NCT01911676
Translational Neuroscience Optimization of GlyT1 Inhibitor

Consent Form – Approved by IRB on 7/12/2018

COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL
YALE UNIVERSITY SCHOOL OF MEDICINE—CONNECTICUT MENTAL HEALTH CENTER

Study Title: Translational Neuroscience Optimization of GlyT1 Inhibitor
Principal Investigator: Deepak Cyril D'Souza, M.D.
Funding Source: National Institutes of Health, National Center for Advancing Translational Science

Sub-study 2: Patients with Schizophrenia or Schizoaffective Disorder

Invitation to Participate and Description of Project

You are invited to take part in a research study designed to test a new potential investigational medication for treating schizophrenia. An investigational drug is one that has not been approved for sale by the United States Food and Drug Administration (FDA). The medication is called PF-03463275 and it has been thoroughly tested for safety in human subjects. This medication interacts with a receptor in the brain called the NMDA receptor and may reduce cognitive deficits. This study will also compare the effects of PF-03463275 with a placebo to see if taking PF-03463275 is better than taking placebo. Placebo is a capsule that looks like PF-03463275 but has no drug in it. In this study we are testing this medication's effects on thinking and cognition in patients with schizophrenia or schizoaffective disorder as described below.

You have been asked to participate because you have been diagnosed with schizophrenia or schizoaffective disorder and you are currently being treated with an antipsychotic, except clozapine. You have not required inpatient hospitalization for at least 3 months prior to screening and you are not addicted to drugs or alcohol. Despite this treatment, you may still be experiencing difficulty with your cognition. Cognition is the way people think, and it includes abilities like paying attention, focusing, remembering things, and solving problems.

Over the phone, you were asked a series of questions about psychiatric and medical symptoms that you may have experienced during your lifetime. These questions were used to determine whether you were likely to meet study requirements. Since the results of this telephone-screening interview indicated that you may qualify for this study, we have invited you for an additional set of interviews and lab tests requiring an outpatient visit to the Connecticut Mental Health Center (CMHC), Clinical Neuroscience Research Unit at 34 Park St. New Haven, CT.

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed decision. This consent form gives you detailed information about the study, which a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, and possible benefits. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form. Please note that you will be told of any significant new findings that are developed during the

course of your participation in this study that may affect your willingness to continue to participate.

Description of Procedures

If you agree to participate in this study, you will complete a screening session. If we feel this study is appropriate for you, we will schedule you for a baseline visit and 2 study periods. Each study period will last a minimum of 5 weeks, and will be separated by a washout lasting approximately 3 weeks. During each of your study periods you will be randomly assigned to take placebo or active PF-03463275 twice daily in addition to your antipsychotic medication. During the week that you take active PF-03463275, you will be randomly assigned to take either a 40 mg dose or a 60 mg dose. Neither you nor the study doctor and the research clinic staff, who work with you, will know which pill you are taking. You will begin taking study medication during the first week of each study period, and you will be assessed for side effects and will meet with research staff and a study doctor. If the first week of taking the study medication goes well you will begin cognitive remediation training that will last for approximately 4 weeks. The cognitive remediation training will require you to come to a computer lab at the West Haven VA for approximately 5 hours each week.

Each treatment period may be extended by up to 14 days, to provide scheduling flexibility in extenuating circumstances, which would obstruct your progress in the study, such as departmental closings and scheduling conflicts.

The study periods will be separated by a "washout period", which must last approximately 21 days. The study period extensions will allow for scheduling flexibility for circumstances in which you require more than the standard amount of time to complete study procedures.

In extenuating circumstances, for ease of participation, you may be given the opportunity to stay overnight at the Connecticut Mental Health Center (CMHC) located at 34 Park Street, New Haven, CT or at a hotel close to the CMHC for a portion of your participation at the Principal Investigator's discretion, so that you do not have to travel back and forth from home. In the event that you do stay at the CMHC, you will engage in routine admission procedures on which include evaluation by both a doctor and a nurse, a physical examination, measurement of height and weight, vital signs, ECG, and routine clinical laboratory tests. You will not receive any additional compensation for any overnight stays. Your compensation will occur as described in the Economic Considerations section.

