Cover Page

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Protocol Title: Effect of Lorcaserin on Cannabis Withdrawal and Self-administration

Principal Investigator: Margaret Haney, PhD

Email: mh235@cumc.columbia.edu

Telephone: 646-774-6153

Office: [redacted] Cell [redacted]

Lay Summary

This section is intended to provide a basic overview of the study including a description of its purpose, methods, and subject population. The summary should provide a concise overview of the study for non-scientific and scientific members of the IRB. Please avoid medical or technical terminology. In general, the abstract of a grant does not provide a suitable lay summary.

Please also paste of a copy of the Lay Summary into the PRISM PSF Form.

In order to improve treatment outcome for cannabis use disorder (CUD), we have developed a laboratory model to investigate the effects of potential treatment medications on cannabis withdrawal and on the subjective and reinforcing effects of cannabis in non treatment-seeking, cannabis smokers. In this study, we are interested in testing how lorcaserin (10 mg, BID) influences the effects of cannabis and the choice to smoke cannabis in this human laboratory model of cannabis administration. Lorcaserin is a well tolerated, selective 5HT2c agonist that is FDA-approved for the treatment of obesity. 5HT2c receptors are abundant in areas rich in dopamine neurons (Abramowski et al., 1995) and are involved in modulating impulsive behaviors and reactivity to drug-related cues (Anastasio et al., 2013; Cunningham and Anastasio, 2013). Recent preclinical data show that lorcarserin reduces THC self-administration and relapse in non-human primates (Justinova et al., unpublished). We hypothesize that lorcaserin will decrease cannabis withdrawal symptoms and cannabis relapse in this human laboratory model.

Background, Significance, and Rationale

In this section, provide a brief summary of the status quo of the relevant work field, and how the proposed study will advance knowledge. Specifically, identify the gaps in knowledge that your project is intended to fill. If no gaps exist that are obviously and directly related to your project, explain how your proposed research will contribute to the overall understanding of your field. Describe potential impacts of your project within your field of study and in a broader context. Provide a critical evaluation of existing knowledge. The literature review does not have to be exhaustive.

Cannabis use is increasing (SAMHSA, 2012) and numbers are likely to rise further with legalization; residents of states with medical cannabis laws have higher odds of cannabis use and higher rates of DSM-V abuse/dependence compared to states without these laws (Cerdá et al., 2012). Almost 20% of patients entering treatment for substance use disorders have a diagnosis of cannabis use disorder (CUD; SAMHSA, 2013), yet their outcome is poor. Only 15%–37% of patients achieve continued abstinence from cannabis following clinical treatment (MTPRG, 2004; Budney et al., 2006; Kadden et al., 2007; Levin et al., 2011). There is a clear need for FDA-approved pharmacological options to improve cannabis

treatment outcomes. Human laboratory studies provide a powerful means of investigating potential medications for drug treatment, and are an important precursor to guide expensive clinical trials (Koob et al., 2009).

The overall aim of this study is to test the effects of lorcaserin on a range of clinically-relevant behaviors: cannabis self-administration under non-abstinent conditions, relapse to cannabis use, mood, sleep, food intake, and cognitive task performance. This drug is of interest because 5HT2c agonists influence behaviors motivated by a wide range of reinforcers. In preclinical studies, 5HT2c agonists, including lorcaserin, reduce the stimulant, discriminative stimulus and reinforcing properties of nicotine, ethanol and cocaine, as well as reinstatement of nicotine and cocaine seeking (Grottick et al., 2000; Fletcher et al., 2012; Cunningham et al., 2011; Higgins et al., 2013; Collins et al. 2016). These effects persisted with repeated medication administration (e.g., Yamauchi et al., 2004), essential for a treatment medication. Similar to obesity, the indication for which lorcaserin is approved, substance use disorders reflect learned behaviors that persist despite negative consequences (e.g., Bickel et al, 1999; Fields et al., 2009). Lorcaserin is currently in clinical testing as an aid for smoking cessation (ClinicalTrials.gov: NCT02044874) and a treatment for cocaine-use disorder (studies NCT02680288, NCT02537873).

