# Cannabinoid Medication for Adults with OCD

# NCT02911324

# 1/7/2020

## Background, Significance and Rationale

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The two first-line treatments for OCD are a class of medications called serotonin re-uptake inhibitors (SRIs) and a type of cognitive behavioral therapy called exposure and response prevention (EX/RP). But more than a third of patients with OCD do not respond to these treatments, and less than half become well. Thus new treatment approaches are needed.

EX/RP is thought to involve fear extinction learning. Recent research suggests that modulators of the cannabinoid system**,** such as nabilone (a synthetic cannabinoid that is thought to be a CB(1) agonist), may enhance fear extinction learning and therefore could enhance EX/RP. However, nabilone could also work via cortico-striatal circuits (which have high levels of cannabinoid type 1 receptors) directly reducing repetitive behaviors such as those seen in OCD (i.e., compulsions). To test both ideas, we propose a small pilot randomized trial to explore the effects of nabilone on its own for four weeks versus in combination with EX/RP in 20 adults with OCD (10 per arm).

This proof-of-concept study will investigate whether the administration of nabilone in adult OCD patients is feasible and/or well-tolerated. The intent is to collect pilot data to support future grant applications.

## Specific Aims and Hypotheses

Specific Aims and Hypotheses
The goal of this pilot study is to investigate whether the administration of nabilone in adult OCD subjects is feasible and/or well-tolerated. The intent of this protocol is to gather pilot data.

## Description of Subject Population

### Sample #1

Specify subject population
Adult individuals with OCD
Number of completers required to accomplish study aims
20
Projected number of subjects who will be enrolled to obtain required number of completers
25
Age range of subject population
18-60

Gender, Racial and Ethnic Breakdown
Based on the community from which we will be drawing subjects and proportions to those encountered

during previous clinical trials at this site, we expect the sample to be approximately 5% Hispanic and 95% Non-Hispanic; racially there will be 89% White, 9% Black, 2% Asian. Based upon the prevalence of OCD, it is expected that the sample will be approximately 1:1 =male:female.
Description of subject population
Female and male adults with a diagnosis of OCD and clinically significant symptoms (i.e., a Y-BOCS score of at least 16). Minorities and females will be well represented in this study.

## Recruitment Procedures

Describe settings where recruitment will occur
Recruitment will draw from the broadest possible population with respect to gender and ethnic origin. Participants will be enrolled through the Anxiety Disorders Clinic, located on the third floor of the New York State Psychiatric Institute.
How and by whom will subjects be approached and/or recruited?
OCD patients will be recruited by a physician or mental health practitioner referrals, or patient or family referrals following advertisement of our work.
How will the study be advertised/publicized?

IRB-approved advertisements and flyers will be posted both online and in the local community (e.g., in and around the CUMC campus). Online advertisements may be posted on websites dedicated to obsessive compulsive disorder or psychiatry research [e.g., our own clinic website (www.columbia-ocd.org), www.ocfoundation.org, Columbia clinical trials website] and on community websites (e.g., Craigslist.org, Myspace.com, Facebook.com, Friendster.com, Livedeal.com, Citynews.com, Adwords.google.com, ResearchMatch.org and Topix.net). For web-based forums or discussion groups that are open only to patient members, permission to recruit will be obtained from group leaders prior to posting.

We would like to use RecruitMe for recruitment. RecruitMe is a recruitment website launched by the Clinical Trials Office at Columbia University Medical Center and is meant to connect those that want to participate in research studies to the investigators that conduct them. To begin using RecruitMe, the volunteer will search for a medical condition or research field of the user's interest and answer a few eligibility questions. If the volunteer pre-qualifies for a study, he or she may either reach out directly to the research team or if he/she leaves their contact information a member of that research team will reach out to them. RecruitMe also allows users to join a research registry which will notify users via email whenever a study or clinical trial of interest enters the database. Investigators that join RecruitMe will have the ability to create a profile and submit their study for review. Upon approval from members of the Clinical Trials Office, their study will be visible to users that visit
RecruitMe.

Do you have ads/recruitment material requiring review at this time?
No
Does this study involve a clinical trial?
Yes
Please provide the NCT Registration Number

NCT02911324

## Concurrent Research Studies

Will subjects in this study participate in or be recruited from other studies?
Yes
Describe concurrent research involvement
Will subjects in this study participate in or be recruited from other studies?

Yes. Eligible subjects who have finished other studies in the Anxiety Disorders Clinic will be offered participation if they are eligible. These protocols will include:
IRB#7405 Effects of Marijuana on Symptoms of OCD (provided they test negative for THC after study completion)
IRB#6628. Attaining and maintaining wellness in OCD
IRB#7000. Control and Reward Circuits in OCD
IRB#7127 Toward Precision Medicine for OCD
IRB#7059 Pilot study of personalized-computerized inhibitory control training for OCD
IRB# 6837 Internet Based Treatment for OCD (iCBT)

Participants will be allowed to participate in other studies at our center at the same time if these studies do not involve treatment (e.g. IRB#7127 Toward Precision Medicine for OCD).