Screening

The study will begin with two screening visits that will take place at CMHC, 34 Park Street, New Haven, CT. The purpose of the screening visit is to find out if you meet all of the requirements to take part in this research study. Before any study-related procedures are performed, you will be asked to read and sign the informed consent, if you wish to participate. The following tests and procedures will be performed to determine if you qualify:

- Review of your medical, surgical and psychiatric history
- Review of your current and past medications (prescription, non-prescription, and dietary supplements)
- Physical examination

- Measurement of your height, weight, and vital signs (blood pressure, heart rate, respiration rate and temperature)
- Completion of questionnaires related to your current diagnosis of schizophrenia and suicidal thoughts/behaviors
- Electrocardiogram (ECG - a test that measures the electrical activity of your heart)
- Genetic testing: A small sample of your blood (about a tablespoon) will be taken for genetic analysis. Genes are the structures inside your cells that were passed to you from your mother and father, that make you more like your relatives than like strangers. The genes provide the "blueprints" or "plans" your cells follow as they make proteins, which in turn are the building blocks for your body and brain. DNA is the chemical that makes up genes. In this study, we will test for the gene of a particular enzyme that metabolizes the study medication. This is a part of screening for this study. In addition, we will want to look at your blood to learn if your genes affect your response to the study drug. We plan to keep your DNA samples indefinitely (as long as possible) in the laboratory and they may be used for other analyses that will allow us to better understand cognitive function and psychiatric illnesses in the future. These analyses may include information regarding other things that you tell us about yourself or that we learn about you in the course of this project. Your identity will be carefully guarded. We may study many different genes in the course of this research, and will retain the DNA sample in the laboratory indefinitely.
- Laboratory tests including:
    - Tests for hepatitis B, C and HIV/AIDS. Positive HIV, hepatitis B, or C results will be reportable to the Connecticut Department of Public Health.
    - Pregnancy testing for women who are able to become pregnant. The result of the pregnancy test must be negative for you to qualify to participate in this study
    - Routine Urine analysis
    - You will be asked to breathe into a device called a breathalyzer that will measure your blood alcohol content
    - Drug testing for illegal drugs of abuse. You will not be allowed to participate in this study if you test positive for illegal drugs

If you have completed a prescreening visit, relevant assessments may be incorporated in to the screening for this study with your permission.

You will undergo a detailed psychiatric and physical evaluation with a doctor. Additionally you will be asked to complete a few tasks measuring thinking, memory, attention and perception. All these procedures will take approximately 4 hours.

If you do not fit study requirements, you may be excluded from the study. In that case we will discuss with you the findings and will advise you about appropriate follow-up. In this case you cannot participate in further study visits and you will be discharged from the study.

Study Periods

If you are found to be eligible after the screenings, you will be scheduled for the Baseline visit and 2 study periods. Each study period will last a minimum of 5 weeks, and will be separated by a washout lasting approximately 3 weeks. During each of your study periods you will be randomized to either PF-03463275 or placebo. During the study drug phase of the study we will schedule a time for you to come to the Learning Based Recovery Center (LBRC) at the West Haven VA for cognitive remediation training for up to 5 hours a week for approximately 4 weeks per study period. We will also schedule weekly visits at the Connecticut Mental Health Center to monitor how you are doing. The study periods will be separated by a "washout period", which must last approximately 21 days, but may be extended per the discretion of the PI.

During study participation, you will be required not to drink grapefruit juice and not to take certain medications that may interfere with the study medication. All your current medications will be reviewed at each visit. You will also be asked to provide blood and urine samples for routine lab tests to check on your health, and to test for alcohol, and drugs of abuse. Women of childbearing potential will have urine pregnancy tests throughout the study. You will have evaluations that will include physical and psychiatric examinations, vital sign measurements and ECGs. You will be asked to answer questions about your schizophrenia symptoms and daily activities. Also, at these visits, we will measure your heart rate, blood pressure and respiration and give you the study medication. You will take the study medication each morning and evening for the entirety of each dosing period. Though we do not expect any difficulties, we will provide you with a 24-hour phone number so you can reach a physician if you have concerns about the medication at any time. Your total participation in this study will last approximately 16 weeks.