In non-human primates, pretreatment with 5-HT2c agonist lorcaserin dose-dependently reduced THC self-administration behavior at a dose (4 µg/kg/inj.) that maintains high rates of drug taking behavior. In a model of relapse, lorcaserin also dose-dependently reduced cue-induced reinstatement of previously extinguished THC-seeking behavior. However, lorcaserin did not affect THC priming-induced reinstatement. At the doses that affected THC self-administration and reinstatement, lorcaserin did not reduce food-maintained self-administration under the same schedule of reinforcement (Justinova, unpublished data). These findings suggest that lorcaserin could be a novel treatment for CUD.

Specific Aims and Hypotheses

Concisely state the objectives of the study and the hypothesis or primary research question(s) being examined. There should be one hypothesis for every major study procedure or intervention. For pilot studies, it is important not to overstate the study's objectives. If there are no study hypotheses, describe broad study goals/aims.

The overall aim is to test the effects of lorcaserin on a range of clinically relevant behaviors: cannabis self-administration, relapse to cannabis use, mood, sleep, food intake, and cognitive task performance. We hypothesize that lorcaserin will attenuate cannabis' positive subjective effects and facilitate abstinence initiation, i.e., reduce cannabis self-administration under non-abstinent conditions, as well as reducing relapse to cannabis use.

Inclusion/Exclusion Criteria

This section details your study sample(s) and addresses the requirement for risk minimization.
You may choose to divide your sample by population (healthy controls vs. subjects) or by procedure (subjects who will have an MRI) and then define different sets of criteria for each.

For each sample, create or insert a table to describe detailed criteria for study inclusion and exclusion and the method you will use to ascertain each criterion. The method of ascertainment may describe tests, scales and instruments. When relevant, indicate the level of training of the person who will make the assessment (e.g. clinical interview by a psychiatrist).

Inclusion/Exclusion Criteria needs to be numbered and listed in outline form (see Table template below).

Name the subject group/sub sample

Healthy Cannabis Smokers

CRITERION	METHOD OF ASCERTAINMENT
Inclusion:	
1. Current cannabis use: average of 2 cannabis cigarettes per day at least 6x/ week for the past 4 weeks	Self-report during clinical interviews (telephone, psychologist, physician), urine toxicology
2. Able to perform study procedures	Practice sessions, physician's physical and mental status examination
3. 21-50 years of age	Legal identification
4. Women practicing an effective form of birth control (condoms, diaphragm, birth control pill, IUD)	Self-report during clinical interview, physician's evaluation
5. English Speaking	Clinical interview, ability to complete screening paperwork
6. Able to give informed consent	Clinical interview, physician's mental status examination
Exclusion:	
1. Current diagnosis of an eating disorder (anorexia, bulimia, etc.) or have lost more than 10% of their body weight within the last 3 months and a known sensitivity, allergy or contraindication to lorcaserin or similar medications	Medical history, physical examination
2. Current, repeated (>2x/week) illicit drug use other than cannabis	Clinical interview, physicians evaluation, urine toxicology
3. Presence of any clinically significant cardiovascular, respiratory, renal, gastrointestinal, hematologic, neurologic, pulmonary, immunologic, hepatic, endocrine, or other abnormality	Medical history, physical examination, 12-lead ECG, laboratory tests (Chem panel, CBC, urinalysis)
4. History of heart disease and cardiac risk factors (congestive heart failure, edema, unstable angina, or cardiac arrhythmias), blood pressure > 140/90, severe chronic obstructive pulmonary disease, uncontrolled hypertension or diabetes, or other medical condition that would make participation hazardous	Self-report, clinical interview, abnormal ECG, Medical history, physical examination
5. Interest in treatment for cannabis use	Self-report, clinical interview
6. Current parole or probation	Self-report, clinical interview
7. Current pregnancy or lactation	Clinical interview, physical examination, pregnancy testing (serum HCG)

8. Recent history of significant violent behavior (past year)	Self-report, clinical interview
9. Current Axis I psychopathology requiring medical intervention (e.g., bipolar disorder, major depressive disorder, suicide risk, schizophrenia)	Clinical interview; diagnoses determined by a clinical interview via the SCID, as confirmed by the psychiatric evaluation
10. Current use of any prescription or over-the-counter medication	Clinical interview, medical history, physical examination

Study Procedures

Provide a clear, concise narrative of study procedures with special attention to the subjects' involvement. Detail the overall study timeline and location of study procedures, list all interventions, assessments and interviews, estimate the duration of each procedure, provide dosing schedules, identify study personnel involved in each procedure, and provide credentials for relevant personnel. For complicated study designs, we strongly encourage attaching tables, flow-charts, and study algorithms.

