, with CAPS score of 50 or higher. They must have either had at least one unsuccessful trial with an SSRI or they must have refused medication.

Primary Outcome Measure: Clinician-Administered PTSD Scale (CAPS)
Other Measures: Beck Depression Inventory (BDI) (efficacy), Global Assessment of Functioning (GAF) (efficacy), Columbia Suicide Severity Rating Scale (C-SSRS) (Safety), daily record of cannabis use.

***Study Procedures**:* After giving written informed consent, participants will undergo screening to ensure that they meet all inclusion criteria without meeting any exclusion criteria. Their PTSD symptoms will be assessed with CAPS, symptoms of depression will be assessed with BDI, and general psychological function will be assessed with GAF. Participant suicidality will be assessed at baseline with the C-SSRS. All participants will undergo a 30-minute introductory session wherein they will receive information about what to expect after smoking cannabis. Ten participants will receive two grams per day of placebo cannabis, ten will receive two grams per day of 6% THC cannabis and 10 will receive two grams per day of 12% THC cannabis. Participants will record the amount, time and frequency of cannabis self-administration for six weeks. At the end of this interval, symptoms of PTSD and depression will be assessed again, and general life function will be assessed with GAF. Suicidality will be assessed again via C-SSRS. After discontinuation of cannabis, participant PTSD and depression symptoms, general life function and suicidality will be assessed for a third time three weeks later (nine weeks after study enrollment). The blind will be broken for each individual after the third assessment, and participants who received placebo cannabis will undergo an open-label study segment following identical study procedures, with participants choosing to receive either 6% or 12% THC cannabis. Participants will complete daily diaries for another six weeks, and assessments will be performed six weeks and nine weeks after entering this second segment or "Stage 2."

Inclusion Criteria

Individuals eligible to be enrolled into this protocol are participants who:

1. Meet DSM IV criteria for current PTSD of at least six months.
2. Have a CAPS score of 50 or higher, indicating moderate to severe PTSD symptoms.
3. Have had unsuccessful treatment (defined as still meeting PTSD criteria post-treatment) with one of the following:
    a. Treatment with a selective serotonin uptake inhibitor (SSRI), mirtazapine or a monoamine oxidase inhibitor.
4. Are at least 18 years old
5. Are willing to commit to medication dosing, and follow-up sessions and to complete evaluation instruments.
6. Agree not to change the type or frequency of current psychotherapy, nor change therapists until after the third experimental session (if they are concurrently seeing an outside therapist)
7. If female participants of childbearing potential, must be willing to have pregnancy tests and must agree to use an effective form of birth control
8. Are literate. They must be proficient in reading English, and they must be able to effectively communicate with the therapists and other site personnel.

Exclusion Criteria

Individuals not eligible to be enrolled into this protocol are those who:

1. Are pregnant or nursing, or of child bearing potential and not practicing an effective means of birth control.
2. Have a history of or current primary psychotic disorder or bipolar affective disorder type 1 or borderline personality disorder.
3. Diagnosed with dissociative identity disorder or an eating disorder with active purging, or borderline personality disorder.
4. Have evidence of significant, uncontrolled hematological, endocrine, cerebrovascular, cardiovascular, coronary, pulmonary, gastrointestinal, or neurological disease. (Participants with hypothyroidism who are on adequate and stable thyroid replacement will not be excluded).
5. have any allergies to the study material
6. Would present a serious suicide risk or who are likely to require hospitalization during the course of the study.
7. Meet DSM-IV criteria for substance abuse or dependence for any substance save caffeine or nicotine in the past 60 days.
8. Are not able to give adequate informed consent.
9. Have any current problem or a history of substance abuse which, in the opinion of the investigator or medical monitor, might interfere with participation in the protocol.

Schedule of Events and Procedures

Visit #	Pre-Study	V1	Self-Admin	V2	V3
Type of Visit	Screening may take place over more than one day	Preparatory Session	Six weeks	Assessment / Evaluation 2	Assessment/Evaluation 3
Approximate Study Day	Up to one month prior to Visit 1	1		6 w post V1	9 wk post V1
Visit Timing and Windows		At least 3 w post screen		-5 d + 4 day	-5 d + 4 day
Provide Consent Materials/Informed Consent	X				
Medical and Psychiatric History (by interview)	X				
General Physical Exam (BP, Pulse, Temp, brief systems check)	X				
Clinical Laboratory Tests, including HIV test	X				
Collect Concomitant Medication	X	X			
Study Enrollment after meeting Inclusion/Exclusion		X			
General Well-Being		X			
Drug Screen					
Pregnancy Screen (if applicable)	X				
Complete Randomization Procedure		X			
CAPS	X		X	X	X
IBDI	X		X	X	X
GAF	X		X	X	X
C-SSRS	X	X	X	X	X
Daily cannabis use diary			X	X	
Provide information on cannabis experience		X			
Adverse Events Requiring Dr. Visit			X	X	X
Spontaneously Reported Side Effects			X	X	X
Adverse Events that are of Concern to the Participant			X	X	X
Serious Adverse Events		X	X	X	X
Unblinding					X
Study Termination					X*

*If placebo cannabis, then participant continues to Stage 2, which will follow identical procedures