Your compliance to the study medication will be monitored by weekly self-report and pill counts at study visits and using the Cellphone Assisted Remote Observation of Medication Adherence (CAROMA) method. This is basically a method that allows us to confirm that you are taking the study medication visually using the camera of a cellphone. CAROMA may be used 1 - 2 times per day during the treatment period to confirm compliance. Flexible scheduling will be maintained regarding time and days of CAROMA depending on your availability and frequency of in person visits. This will only occur on weekdays. You will be provided with a cellphone with the hardware, software and service necessary to video. The phone will have service that is restricted. Prior to beginning study medication (PF-04457845 or placebo), you will be trained how to use the phone and also trained on the protocol for doing the compliance checks. For this training, you will be placed in one office with the phone. A research staff member will video call you from another location in the clinic and observe you consuming one M&M candy with a glass of water. Once successfully trained in the clinic, you will be loaned the phone to take home for one trial visit. This is to ensure that 1) you understand how to use the phone and 2) that you have adequate cell service at home.

If you have demonstrated that you understand how the video calling works, you will be called during the week while you are taking the study medication at a predetermined time. You will be observed removing study medication from the packaging and swallowing the medication with water. In addition, we will also ask you how you are feeling since you have started the study medication. You will receive additional compensation for CAROMA visits which is outlined in the "Economic Considerations" section. If you are not contactable, it will be assumed that you have been noncompliant and will not receive payment for CAROMA visits. At the end of the study, you will receive a return fee for returning the phone to us.

EEG Session

In addition to the assessment procedures described above, you will be asked to participate in electroencephalographic (EEG) recording sessions. EEG measures your brain waves, and we use it to try to understand how the brain processes information in different situations. You will first be fitted with a nylon cap, to which sensors used for EEG recording will be attached. The sensors do not make direct contact with your scalp. To make this connection, a gel is inserted through holes in the cap.

This gel is made for this purpose and can easily be washed out of your hair with warm water after the experiment. You will be seated in front of a video display in a dimly lit recording room, and asked to wear foam insert earphones. During EEG recording you will be asked to view images on the video display. These images are simple shapes, including a circle and a square checkerboard, and they will be presented at different rates in two conditions. In one condition you will be asked to press a button on a keypad to certain images and to withhold the button press to others. In another condition one of these images will be shown very quickly, so that it appears to "flicker" on and off. Under this condition you will only be asked only to look at the flickering image, and will not need to press any buttons. In another condition you will be asked to memorize short lists of letters. The EEG recording sessions, including set up time and experiments, will take approximately 90 minutes each.

Cognitive Remediation

All participants will have the opportunity to receive computer-based cognitive training using commercially developed software. A series of exercises involving attention, memory, and processing speed skills will be combined over individual sessions lasting a minimum of approximately 45 minutes and a maximum of approximately 2 hours, depending on your schedule preference. We ask that you complete 5 sessions over each 4 week training period. We recommend a schedule of 1-2 training sessions per day, 3 to 5 days per week. You will participate in approximately 40 sessions over the course of the study. The program will instruct you on what exercises to use and how to do them. Generally the more you practice these exercises the better you get at them, so a consistent training schedule is encouraged for best results. Cognitive training will be completed at a monitored computer laboratory located at VA Connecticut (Bldg 14), which will be available to you from approximately of 10:00 am to 12:00 pm each morning and from approximately 1:00 pm to 3:00 pm in the afternoon. This schedule will regularly be maintained Monday through Friday, unless in extenuating circumstances. No prior computer experience is necessary, an assistant will be available to help answer your questions as needed. We will make every effort to create a schedule that is most convenient to you and that does not interfere with work or other activities.