General design: This within-subject study will have two 11-day inpatient phases, with one phase testing lorcaserin and the other phase testing placebo maintenance in counter-balanced order. In between the two inpatient phases, there will be a minimum 7-day outpatient period with no medication administration to provide time for medication clearance and the resumption of daily cannabis use. Inpatient phases will be preceded by two brief outpatient days of lorcaserin administration and a move-in day so that by Day 1 of each inpatient phase, participants will have achieved steady state conditions (3 days of 10 mg BID lorcaserin administration). On outpatient dosing days, participants will take their AM capsule under observation and will take their PM capsule (2030) at home. On the third day (move-in day), they will take their AM capsule under observation and then receive their PM capsule after moving into the laboratory. While inpatient, AM and PM capsules will always be administered under observation.

Outpatient Dosing Visits: Participants will undergo two outpatient dosing visits immediately prior to each inpatient phase. On outpatient dosing days, participants will be administered capsules (lorcaserin or placebo, depending on phase) at 0900 under observation and will take their PM capsule (2030) at home. During outpatient dosing visits and move-in day, research staff will measure vital signs, urine toxicology, conduct at Timeline Followback and document any reported side effects from the medications. Staff will also ask about any medication or dietary supplement use. Participants will move into the residential laboratory (NYSPI, Division on Substance Use) the morning of the third outpatient dosing visit. They will be given the option to contribute a DNA sample on move-in day. We will over-enroll during the first outpatient phase, starting up to 7 individuals on medication, in order to ensure that we will have the maximum number of participants that can stay in the residential laboratory (n=4) on move-in day.

Inpatient Phase: Immediately before the onset of each new medication phase, female participants will have a urine pregnancy test. The overall design and daily inpatient schedule is outlined in the attached tables (Table 1 and 2). We will assess vital signs each morning. On move-in day, we will instruct participants on how to smoke marijuana using the paced puffing procedure and will inform them that this is the strength available for self-administration. On the first full inpatient day (day 1), participants will smoke experimenter-administered cannabis 6 times (3 puffs/occasion). The purpose of this day is to standardize cannabis exposure prior to abstinence initiation. During the next 3 days (days 2-4; Table 1), participants will have the opportunity to purchase individual puffs of cannabis at $2/puff, at 6 time points. This measures the reinforcing effects of cannabis under nonabstinent conditions, and will reveal whether a medication facilitates *abstinence initiation*. On day 5, cannabis will be experimenter administered at 6 time points in order to again standardize cannabis exposure and assess medication effects on cannabis subjective ratings. On days 6-8, no cannabis

Table 1: Representative Dosing Schedule

Day	Outpt (2 days)	Move-in	1	2	3	4	5
Phase	Medication Initiation	Predose	Subj-effects	Abstinence Initiation* →			Subj-effects
Cannabis	none	7.0%THC	7.0%THC	7.0%THC	7.0%THC	7.0%THC	7.0%THC
Lorcaserin (mg BID)	10	10	10	10	10	10	10
Day	**6**	**7**	**8**	**9**	**10**	**11**	**Move-out**
Phase	Withdrawal →			Relapse →			
Cannabis	none	none	none	7.0%THC	7.0%THC	7.0%THC	
Lorcaserin (mg BID)	10	10	10	10	10	10	

Outpt=Outpatient. *Order of abstinence initiation and withdrawal/relapse phases will be counter-balanced.