Before and after finishing the study, participants will be allowed to participate in other treatment and non-treatment studies at our center if they meet the eligibility criteria for those studies (including time off medication prior to entry).

Subjects will be re-screened if there is a delay of more than 4 weeks between screening and participation (and the physical exam and laboratory tests will be repeated if older than 3 months).

Describe concurrent research involvement
All participants in the current study will be screened under “IRB #7094R- Anxiety Disorders Clinic and Hispanic Treatment Program Screening and evaluation Process."

## Inclusion/Exclusion Criteria

Name the subject group/sub sample
Adult OCD subjects
Create or insert table to describe the inclusion criteria and methods to ascertain them

| Inclusion criteria | |
|---|---|
| CRITERION | METHOD OF ASCERTAINMENT |
| 1) Patient must be 18-60 years of age at the time of | Clinical Interview |

| | |
|---|---|
| consent | |
| 2) Patient must be physically healthy and, if female, must be non-pregnant. Females of childbearing potential must comply with contraceptive restrictions noted in the protocol. | Clinical interview and physical examination (including EKG and blood and urine tests) by trained M.D, and as part of screening. |
| 3) Patient must fulfill DSM-5 criteria for OCD, OCD being the principal disorder (i.e., currently the most severe and needing of treatment) and have had OCD for at least one year | Clinical Interview by trained M.D. or Ph.D. and results of SCID |
| 4) Patient with a Y-BOCS score of greater than or equal to 16 prior to entering trial. | Clinical interview and assessment by trained rater |
| 5) Patient is off all psychotropic (except selective SRIs) and other types of drugs likely to interact with nabilone (e.g., antihistamines or anticholingeric drugs). Patients taking a selective SRI must be on a stable dose for 6 weeks prior to study entry. Note: Subjects on clomipramine will be excluded because both clomipramine and nabilone can cause orthostatic hypotension. | Clinical interview |
| 6) Each patient must have a level of understanding sufficient to provide written informed consent to all required study tests and procedures. | Clinical interview |
| 7) Subject must be able to tolerate a treatment-free period | Clinical Interview |

Create or insert table to describe the exclusion criteria and methods to ascertain them

| Exclusion criteria | |
|---|---|
| 1) History of violence. | Psychiatric evaluation |
| 2) Presence of psychotic symptoms or lifetime history of schizophrenia, bipolar disorder, substance-induced psychotic disorder, or psychosis due to a general medical condition. | Psychiatric evaluation/SCID |
| 3) Presence of developmental disorder or intellectual disability. | Clinical interview |
| 4) Severely depressed patients with HAMD-17 (17-item Hamilton Depression Rating Scale) >25 or judged clinically to be at risk of suicide. | Clinical Interview/SCID and HAMD-17 |
| 5) OCD patients with primary symptoms of hoarding | SCID/Y-BOCS check-list |
| 6) Female patients who are either pregnant or nursing. | Clinical interview, medical exam, and blood pregnancy test |

| | |
|---|---|
| 7) Patients planning to commence EX/RP during the period of the study or currently in EX/RP treatment. | Clinical interview |
| 8) Current substance use disorders (meeting criteria within the past year, with the exception of nicotine) or positive urine toxicology at screening, or any adverse reaction to a cannabinoid (e.g., panic attack with THC use). | Clinical interview and urine toxicology. |
| 9) History of any significant medical condition (e.g., hypotension) that might increase the risk of participation given the known side effects of nabilone. | Clinical interview and medical examination |

## Waiver of Consent/Authorization

Indicate if you are requesting any of the following consent waivers
Waiver of consent for use of records that include protected health information (a HIPAA waiver of Authorization)
No
Waiver or alteration of consent
No
Waiver of documentation of consent
No
Waiver of parental consent
No

## Consent Procedures

Is eligibility screening for this study conducted under a different IRB protocol?
Yes
Indicate NYSPI IRB #
6112R
Describe Study Consent Procedures
A member of the clinic (MD psychiatrist) will meet with prospective subjects to discuss the study. The staff member will review the consent form and answer any questions.
Indicate which of the following are employed as a part of screening or main study consent procedures
✓ Consent Form

## Persons designated to discuss and document consent

Select the names of persons designated to obtain consent/assent
Campeas, Raphael, MD
Kayser, Reilly, MD
No
Type in the name(s) not found in the above list

## Study Procedures

Describe the procedures required for this study
Screening/initial evaluation
Patients deemed eligible following screening (by phone or in person) will undergo with their consent: 1) an evaluation by a senior clinician (M.D. or Ph.D.); 2) a Structured Clinical Interview for DSM-5; 3) a Y-BOCS to assess OCD severity; and 4) a medical evaluation (i.e., history, physical, routine blood tests [including blood pregnancy test for females], urine toxicology, and EKG). Those who meet entry criteria will provide written informed consent.