It is important for you to know that that there is a new law in Connecticut (Public Act 13-3), that may affect you if you participate in this study. The law requires hospitals to report to the Department of Mental Health and Addiction Services (DMHAS) the names of all persons who are voluntarily admitted for psychiatric care. Under the law, DMHAS will report to the Department of Emergency Services and Public Protection (DESPP) the names, addresses, birthdates and social security numbers of all persons who are voluntarily admitted and who are

registered gun owners or who apply for a gun registration within six months of admission. The DESPP will revoke the gun permit, confiscate the gun and deny new permits for six months after the admission. You will be affected by this law only if you legally own a gun or are planning to register for one in the next six months.

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.

You will be told of any significant new findings that are developed during the course of your participation in this study that may affect your willingness to continue to participate.

Risks and Inconveniences

There may be side effects that are not known at this time. You will be told of any significant new findings that are developed during the course of your participation in this study that may affect your willingness to continue to participate.

***Possible risks from participation in this study include*:**

- Risks associated with blood drawing
- Risks associated with cognitive remediation
- Risks associated with electroencephalography (EEG)
- Risks associated with the study drug
- Risks associated with any medication
- Risks associated with genetic testing
- Risks to embryo, fetus and nursing infants

Risks associated with blood drawing*:* Drawing blood and inserting an intravenous line (IV) into an arm vein are safe and standard medical procedures. Sometimes a bruise will occur at the puncture site and rarely a blood clot or infection will occur in the vein. You should not donate blood for at least eight weeks after the study. The total volume of blood collected during this study will be up to 36 tablespoons, including blood drawn for the screening and blood drawn during the dosing period. This amount of blood is much less than the amount of a typical donation to a blood bank.

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Risks from Cognitive Remediation: There are no known physical risks associated with computer-based cognitive remediation. Fatigue and frustration during training are possible. If this occurs, you will be encouraged to take breaks, during which you can drink coffee or halt training for the day. Research staff will monitor you during training and may advise you to seek further treatment if symptoms worsen as a result of participation in the study.

Risks of EEG Testing: There are minimal risks associated with EEG/ERP recording. A conductive gel is applied, which can be easily washed out of your hair with warm water. A shower facility for hair washing and sterile linens are available in the laboratory. Electrode caps

and sensors will be washed and sterilized between subjects to minimize the risk of transmitting infection.

Risks from the administration of Study Medication PF-03463275: To assure your safety, we will thoroughly screen you medically and will check your pulse, blood pressure, and respiration on each study visit. We will also conduct a detailed psychiatric examination and ask about your symptoms at each telephone or in-person visit. In addition, we provide a 24 hour number so you can contact the study doctor at any time if you become concerned. Your total participation in this study will last approximately 16 weeks.

The study medication (PF-03463275) has been tested for safety and has been used in a number of clinical trials in healthy subjects and in two separate studies in patients with schizophrenia. In one study, patients with schizophrenia received doses of 5 mg- 25mg every 6 hours for 1 week. These doses were well tolerated with no serious adverse events related to the study medication. In a separate study patients with schizophrenia received 30 mg twice daily for 1-12 weeks. Patients tolerated the medication well overall. The most common side effects (>10%) reported in both these studies included headaches, sleepiness or less sleep, dry mouth and increased urination. Less common side effects (1-10%) included dizziness, restlessness, thirstiness, palpitations, blurry vision and flashing lights, nausea and stomach problems. One patient experienced high heart rate and decreased blood pressure but this resolved on its own. In the previous study done here at Yale, 20 mg twice daily, 40 mg twice daily and 60 mg twice daily were tested, and were very well tolerated. In addition to the above listed side effects, you may also experience increased anxiety or a worsening of your psychiatric symptoms. In case of worsening of your symptoms, we may ask you to come in for an evaluation with the study doctor. If needed, for your safety, you may be escorted to an emergency room for an evaluation and even admitted to an inpatient unit.