will be available. This period will assess medication effects on cannabis withdrawal. For the remaining inpatient days (days 9-11; Table 1), participants will be presented with 6 opportunities throughout the day to purchase individuals puffs of cannabis ($7 first puff, $1 subsequent puffs). These days provide a laboratory measure of cannabis relapse. Money spent on cannabis during the inpatient phase is deducted from the total study pay at the end of the study. Participants will move out on Day 12 after passing the field sobriety test. Note, we will counter-balance the cannabis self-administration and relapse conditions across inpatient phases so participants are not able to predict the study schedule in the subsequent inpatient phase; sometimes the withdrawal and relapse condition will occur first and the abstinence initiation condition will occur second. Throughout each day, participants will wear an Actiwatch Activity Monitoring System (Actiwatch: Respironics Company, Bend OR), which tracks gross motor activity, and provides objective data on the number of hours slept and the number of awakenings (Perez et al., 2008). The Actiwatch is the size of a wristwatch. It will be removed briefly each evening in order to download that day's data. Participants will also give a urine sample each morning upon awakening. We will conduct a urine toxicology twice/week; we will also measure extracellular vesicles in urine on certain inpatient days to look for biomarkers of recent marijuana use (potential preliminary data for future grant funding).

Table 2: Inpatient Schedule

0815	Wake up
	Subjective-Effects Battery
	Sleep questionnaire
	Tobacco Cigarettes
	Weigh In, BP/HR Receive Food Boxes
0830	Medication administration
0900	Task and Subjective-effects Batteries
0945	Choice of 0, 1, 2, or 3 puffs
1000	Cannabis administration*
1030	Task and Subjective-effects Batteries
1115	Choice of 0, 1, 2, or 3 puffs
1130	Cannabis administration
1215	Task and Subjective-effects Batteries
1245	Choice of 0, 1, 2, or 3 puffs
1300	Cannabis administration
1315	Task and Subjective-effects Batteries
1415	Choice of 0, 1, 2, or 3 puffs
1430	Cannabis administration
1445	Task and Subjective-effects Batteries
1545	Choice of 0, 1, 2, or 3 puffs
1600	Cannabis administration
1615	Task and Subjective-effects Batteries
1700	Recreation period starts
2030	Medication administration
2145	Choice of 0, 1, 2, or 3 puffs
2200	Recreation period ends
	Cannabis administration
	Subjective-Effects Battery
2400	Lights out

*On experimenter-administered days, participants will not be required to purchase puffs but will be given cannabis at no cost at the 6 times indicated. On self-administered days, cannabis will only be administered if participants choose to purchase it. All medication administration is double-blind.

Debriefing: Participants spend the morning after completion of the final inpatient phase being debriefed regarding the study design. Participants are encouraged to ask questions and provide recommendations for improving the experience (e.g., food, movies, computer games). Following debriefing, the investigator will discuss options for cannabis treatment,

and will give participants a pamphlet for our clinic (STARS), where cannabis-specific treatment studies are underway. It will be emphasized that treatment is always an option, they can always contact us for referral information, or call STARS directly, if they are ready to stop smoking cannabis. We are careful to only enroll non-treatment seekers into our studies, so it is unusual for participants to express interest in treatment. However, the investigator will emphasize that treatment for cannabis use may be of interest in the future. We will also do a 12-lead ECG on the final study day. Participants will not leave the laboratory until a study physician approves the ECG.

Criteria for Early Discontinuation

Define criteria that will be used to exit or drop subjects from the study. Indicate the time points when such criteria will be applied, and describe the rating instruments, parameters, and thresholds that will lead to a decision to terminate a subject's participation. In addition, explain procedures for managing subjects who are dropped from the protocol.

For treatment studies: To minimize risks to subjects, operationalized drop-out criteria should be defined so that subjects who worsen, or in some cases, fail to improve, are removed from the study and offered standard care. The threshold for drop-out should consider the level of risk associated with non-improvement for the specific disorder, the availability of alternatives, and the typical required duration of treatment. For example, emergence of suicidal intent, or psychosis, should prompt immediate clinical evaluation and withdrawal from the study.