Randomization and Treatment Intervention
After the baseline evaluation, participants will be randomized to one of two groups. Randomized assignments (stratified by SSRI use) will be generated using a random number generator in SPSS.

Group 1 (n=10) will receive nabilone at 1 mg BID over 4 weeks. (Note: These patients will be offered EX/RP at no cost in open treatment after the 4 weeks of the trial).

Group 2 (n=10) will receive nabilone at 1 mg BID plus therapist-guided EX/RP (as described below) during 4 weeks.

All subjects will meet weekly with a study psychiatrist to receive nabilone and to review side effects.

Those randomized to EX/RP will also meet with a study therapist (MA or PhD-level) to receive 9 sessions of EX/RP (i.e., a treatment planning session plus 8 sessions of EX/RP) over four weeks according to a treatment manual. Following standard procedures, EX/RP will include therapist-aided exposure, self-guided exposure as homework, ritual prevention, and education about relapse prevention.

Assessments (independent evaluator)
An independent evaluator (Master's level or above) who is not involved with study treatment will assess global psychopathology (CGI); OCD symptoms (YBOCS); sensory phenomenon (Sao Paulo Sensory Phenomena Scale), depressive symptoms (HAM-D) **and at follow-up, any changes in treatment since study end and adherence to EX/RP lifestyle**. Subjects will also complete self-reports that assess depression and anxiety (DASS) and quality of life (Q-LES-Q). Subjects will be evaluated at weeks 0, 1, 2, 3, and 4 and also 1 month after study end (week 8, by phone or in person).

You can upload charts or diagrams if any

## Criteria for Early Discontinuation

Criteria for Early Discontinuation
Participants are free to withdraw from the study at any time for any reason. Study doctors are to discontinue patients from the study if patients:
- Request early discontinuation or withdraw consent.
- Experience a serious or intolerable adverse event that prevents the patient from continuing.
- In the Investigator's opinion, are experiencing a clinically significant deterioration in OCD (i.e., YBOCS score six points greater than their baseline at any time point).
- In the Investigator's opinion, are experiencing a clinically significant deterioration in a comorbid condition such as major depression. For example, if a patient became suicidal or their symptoms of depression increased such that the depressive symptoms were much or very much worse relative to baseline and the HDRS-17 is no longer <25, they would be discontinued from the study.
- Commit a protocol violation, including lack of compliance.
- Are "lost to follow-up."
- Encounter other conditions (such as administrative issues or pregnancy).
If a patient discontinues from the study at any time at their own request or at the study doctor's discretion, the reason(s) for discontinuation are to be recorded by the study. Subjects will be asked to return to the study site for final safety assessments as scheduled for the final study visit. Patients withdrawing from the study for reasons related to the study medication (usually adverse events) will be followed until the event(s) have resolved or no further action is required.

## Blood and other Biological Samples

Please create or insert a table describing the proposed collection of blood or other biological specimens
N/A

## Assessment Instruments

Create a table or give a brief description of the instruments that will be used for assessment
- Structured Clinical Interview for DSM-5 (SCID, 1-2 hours) The SCID is a semi-structured clinician rated instrument that assesses the major adult Axis I disorders in DSM-5
- Yale-Brown Obsessive Compulsive Scale (Y-BOCS, 45 minutes) This is a semi-structured clinician rated instrument used to measure obsessions and compulsions separately over five separate dimensions (time consumed, distress, interference, degree of resistance, control). This is the gold-standard measure of OCD

symptoms.
- Clinical Global impression (CGI, 1 minute). This is a clinician rated instrument for rating global psychopathological severity.
- 17-Item Hamilton Depression Rating Scale (HDRS-17, 5 minutes). This is a clinician rated instrument for rating depression.
- Sao Paulo Sensory Phenomena Scale (SPSPS, 6 minutes). This is a clinician rated instrument for rating sensory phenomena associated with OCD.
- Depression Anxiety Stress Scales (DASS, 5 minutes): 21-item self-report measure that assesses depression, anxiety, and stress experienced in the past week.
- Quality of Life Enjoyment and Satisfaction Measure (Q-LES-Q, 4 minutes): Self-report questionnaire that assesses subjects' satisfaction and enjoyment in daily life.
- PhenX Toolkit Hand Dominance Measure: This measure assesses one's handedness, and is based off of the Edinburgh Handedness Inventory (2 minutes)
- Intolerance of Uncertainty Scale: 27-item self-report questionnaire that assesses a person's ability to tolerate uncertainty. (4 minutes)
- Spielberger State-Trait Anxiety Inventory (STAI): 40 item self-report questions that assesses state and trait anxiety (6 minutes)
- Patient EX/RP Adherence Scale (PEAS, 5 minutes): This 3-item scale is used by a therapist to assess subject adherence to EX/RP homework and targets the quantity and quality of exposures and the degree of ritual prevention.
- Side Effect Checklist (SECL, 3 minutes): Side Effect Assessment: possible side effects will be rated on a scale from 0 (none) to 3 (severe). Weight, blood pressure and heart rate will be assessed at each visit.