General Risk of Allergic Reaction: Any drug, including PF-03463275, may cause allergic reactions. Allergic reactions can become serious and require immediate treatment in a hospital or emergency room. If you have a very bad allergic reaction, you could die. Some things that can happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

- rash
- hives
- having a hard time breathing
- wheezing sounds when breathing
- sudden drop in blood pressure (making you feel dizzy or lightheaded)
- swelling around the face, mouth, lips, throat or eyes
- fast pulse
- sweating

You should get medical help and notify the study doctor or study staff immediately if you have any of these or any other side effects during the study. You will be checked regularly for any symptoms and will be treated for them as needed. If your study doctor feels that there are any problems, you will be withdrawn from the study and followed by the study doctor for the necessary time period.

Risks Associated with Genetic Testing: Under some circumstances, it can be a risk for genetic information about you to be known. Variation in some genes is known to be directly related to risk for certain illnesses, and other genes we may study in your DNA may be shown at some point in the future to be related to illness. The results obtained from the research that involve your DNA sample will not be given to you or the study physician. These test results are for research only. The DNA test results will not be put in your medical records. (If you want to know your risk for genetic diseases, we will refer you to a genetic counselor.) Additionally, the biological materials that we collect from you will be identified by code number rather than by name to maintain confidentiality. We hope that this will prevent any information that could cause you trouble in the future from becoming known to anyone other than the scientists working on this study. We believe that the chance of this information becoming known to others in such a way that it would be harmful to you is small.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most employers, except those with less than 15 employees, to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance

Your genetic data and relevant clinical information may be submitted to the National Institutes of Health (NIH) Genome-Wide Association Studies (GWAS) database where it can be used for future research. All data will be de-identified and will not carry any identifiers prior to submission. With your permission, the research data collected in this database will be used by qualified researchers to study the genetic basis of psychosis, and other diseases. All information will be de-identified prior to submission to the NIH GWAS and/or other restricted-access scientific database. De-identified means that the researchers will use your information without knowing your identity. The genetic data that you have donated for this research study may be sent to the NIH GWAS (and/or other restricted-access scientific database) and may include the following information about you: [age at sample collection, gender, race].

In addition to the referenced risks, there is the possibility that unforeseeable risks could occur as a consequence of your participation in this study, from the study drug PF-03463275,

Reproductive Risks:

Men: If you are a man, you must be either surgically sterile (vasectomy), sexually inactive, or agree to using a barrier method (condom) of birth control from the time of the Screening Visit through the end of the Follow-up Period.

Women: If you are a woman, you cannot be in this study if you are pregnant, planning to become pregnant during the study or nursing a child.

If you are able to become pregnant, you must agree to use a double barrier method of birth control from the start of the Screening Period through the end of the Follow-up Period:

1. Physical barrier (such as condoms or intrauterine device [IUD]), and
2. Chemical barrier (such as birth control pills, spermicidal jellies or foams).

A diaphragm must be used with spermicidal jelly or foam. The combination of a diaphragm and spermicidal jelly or foam counts as a single barrier. Ask the study doctor if you have questions about the birth control requirements of the study. Some methods of birth control will not work while you are taking certain drugs.

If you are pregnant or nursing a child while taking PF-03463275, there may be risks to your unborn baby or nursing child. Nobody knows what these risks are right now. Some drugs cause women to have their babies prematurely (early) or to have babies with birth defects.

Benefits

You may or may not receive any direct medical benefit from being in this study. However, information learned from this study may help us to better understand the biological bases of memory and to develop more effective medications for people with schizophrenia. Your condition may get better, it may get worse, or it may stay the same.