Participants will be removed from the study and assessed by a member of the clinical staff if, at any stage during participation, they: 1) experience a panic attack, as diagnosed by DSM-V criteria; 2) experience significant psychological deterioration as indicated by self-reported anxiety or depressed mood producing clinically significant distress beyond the discomfort typically experienced during cannabis withdrawal; 3) report suicidal ideation; or 4) show functional deterioration as indicated by inability to comply with study procedures or erratic or aggressive behavior. Experienced research staff will monitor participants for any potential medical or psychiatric issues over the course of the study in concert with the medical director, Dr. Frances Levin. If a patient is removed from the protocol, clinical staff will undertake a risk assessment and determine the appropriate course of action, including but not limited to admittance to the emergency department of Columbia University Medical Center, and referral for outpatient treatment. Participants may also be discontinued if they fail to follow the study procedures.

Blood and other Biological Samples

Describe how the sample will be used and indicate, when relevant, the amount of the sample. The IRB wants to know that the sample is sufficient for the purposes of the study, but that sampling is limited to what is minimally necessary.

If you've indicated that you intend to store a sample for future use, indicate where the sample will be stored, how long the sample will be stored, and to what purposes the sample will eventually be put. Check the IRB website at http://irb.nyspi.org/irbdnn/Policies/GeneticResearch/tabid/96/Default.aspx for specific guidance and additional information about future use of DNA samples.

We will do a complete blood chemistry and a plasma pregnancy test (15 ml blood) at screening. If participants opt to participate in the genetics study (IRB #6929R), and if we collect blood rather than buccal samples, an additional 15 ml may be drawn on an inpatient study day, totaling up to 30 mls.

The collection of DNA/RNA will enable direct study of possible genetic contributions to both the patterns of behavioral response and biological measures associated with both illness and health. These samples will be used to investigate genetic contributions to drug use, abuse, and dependence. Although the focus of the research is on the study of addiction, we ask participants to indicate in their consent form whether they would also allow their DNA to be used for research on other (unforeseen) disorders. The measurement of DNA is optional, and it will be made clear to individuals that they are not required to volunteer for this component in order to participate in the main studies. Blood, cheek swab

or saliva samples will be de-identified by Dr. Haney. Blood plasma (2 ml) and saliva samples will be will be stored at -80 °C until they are shipped out for analysis. Dr. Haney will code samples with an ID number and have sole access to the codes. The samples will be sent to Dr. McGeary at Brown University or to Dr. Regina Santella of the Biomarkers Shared Resource center of Herbert Irving Comprehensive Cancer Center of CUMC with the accompanying ID number, age and gender. Drs. John McGeary and Santella has agreed to collaborate with us on these studies. They will not have access to any identifying information including the name, birthday, social security number, telephone number, or address of the participant. Once the samples are sent to the Biomarkers Shared Resource center or to Brown University, they will be stored in a repository to which only Drs. McGeary and Santella and his staff will have access. Cell lines will not be grown from the samples. Once the RNA and DNA has been extracted from the samples and analyzed for polymorphisms and biomarkers of interest, the data will be sent to Dr. Haney with the accompanying serial number.

Assessment Instruments

List all assessment instruments, indicate who will administer them, and provide an estimate the duration of each. The IRB wants to know that assessments instruments are appropriate measures for the purposes of the study and are no more burdensome than is necessary. The IRB will consider the burden of assessment instruments (in terms of time, sensitivity of material, etc.) in the risk/benefit analysis. Please attach copies or otherwise provide all non-standard instruments.

Screening Instruments:
Telephone Interview: 10 min
Drug Use History Questionnaire: 10 min
General Health Questionnaire: 5 min
Medical History Questionnaire: 10 min
Beck Depression Inventory: 5 min
Barratt Impulsiveness Scale: 10 min
Trauma Assessment for Adults: 5 min
Michigan Alcoholism Screening Test (MAST): 5 min
Physical and Psychiatric Examination: 30 min
Laboratory Tests: 30 min
PhD Interview (MINI SCID and drug use history interview): 30 min

Objective Sleep Measures: Participants will wear an Actiwatch Activity Monitoring System that tracks gross motor activity (Actiwatch®: Respironics Company, Bend, OR; Kushida et al., 2001) and records objective sleep outcomes (hours slept, number of awakenings). We have used this system effectively to demonstrate perturbations in sleep as a function of cannabis withdrawal (e.g., Haney et al., 2010, 2013b).