Please attach copies, unless standard instruments are used

## Off label and investigational use of drugs/devices

Choose from the following that will be applicable to your study
✓ Drug
Select the number of drugs used in this study
1

### Drug #1

Name of the drug
Nabilone
Manufacturer and other information
Nabilone is a synthetic cannabinoid that is FDA-approved for the treatment of chemotherapy-induced nausea and vomiting and has also been used as an adjunct therapy for chronic pain management. It acts on the brain’s endocannabinoid system and is similar to tetrahydrocannabinol (THC), the primary psychoactive compound found naturally in Cannabis (or marijuana). Thus, nabilone is a controlled substance, and it may produce subjective effects in some that are similar to a marijuana-like “high.”

Approval Status
No IND is required
Choose one of the following options
FDA conditions are met (see 'Rules')
Explain

The protocol meets FDA's rules for waiver of IND. These rules include:

1. The study drug is lawfully marketed in the United States;
2. The study is not intended to be reported to the FDA as a well-controlled study in support of a new indication or use; or support any significant change in the drug's labeling;
3. The study is not intended to support a significant change in the advertising for a prescribed drug;
4. The study does not involve a change in route of administration, dosage level, patient population, or other factors that significantly increases the risks associated with use of the drug product;
5. The study complies with IRB evaluation and informed consent requirements; and
6. The study sponsor and/or investigator do not represent in a promotional context that the drug is safe and effective for the purposes in which it is under investigation.

## Research Related Delay to Treatment

Will research procedures result in a delay to treatment?
Yes
Maximum duration of delay to any treatment
Half of the patients will receive an evidence-based treatment (EX/RP) from the outset. The other half will be offered EX/RP after the trial termination and therefore the maximum time from the time of consent to beginning EX/RP for this group will be ~~8~~ **4** weeks. Dr. Simpson and her clinical team will be in contact with the OCD patients every week from the time of signing consent for this study throughout the study to evaluate their ability to continue in the protocol. If a patient suddenly meets any exclusion criteria (e.g., active suicidal ideation) or no longer met the inclusion criteria of being "able to tolerate a treatment-free period," the patient would be removed from the study and referred for treatment. Patients may refuse to participate at any point and seek outside treatment.
Maximum duration of delay to standard care or treatment of known efficacy
Same as above.
Treatment to be provided at the end of the study
Upon completion of the trial, participants in group 1 (medication only) will be offered the same EX/RP treatment received by participants in group 2 (medication plus EX/RP).

## Clinical Treatment Alternatives

Clinical treatment alternatives
Subjects do not have to participate in this study to receive treatment for OCD. There are two evidence-based

first-line treatments for OCD. The first is a class of medications called Serotonin Reuptake Inhibitors (SRIs). The second is EX/RP. Subjects will have these treatment options explained to them by the study doctor, and they will be offered the option to receive outside referrals for one or both of these treatments rather than participating in the study.

## Risks/Discomforts/Inconveniences

Risks that could be encountered during the study period
Risks associated with assessments:
Patients are assessed in person by experienced clinicians for discomfort or frustration associated with psychiatric interviewing or filling out questionnaires. Study clinicians are skilled at dealing with these events and will make efforts to help clients to feel as comfortable as possible (e.g., by giving breaks during an evaluation, offering encouragement).

Risks associated with EX/RP:
In EX/RP (an evidence-based treatment for OCD), patients confront feared situations that are expected to produce moderate levels of distress initially. This initial fear reaction is essential to the treatment, as it allows the patient to habituate to situations in which he or she is excessively or irrationally fearful.

Risks associated with nabilone: (see package insert):
Chemically, nabilone is similar to the active ingredient found in naturally occurring Cannabis (marijuana) or THC. It is thought to interact with the cannabinoid receptor system in the brain.
According to the package insert approved by the FDA, the most common adverse reactions to nabilone in controlled clinical trials were drowsiness, vertigo, dry mouth, euphoria (feeling "high"), ataxia, headache, and concentration difficulties. Caution is recommended when administering nabilone in combination with any CNS depressant. The effects of nabilone have not been studied in pregnant or nursing women.