Economic Considerations

- The total amount that you may be compensated is **$1,555** if you participate in the entire study.
- In addition to the compensation for each in-person visit, subjects will be compensated $5 for completing each compliance monitoring or CAROMA visit by phone. CAROMA visits will only be completed on weekdays that the research clinic is open. Subjects may earn up to $350 dollars for completing all possible CAROMA visits.
- You will receive compensation only for study visits that you attend.
- Payments for screening, baseline and week 1 will be made in cash. All other payments will be made via check or debit card unless otherwise requested by the subject or subject's conservator and agreed upon with the P.I. of the study.
- After your first payment milestone you will receive your Bank of America pre-paid debit card in the mail. You will need to activate the card over the phone. Any subsequent milestones payments will automatically add additional funds to your card.
- To encourage participation in cognitive training, additional incentive payments will be dispensed for cognitive training activity, amounting up to $440. Training will be administered over approximately 8 weeks, during which you will be asked to complete approximately 5 sessions per week, for a total of about 40 sessions. Incentive payments will be earned in blocks of 5 sessions, and dispensed according to the schedule outlined in the Economic Considerations Table. A maximum of 5 sessions can be completed each week, and no additional incentive payments will be made after 40 training sessions. A partial payment may be made at the final training session based on the percentage of training you complete toward the next payment point.
- All study procedures and medication will be provided free of charge. There will be no costs to you as a part of this study.

NCATS Sub-study 2 Economic Considerations		
Sub-study 2Visit	**Amount**	**Method**
Screening Visit 1	$25	Cash
Screening Visit 2	$25	Cash
Baseline	$75	Cash
Period 1		
Week 1	$75	Cash
Week 2	$100	Debit Card
Cog Rem-Session 5	$20	Debit Card
Week 3	$100	Debit Card
Cog Rem- Session 10	$30	Debit Card
Week 4	$100	Debit Card
Cog Rem- Session 15	$40	Debit Card
Week 5	$100	Debit Card
Cog Rem- Session 20	$50	Debit Card
Washout Week 1	$20	Debit Card
Washout Week 2	$20	Debit Card
Period 2		
Week 9	$100	Debit Card
Cog Rem- Session 25	$60	Debit Card
Week 10	$100	Debit Card
Cog Rem- Session 30	$70	Debit Card
Week 11	$100	Debit Card
Cog Rem- Session 35	$80	Debit Card
Week 12	$100	Debit Card
Cog Rem- Session 40	$90	Debit Card
Follow- Up	$75	Debit Card

Confidentiality

Any identifiable information that is obtained in connection with this study will remain confidential and will be disclosed only with your permission or as permitted by U.S. or State law. Examples of information that we are legally required to disclose include abuse of a child or elderly person, or certain reportable diseases. Information that contains your identity will be stored in a locked file on a locked unit or be password-protected on a computer. To protect your privacy, DNA samples will be labeled with a numeric code. Information linking this numeric code with your identity will be stored in a site separate from that where your DNA is stored. The geneticist and other personnel who work with DNA will have no access to any information that personally identifies you.

When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity unless your specific consent for this activity is obtained. 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.

If you decide to be in this study and you will be visiting the Connecticut Mental Health Center (CMHC) as part of your study procedures, some information about your participation in this research study will become part of your CMHC medical record. If you do not already have a medical record at CMHC, one will be made for your visit. The information that will be entered into your medical record will include the following: medical and psychiatric history, consent form, screening procedures, progress notes, nursing notes, lab test results, and results from physical exams.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and telephone number. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for ten years, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.

The information about your health that will be collected in this study includes:

- *Research study records*
- *Medical and laboratory records of only those services provided in connection with this Study.*
- *The entire research record and any medical records held by the Connecticut Mental Health Center*
- *The following information: Physical examination, results of blood and urine tests (including results of the testing for alcohol, tobacco, drugs of abuse, and communicable diseases, as well as genetic testing), questionnaires and evaluations, ECG's, and other tests and procedures you have as part of the study.*
- *Records about phone calls made as part of this research*
- *Records about your study visits*
- *Records about any study drug you received*

Information about you and your health which might identify you may be used by or given to:

- *The U.S. Department of Health and Human Services (DHHS) agencies*
- *Representatives from Yale University and the Human Investigation Committee (the committee that reviews, approves, and monitors research on human subjects), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.*
- *Those individuals at Yale who are responsible for the financial oversight of research including billings and payments*
- *The Principal Investigator: Deepak D'Souza, MD*
- *The Yale institutional review board*
- *The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about the new drug product involved in this research. The*

information may also be used to meet the reporting requirements of drug regulatory agencies.