Subjective Effects: A 3-minute series of visual analog scales (VAS) in which participants indicate how they are feeling at that moment will be done 8 times/day. Mood states including symptoms of cannabis withdrawal (e.g., I feel irritable), positive subjective effects (e.g., I like the cannabis), medication effects (e.g., I feel sedated) and drug craving (e.g., I want to smoke cannabis) are assessed. In addition, subjective ratings of the previous night's sleep are measured each morning.

Tobacco Cigarette Smoking: Cigarette-smoking participants will be provided with cigarettes and a lighter upon request. They will report each cigarette prior to smoking it by scanning it with a bar code scanner. At the end of each day, the number of cigarettes smoked will be verified by removing and counting the remaining cigarettes and butts. Cigarette use is an important predictor of cannabis relapse (Haney et al., 2013a).

Performance Battery: A 25-minute battery, comprising a Digit-Symbol Substitution Task, Divided Attention Task, Rapid Information Processing Task, Repeated Acquisition Task, and an Immediate and Delayed Memory Task (see Foltin and

Evans, 1993) will be completed 6 times/day. The battery assesses subtle changes in mental acuity, learning, and working memory, which could impact the medications' practical utility in the clinic.

Self-Report Questionnaires:
Drug Effects Questionnaire: 1 min Cannabis Rating Form (MRF): 2 min State Anxiety Inventory: 1 min
Visual Analog Craving Scales (CAS): 3 min Beck Depression Inventory: 5 min

Food Intake: A wide range of food items are available ad libitum. Participants scan each item with a bar code scanner before consumption, which tracks timing as well as caloric and macronutrient content.

Additional Behavior: Social Behavior

Physiological Measures:
Qualitative Urinalysis: Collected daily; analyzed biweekly
ActiwatchTM: Worn daily, measures activity
ECG at study termination, heart rate and blood pressure daily

Research Related Delay to Treatment

Research involving participants who are in need of treatment invariably involves delay to care, and this delay is associated with risk. Scheduling of procedures must be carefully organized to minimize delay. Other delay must involve only that minimally necessary to accomplish the aims of the research while respecting subject well- being and safety. Describe the delay, by virtue of research participation in this study, before a participant can receive treatment of known efficacy or standard care routinely offered in the community.

Research procedures will not result in a delay to treatment since participants are not seeking treatment for cannabis use. Nonetheless, all will be informed of cannabis treatment at STARS in case they change their minds in the future.

Clinical Treatment Alternatives

Describe what other treatment or assessment options are available to subjects who do not participate in research.

Participants are not seeking treatment. The alternative is to not participate in this study.

Risks/Discomforts/Inconveniences

"Risk" is a broad term used to convey the potential for harm, burden, and inconvenience related to research participation. Use this section to provide a comprehensive description of foreseeable physical, psychological, social, interpersonal, and economic risks introduced by the research. Include the source of the information. Consider both the probability and magnitude of harm and its impact. Describe the foreseeable harms associated with the research (untoward effects of a medication) and those related to delay to individualized treatment. Include data from the literature, and local data, if available, on risk rates and subject experiences with research procedures. Describe procedures in place to minimize risk. In general, please create a numbered list of risks/categories of risk, and in general put the list in the order of significance or level of risk, the most significant risks first followed by others.

Cannabis: Possible side effects of smoked cannabis include: sedation, gait disturbance, tiredness, sadness, anxiety, concentration difficulties, increased heart rate, palpitations, dizziness, sleep disturbance, changes in food intake, restlessness, confusion, sleepiness, clumsiness, gastrointestinal upset, headache, nausea, dry mouth, pallor, flushing, sweating, and slurred speech. Side effects associated with cannabis withdrawal, e.g., sleep difficulty, irritability, upset

stomach, restlessness, anxiety and loss of appetite may also occur. All participants are fully informed of the side effects that they might experience, and because all currently smoke cannabis, these effects should be familiar to them.