Accurate estimates of the estimates of the incidence of adverse events associated with any drug are difficult to obtain because these estimates are influenced by factors such as drug dose and detection technique. The table presented below indicates the relative frequency of adverse events in placebo controlled clinical trials.

Incidence of Adverse Reactions in Placebo-Controlled Studies

| Adverse Event | Nabilone (n=132) Percent | Placebo (n=119) Percent |
|---|---|---|
| Vertigo | 52% | 3% |
| Drowsiness | 52% | 5% |
| Dry Mouth | 36% | 2% |
| Ataxia | 14% | 0% |
| Euphoria | 11% | 1% |
| Sleep Disturbance | 11% | 1% |
| Dysphoria | 9% | 0% |
| Headache | 6% | 0% |

| | | |
|---|---|---|
| Nausea | 4% | 0% |
| Disorientation | 2% | 0% |
| Depersonalization | 2% | 1% |

Nabilone is a Schedule II controlled substance. However, the abuse potential of nabilone has been found to be low compared to other cannabinoids (Ware and Arnaud-Trempe, 2010).

Describe procedures for minimizing risks

1. Subjects with medical and psychiatric co-morbidity (e.g., psychosis) that make participation unsafe will not be eligible.
2. Subjects with a history of substance use disorder in the last year or an adverse experience with a cannabinoid will be excluded.
3. Subjects who enroll in the study will be assessed and monitored weekly by study physicians and an independent evaluator. Worsening of clinical symptoms or adverse side effects from nabilone can lead to study discontinuation.
4. A low dose of nabilone will be used (1 mg BID).

## Methods to Protect Confidentiality

Describe methods to protect confidentiality

All records will be kept confidential to the extent permitted by law. Paper records will be stored in locked files; electronic data will be saved on computers protected by passwords, secure logon, and data communications security procedures. The patient's name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. Records will only be available to research staff, and Federal, State, and Institutional regulatory personnel who may review the records as part of routine audits. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify subjects. At most, the Web site will include a summary of the results. Patients can search this Web site at any time.

In regards to RecruitMe: All participant data will be protected under CUMC security policy. Only site administrators (also known as super users) will have full access to participant data. The data is limited to

basic contact information (i.e. name, phone, address) as well as their date of birth. Users that express interest in a specific study will have their contact information given to the study research team by a SA. SAs will be the only persons with access to the contact information. An automatic notification message will go out to investigators indicating that a person has expressed interest in their study. The message will also indicate that they will receive the contact information from the SA within a few days. Prospective participants will be required to accept the Terms of Service (TOS) within the Registry Form. By accepting the TOS, users will give their consent to have their contact information be stored on CUMC's secure database as well as allow investigators access to their information.

*Will the study be conducted under a certificate of confidentiality?*
No

## Direct Benefits to Subjects

Direct Benefits to Subjects
All of the patients in our study will be offered the gold standard psychotherapy for OCD (EX/RP), either in combination with the novel medication or in isolation in open treatment in our clinic after the four week medication trial. In addition, the findings of this study will increase knowledge of how to improve OCD treatment.

## Compensation and/or Reimbursement

Will compensation or reimbursement for expenses be offered to subjects?
Yes
Please describe and indicate total amount and schedule of payment(s).
Include justification for compensation amounts and indicate if there are bonus payments.

Participants will be compensated $100 for completing the independent assessment and the cognitive testing (paid in cash during your visit at Week4). Additionally, participants can earn between $24 and $60 in two of the cognitive tasks (paid in cash at the end of the cognitive testing session at Week0).

## References

References

Ware, M.A. & St. Arnaud-Trempe, E. (2010). The abuse potential of the synthetic cannabinoid nabilone. Addiction, 105(3), 494-503

**CONSENT FORM- COVER SHEET**

**CANNABINOID MEDICATION FOR ADULTS WITH OCD**

## Overview

Below is a summary of the study that you are asked to participate in. This outline is meant to be a guide for you to use while considering the study and reading the consent form. It is not meant to replace the consent form, which you will have to sign if you decide to participate in the study. The consent form contains detailed information about the study and about the risks which you will need to consider before making your decision. Read the consent form carefully and discuss it with others before deciding to take part. And remember that, even if you do agree to participate, you can change your mind at any time.

## Participation is Voluntary

As with all research, this is a voluntary study, and you do not have to participate if you do not want to. Also, you may stop participating at any time.

## Alternatives

Serotonin reuptake inhibitors (SRIs) are the standard medications for OCD. CBT consisting of EX/RP is the standard non-medication treatment. Adding EX/RP or antipsychotic medications like risperidone (Risperdal) to SRI medication are standard methods for attempting to improve upon (i.e., augment) SRI response in OCD.