- *Drug regulatory agencies in other countries*
- *Governmental agencies to whom certain diseases (reportable diseases) must be reported*
- *Health care providers who provide services to you in connection with this study.*
- *Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan.*
- *Co-Investigators and other investigators involved in this study, including but not limited to Dr. Mohini Ranganathan, Dr. Morris Bell, Dr. Naomi Driesen, Dr. Jason Johannesen and Joshua Kenney*
- *Study Coordinator and Members of the Schizophrenia Neuropharmacology Research Team*
- *Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study*

If as part of the study, transportation (i.e. cab), overnight stay, or other services are provided or paid for by the study, your name will need to be released to the company in order to provide services. In addition, part of your compensation in this study will be provided via a Bank of America pre-paid debit card. To issue the debit card and receive your ePayments for the research procedures you complete, your name, address, and telephone number will be shared with Bank of America.

Some of the individuals or agencies listed above may not be subject to HIPAA and therefore may not be required to provide the same type of confidentiality protection. They could use or disclose your information in ways not mentioned in this form. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

By signing this form, you authorize the use and/or disclosure of the information described above for this research study. The purpose for the uses and disclosures you are authorizing is to ensure that the information relating to this research is available to all parties who may need it for research purposes.

The information about your health that will be collected in this study includes records of your study visits including study interventions, lab results and relevant phone calls. The researchers involved in this study have obtained a Certificate of Confidentiality (COC) issued by the Department of Health and Human Services. The COC protects the investigators from being forced to release any information in which you are identified, even under a subpoena. The protection offered by the COC does not stop the researchers from reporting information about suspected or known sexual or physical abuse of a child or older person, or a subject's threats of violence to self or others. If any member of the research team is given such information, he or she will make a report to the appropriate authorities.

A Certificate of Confidentiality (CoC) offers protection against compelled identification of research participants by name or other identifying information in any legal proceeding. However, information in a medical record is less secure than information in a research record

and inadvertent or unwanted disclosure of the contents of a medical record is foreseeable given current hospital practices. Thus, even if a CoC is in place, the level of protection against disclosure from the medical record is less.

Representatives from the Yale Human Investigation Committee may inspect study records during internal auditing procedures. However, these individuals are required to keep all information confidential. Authorized representatives of the Food and Drug Administration (FDA) may need to review records of individual subjects. As a result, they may see your name; but they are bound by rules of confidentiality not to reveal your identity to others.

To guard the confidentiality of genetic material, we will do the following:

1) The genetic testing of your DNA is for research purposes only. No results of genetic testing from this study will appear in your medical record.

2) Genetic test results will not be made available to you, your doctors, your other clinicians or any other clinical staff. We do not expect the genetic testing done in this study to become part of treatment for psychiatric problems or addiction at any time during this study or in the next few years to come. If you want to know more about your risks to diseases in which genes play a role, we recommend that you speak with a genetic counselor. We will provide you with names of genetic counselors in the area if you wish to speak with one.

3) Information about your genes will be stored in Dr. Joel Gelernter's laboratory at the West Haven VA Medical Center. These samples will be numerically coded and the key connecting the codes to personal identities will be stored in Dr. D'Souza's laboratory at the Connecticut Mental Health Center. Please note that Research on DNA from your blood will be conducted primarily in the Laboratory of Psychiatric Genetics, Department of Psychiatry, VA Connecticut Health Care System, West Haven Campus, under the supervision of Dr. Gelernter. Dr. Gelernter will be responsible for all uses of your genetic-research blood samples and DNA. It is possible that DNA from your blood sample will be shared with qualified researchers at the VA, Yale or other institutions. Please note that these DNA samples will have absolutely no link to your personal identity. It is possible that Dr. Gelernter will leave VA Connecticut at some time in the future. If this occurs, records of genetic information about your DNA will be maintained in his new laboratory, with all precautions in place to protect your confidentiality that are described elsewhere in this form.