Lorcaserin: Lorcaserin is well tolerated, with no evidence of the side effects commonly associated with 5HT2b or 5HT2a receptor agonists, e.g., abuse, hallucinations, cardiac valve disease (see Smith et al., 2010; Fidler et al., 2011; Shram et al., 2011). Transient and mild side effects include headache, dizziness, fatigue, nausea, dry mouth, constipation, cough, and back pain (Product label; Smith et al., 2010). Participants will be warned of rare but serious side effects include agitation, confusion, hallucinations, irregular heartbeat, depression, thoughts of suicide, and for men, an erection lasting longer than 4 hours. They will also be warned that they should use caution if they drink alcohol, drive a motor vehicle or operate heavy machinery until they know how the medication affects them (although they will be inpatient for all but 2 of the 14 days they take the medication). Participants will not be taking any medications, but will be warned not to take any dietary supplements such as St. John's Wort, tryptophan and drugs that impair metabolism of serotonin, such as dextromethorphan since serotonin syndrome, a potentially life-threatening drug reaction, can occur when two drugs that affect the body's level of serotonin are taken together. They will also be warned about the potential for heart valve problems and changes in white and red blood cells.

Given that only healthy participants will be enrolled and will only receive an active dose of lorcaserin for 14 days, these rare side effects are even less likely. In clinical trials of 1-year duration: 2.4% of patients receiving lorcaserin and 2.0% of patients receiving placebo developed echocardiographic criteria for valvular regurgitation at one year. Decreases in white blood cell count were reported in 0.4% of patients treated with lorcaserin as compared to 0.2% of patients treated with placebo. Decreases in red blood cell count were reported by 1.3% of patients treated with lorcaserin as compared to 1.2% treated with placebo. The participants will be inpatient in a closely-monitored residential laboratory setting within the NY State Psychiatric Institute for 12 of the 14 days they are taking lorcaserin so we will monitor them closely throughout their participation. We will do an ECG at screening and at the end of the study, and assess vital signs each day.

Inpatient Research Designs: There are also minor risks of isolation, boredom, and inactivity associated with living in the residential laboratory. In participants we have tested to date under similar conditions, such problems have been minimal. We describe at length possible difficulties of living in the residential lab before volunteers sign the study consent form.

Phlebotomy: Participants will provide a blood sample during screening; they will be warned that blood drawing may cause slight discomfort at the site of needle entry and may result in a small bruise.

Methods to Protect Confidentiality

Describe the data management plan and the methods you will employ to protect subject privacy and the confidentiality of research data. The section should detail how information will be collected, recorded, coded, stored, transmitted, and as applicable, shared with other investigators so as to minimize risks related to breach of confidentiality. Confirm that identifiers are removed, to the extent possible, from research data, and explain if there are links between subject identity and research data, or if the data is anonymous. Also, indicate where the data is stored, who is responsible for its safekeeping, and who has access to subject identity and codes, if any, which cross-link research data and subject identity. Confirm that identifiable data is not collected, stored, or transmitted by mail, fax, on removable drives, laptops, or via the internet without proper protections, e.g. encryption.

[redacted] records will be kept confidential and will only be accessible to study staff. Screening information, which may have the participant's name, will be kept in a locked filing cabinet. Once a participant is enrolled into the study all further documents will be identified solely by initials and an assigned number.

Direct Benefits to Subjects

Describe only benefits to individual subjects that are likely to accrue during the study itself. Do not include subject compensation or treatment to be provided at the end of the study, as these do not figure into the IRB's risk benefit considerations. Do not describe diagnostic and evaluation components unless subjects receive clinical feedback. Do not describe the anticipated scientific benefits of the research. Some studies offer no direct benefit to subjects.

There are few direct benefits to research volunteers in the proposed study. Prior to study acceptance, all volunteers will have a medical and psychiatric work-up. Thus, even if participants are not accepted into the study, they will benefit from these evaluations. We offer all participants the option of obtaining help to abstain from drug taking. Volunteers understand that they can obtain a referral for drug treatment at any stage of their research participation. We repeat our offer for treatment referral at discharge from the study. We will attempt to obtain a placement in a drug abuse clinic for those people who indicate a desire for help, and will inform all volunteers of our ongoing cannabis-treatment studies conducted within the Division of Substance Abuse. The major benefit of this research from our point of view is scientific. There is clearly a need for better treatment options for cannabis dependence. The model we are proposing to develop will allow us to better understand the effect of a potential treatment medication..

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