## Procedures

-Initial Screening: you have already met with clinic staff to review medical and psychiatric history, and you received a physical exam and blood and urine tests

-Randomization: you will be randomly assigned to receive either the medication nabilone in combination with EX/RP ("medication and EX/RP") or the medication nabilone alone ("medication only") for four weeks

-Nabilone: you will meet weekly with your study doctor to receive the medication nabilone for four weeks

-EX/RP: if you are randomized to the "medication and EX/RP" group, you will also receive 9 sessions of Exposure and Response Prevention (EX/RP) from a study therapist while taking nabilone. If you are randomized to the medication only group, you will be offered 9 sessions of EX/RP at no cost after completing the study.

-Independent Assessments: your symptoms will be evaluated by an independent evaluator during the study and one month after the end of the study by phone

-Cognitive Testing: you will be asked to complete computerized learning/memory tasks before the intervention.

## Risks

This study includes some risks and discomforts (please refer to the consent form for further details and explanations of these risks). These include possible side effects from nabilone such as drowsiness, dizziness/vertigo, dry mouth, and euphoria (feeing "high").

## Benefits:

This research study is not meant to benefit you directly

You may contact the study doctor, Dr. Helen Blair Simpson at 646-774-8110 with any questions.

**CANNABINOID MEDICATION FOR ADULTS WITH OCD**
**Informed Consent for Participation in Research**

**PURPOSE and OVERVIEW:** The purpose of this pilot research study is to test whether a medication called nabilone (Cesamet) on its own or in combination with a form of cognitive-behavioral therapy (CBT) called exposure and response prevention (EX/RP) does not cause unpleasant side effects in participants with obsessive-compulsive disorder (OCD), and to see if participants with OCD find it easy to take the medication repeatedly to help them feel better. Nabilone is a synthetic cannabinoid; it acts on the brain's "endocannabinoid system," which has been hypothesized to play a role in OCD. Nabilone is approved by the Food and Drug Administration (FDA) for the treatment of chemotherapy-induced nausea and vomiting. It is not FDA-approved for treating OCD. You are being asked to participate in this study because you have OCD. This consent form describes the study so that you can decide if you want to participate.

**VOLUNTARY:** Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University. You will be notified of any significant new findings that may affect your willingness to continue to participate.

**ALTERNATIVE TREATMENTS/ALTERNATIVES TO PARTICIPATION:** Serotonin reuptake inhibitors (SRIs) are the standard medications for OCD. These include clomipramine (Anafranil), fluoxetine (Prozac), fluvoxamine (Luvox), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa), and escitalopram (Lexapro). CBT consisting of EX/RP is the standard non-medication treatment. Adding EX/RP or antipsychotic medications like risperidone (Risperdal) to SRI medication are standard methods for attempting to improve upon (i.e., augment) SRI response in OCD.

**PROCEDURES:** All study procedures will take place at the New York State Psychiatric Institute (NYSPI) in New York, NY. Twenty OCD participants will participate. The study consists of several steps:

1. Screening: As part of the screening done in the Anxiety Disorders Clinic (IRB#7094R), you have already met with clinic staff to review your medical and psychiatric history, received a physical exam and tests of your blood and urine (including a urine toxicology and a blood pregnancy test if female), and filled out questionnaires about your symptoms. (Time commitment: approximately 2 hours)
2. Randomization: If you are eligible and sign this consent, you will then be randomly assigned to receive either the medication nabilone in combination with EX/RP ("medication and EX/RP") or the medication nabilone alone ("medication only") for four weeks. This "random assignment" means that you will be placed into one of the two groups by chance (like the flip of a coin). Neither you nor your study doctor can choose in which group you will be placed.
3. Nabilone: **All study participants will receive Nabilone for four weeks.** You will meet weekly with your study doctor to receive the medication nabilone for four weeks and to review any side effects. You will take nabilone twice per day at a fixed dose for four weeks.
4. EX/RP: If you are randomized to the "medication and EX/RP" group, you will also receive 9 sessions of Exposure and Response Prevention (EX/RP) from a study therapist while you are taking nabilone. EX/RP is a form of cognitive-behavioral therapy that involves confronting the things that make you anxious (exposures) while also reducing your compulsive behaviors (response prevention). Therapy sessions will include therapist-supervised exposure, self-guided exposure as homework, and coaching in how to stop rituals. (Time Commitment: 9 EX/RP sessions over 4 weeks).
   Note: If you are in the "medication only" group, you will be offered 9 sessions of Exposure and Response Prevention (EX/RP) therapy at our clinic at no cost once you have completed taking nabilone for four weeks)
5. Independent assessments: Your OCD and related symptoms will be evaluated by an independent evaluator who will not know whether you are receiving nabilone alone or in combination with EX/RP. These evaluations will occur during the study (Weeks 0,1,2,3,4) and one month after the end of the study (Week 8, by phone or in person). (Time Commitment: up to 1 hour per evaluation, 6 evaluations in total).