There is a federal law called the Genetic Information Nondiscrimination Act (GINA) that, in general, makes it illegal for health insurance companies, group health plans, and most employers(except those with fewer than 15 employees) to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

While all efforts are aimed at protecting and guarding your DNA samples, there remains the possibility that Yale University could be compelled by a court or a law enforcement agency to produce such samples. In more than sixteen years of collecting DNA samples here at the Yale University and VA Connecticut Healthcare System, in which many thousands of samples have been collected, no outside agency has ever tried to gain access to any research participant's DNA samples. We believe that the risk of this happening to your sample is small. The records of potential subjects who did not enroll in the study or subjects who withdrew from the study will be retained in the same manner as described above.

In Case of Injury

If you are injured as a result of your participation in this study, treatment will be provided. You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up your legal rights by signing this form.

Voluntary Participation and Withdrawal

Participating in this study is voluntary. You are free to choose not to take part in this study. Refusing to participate will involve no penalty or loss of benefits to which you are otherwise entitled (such as your health care outside the study, the payment for your health care, and your health care benefits). However, you will not be able to enroll in this research study and will not receive study procedures as a study participant if you do not allow use of your information as part of this study.

Withdrawing From the Study

If you do become a subject, you are free to stop and withdraw from this study at any time during its course. If you choose to withdraw after you have received the study medication we will ask you to stay in the clinical unit until it is safe for you to leave.

To withdraw from the study, you can call a member of the research team at any time and tell them that you no longer want to take part. This will cancel any future appointments.

The researchers may withdraw you from participating in the research if necessary. This might happen if you develop serious side effects or if you are not compliant with study procedures.

Withdrawing from the study will involve no penalty or loss of benefits to which you are otherwise entitled. It will not harm your relationship with your own doctors or with Yale-New Haven Hospital and the Connecticut Mental Health Center.

Withdrawing Your Authorization to Use and Disclose Your Health Information

You may withdraw or take away your permission to use and disclose your health information at any time. You may withdraw your permission by telling the study staff or by writing to Dr. Deepak Cyril D'Souza, Clinical Neuroscience Research Unit, CMHC, 34 Park St., New Haven, CT 06519.

If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others until the end of the research study, as necessary to insure the integrity of the study and/or study oversight.

You may also ask that your genetic blood sample be destroyed or that any identifying information be permanently removed from the genetic samples. In this case, your genetic

material can only be studied anonymously in the future. This request should be made in writing to Dr. Deepak Cyril D'Souza, CMHC Ribicoff Research Center, 34 Park St., New Haven, CT 06519.

Possible Participation in Future Studies

We would like to be able to contact you in the future to offer you participation in other studies. Giving your permission for the research team to contact you does not obligate you to answer any future questions or to participate in any future research – you always have the right to decline further participation in research. If you agree to participate in another study, we would ask you to read and sign a new consent form. Please initial if you would like to be contacted to participate in other studies.

I agree to be contacted for future research studies: _____

Participant's Initials

Questions

We have used some technical terms in this form. Please feel free to ask about anything you don't understand and to consider this research and the consent form carefully – as long as you feel is necessary – before you make a decision.

Authorization and Permission

I have read (or someone has read to me) this form and have decided to participate in the project described above. Its general purposes, the particulars of my involvement and possible hazards and inconveniences have been explained to my satisfaction. My signature also indicates that I have received a copy of this consent form.

By signing this form, I give permission to the researchers to use information about me for the purposes described in this form. By refusing to give permission, I understand that I will not be able to be in this research.

Name of Subject:_____

Signature:_____

Date:_____

_____ _____

Signature of Person Obtaining Consent Date

If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203/432-5919.

If you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator*, Dr. Deepak Cyril D'Souza, (203)932-5711 x2594*. If you would like to talk with someone other than the researchers to discuss problems, concerns, and questions you may have concerning this research, or to discuss your rights as a research subject, you may contact the Yale Human Investigation Committee at (203) 785-4688.