6. Cognitive testing: You will be asked to complete computerized memory/learn...g tasks before the intervention (at Week 0). These tasks assess processes that are partly controlled by the cannabinoid system, and may provide clues about factors that influence treatment outcome. This testing session can take up to 3 hours.

**RISKS AND INCONVENIENCES:**

Possible side effects from nabilone: **Nabilone** is a synthetic cannabinoid that is FDA-approved for the treatment of chemotherapy-induced nausea and vomiting and has also been used as an adjunct therapy for chronic pain management. It acts on the brain's endocannabinoid system and is similar to tetrahydrocannabinol (THC), the primary psychoactive compound found naturally in *Cannabis* (or marijuana). Thus, nabilone is a controlled substance, and it may produce subjective effects in some that are similar to a marijuana-like "high." Thus, anyone with a prior adverse experience with marihuana or any other cannabinoid (such as anxiety, panic, paranoia, perceptual distortions) should not participate in this study. Nor should any woman who is pregnant or nursing (since nabilone's effects are unknown).

In controlled clinical trials of nabilone, the most commonly encountered adverse effects (in > 20% of participants) include: drowsiness, dizziness/vertigo, dry mouth, and euphoria (feeling "high"). Other adverse effects included: ataxia, sleep disturbance, dysphoria/depression, visual disturbance, trouble concentrating, hypotension, headache, nausea, disorientation, or depersonalization. Side effects may persist up to a few days after stopping nabilone, until the drug is fully gone from your body. This study will use a low dose of nabilone to minimize any potential adverse effects.

Before taking any other medication, including over-the-counter medications (e.g., cough, cold, and allergy remedies), you must first discuss these medications with your study doctor because of the potential for drug-drug interactions that may change how nabilone, your regular medications, or your supplements work. If you require medications that are not safe to take with nabilone, you will not be able to participate in this study. You will not be asked to stop medications you are currently taking to participate in the study.

When taking any new drug, you should exercise caution and not drive, operate machinery, or engage in other activities requiring mental alertness until you know how the drug will affect you. Because nabilone affects the brain, you must avoid other drugs that affect the brain, including alcohol, sedatives or hypnotics (e.g., benzodiazepines), and stimulants (e.g., amphetamine) since the brain effects are potentially additive. Use of illegal drugs (including marijuana or cannabis) during this study is forbidden.

As with any drug, there may be associated risks and side effects, which cannot be predicted. If your symptoms become worse, if side effects are severe, or if your study doctor feels that taking nabilone is no longer in your best interest, administration of the drug will be stopped. Your study doctor will discuss any further treatment with you. Call your study doctor if you experience any side effects or if anything concerns you, whether or not you think these problems are related to the study drug. You may also call your regular doctor who may be informed (with your permission) by the study staff that you are participating in this study.

EX/RP: EX/RP involves exposure to feared situations; exposures are intended to produce anxiety for therapeutic benefit. Some participants have not been able to complete EX/RP because of this.

Delay in Treatment Initiation: If you are randomized to the "medication only" group, this will delay treatment with EX/RP for 4 weeks. If you have significant worsening of your psychiatric symptoms, we will stop your study participation and refer you to appropriate care.

Questionnaires: Questionnaires take time and ask you about personal things, such as your thoughts and feelings. These interviews may make you tired or upset. If at any time the questions make you uncomfortable or tired, you can choose not to answer specific questions or ask to take a break or stop at any time.

**BENEFITS:** Your OCD symptoms may improve with EX/RP but may not improve with nabilone. What we learn from your experience may help us understand more about the treatment of OCD, and it is possible that others might benefit in the future from your contribution.

**CONFIDENTIALITY:** All records will be kept confidential to the extent permitted by law. Paper records will be stored in locked files; electronic data will be saved on computers protected by passwords, secure logon, and data communications security procedures. Your name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. Records will be available to research staff, and to Federal, State, and Institutional regulatory personnel (who may review the records as part of routine audits). A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

**STUDY COMPENSATION:** You will not be charged for any part of the study, including the interviews, medication, and EX/RP. You will be compensated $100 for participating in the independent assessment and the cognitive testing (paid in cash during your visit at Week4). Additionally, you will earn between $24 and $60 in two of the cognitive tasks (paid in cash at the end of the cognitive testing session at Week0).

**IN CASE OF INJURY:** Federal regulations require that we inform participants about our institution's policy with regard to compensation and payment for treatment of research-related injuries. In case of injury, New York State Psychiatric Institute will provide short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute to provide. In addition, we will provide assistance in arranging follow-up care in such instances. New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you do not give up your legal right to seek such compensation through the court by participating in this research.

**QUESTIONS:** Please ask questions about any part of this form or this study that you don't understand. Take as long as you need to decide whether to participate in the study. You can also contact the Principal Investigator, Dr. Simpson, with questions at (646) 774-8110. You will be notified of significant new findings that may relate to your willingness to continue to participate. If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the New York State Psychiatric Institute Institutional Review Board (IRB) to speak with the IRB Main Office at (646) 774-7155 during regular office hours. An IRB is a committee that protects the rights of human subjects in research studies. You will be given a copy of this consent form to keep.

## DOCUMENTATION OF CONSENT

I voluntarily agree to participate in this research study and have been given a copy of this consent form. I understand that I should not drink alcoholic beverages or use other drugs that affect my brain while I am in this study. If female, I agree to take measures to prevent becoming pregnant while taking nabilone.

NAME_____ (print)
Participant's Name

Signature_____ Date_____
Participant's Signature

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research. I have discussed how to prevent pregnancy with female participants.

NAME_____ (print)
Consenting Investigator's Name

Signature_____ Date_____
Consenting Investigator's Signature

**New York State Psychiatric Institute (NYSPI)**
**Authorization to Use or Disclose Health Information during a Research Study**

**Protocol Number:** 7239 **Principal Investigator:** H. Blair Simpson

**Name of Study:** Endocannabinoid medication for adults with OCD

**Before researchers can use or share any identifiable health information ("Health Information") about you as part of the above study (the "Research"), the New York State Psychiatric Institute (NYSPI) is required to obtain your authorization. You agree to allow the following individuals and entities to use and disclose Health Information about you as described below:**

- New York State Psychiatric Institute (NYSPI), your doctors and other health care providers, if any, and
- The Principal Investigator and his/her staff (together "Researchers"). Researchers may include staff of NYSPI, the New York State Office of Mental Health (OMH), Research Foundation for Mental Hygiene, Inc. (RFMH), and Columbia University (CU), provided such staff is a part of the study, and
- Providers of services for the Research at CU, NYSPI and/or RFMH, such as MRI or PET, or Central Reference Laboratories (NKI), if indicated in the consent form**.**

**1. The Health Information that may be used and/or disclosed for this Research includes:**

☑ All information collected during the Research as told to you in the Informed Consent Form.
☑ Health Information in your clinical research record which includes the results of physical exams, medical and psychiatric history, laboratory or diagnostic tests, or Health Information relating to a particular condition that is related to the Research.
☐ Additional information may include:

2. **The Health Information listed above may be disclosed to:**

☑ Researchers and their staff at the following organizations involved with this Research:
NYSPI

☐ The Sponsor of the Research,

and its agents and contractors (together, "Sponsor"); and
☑ Representatives of regulatory and government agencies, institutional review boards, representatives of the Researchers and their institutions to the level needed to carry out their responsibilities related to the conduct of the research.
☐ Private laboratories and other persons and organizations that analyze your health information in connection with this study

☐ Other (family members or significant others, study buddies, outside agencies etc.) Specify:

3. By giving permission to release your Health Information as described above, you understand that your Health Information may be disclosed to individuals or entities which are not required to comply with the federal and state privacy laws which govern the use and disclosure of personal Health Information by NYSPI. This means that once your Health

Information has been disclosed to a third party which does not have to follow these laws (e.g., a drug company or the Sponsor of the Research), it may no longer be protected under the HIPAA or NYS Mental Hygiene Law requirements but is subject to the terms of the consent form and may be subject to other state or federal privacy laws or regulations.

4. **Please note that:**
   - You do not have to sign this Authorization form, but if you do not, you may not be able to participate in the study or receive study related care. You may change your mind at any time and for any reason. If you do so, you may no longer be allowed to participate in the study. If you withdraw this Authorization the research staff and the Sponsor, if this is sponsored research, may still use or disclose Health Information containing identifying information they already have collected about you as needed to maintain the reliability of the research. Any request to withdraw this Authorization must be made in writing to (enter name and contact information below):

     H. Blair Simpson, MD/PhD, 1051 Riverside Drive Unit 69, New York, NY 10032

   - While the Research is going on, you may not be allowed to review the Health Information in your clinical research record that has been created or collected by NYSPI. When this research has been completed you may be allowed to see this information. If it is needed for your care, your Health Information will be given to you or your Doctor.

5. **This Authorization does not have an end date.**

6. **You will be given a copy of this form after you have signed it.**

**I agree to the use and disclosure of Health Information about me as described above:**

_____ _____

Signature of Participant/ Legal Representative Date

_____

Printed Name of Participant

_____

Relationship of Legal Representative to Participant (if applicable)

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**We also ask you or your legal representative to initial the statements below:**

☐ **I have received a copy of the NYSPI/OMH Notice of Privacy Practices.**