COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
200 FR. 4 (2016-2)

YALE UNIVERSITY SCHOOL OF MEDICINE – YALE-NEW HAVEN HOSPITAL

Study Title: Understanding Factors that Influence Electronic Cigarette Nicotine Delivery Through PET Imaging of Beta-2 Nicotinic Acetylcholine Receptors
Principal Investigator: *Stephen Baldassarri, MD; 300 Cedar St, TAC 455-S, New Haven, CT 06520*
Funding Source: *National Institute on Drug Abuse (NIDA) / National Institutes of Health (NIH)*

Research Study Summary:

The purpose of this research study is to understand factors that affect nicotine delivery from e-cigarettes. We want to include you in this study because you are healthy and currently use nicotine e-cigarettes. This study will involve 1 MRI scan, 2 PET scans (during which time you will vape and e-cigarette), two periods of abstinence from nicotine-containing products (including e-cigarettes and cigarettes), cognitive testing, and blood sampling. The benefits, risks, and alternatives of participating in this study are described in detail below. You will be compensated appropriately for your time spent completing each part of the study as described below. A Research Assistant or the Principal Investigator will also describe the study procedures to you verbally in detail to make sure you fully understand the study.

Taking part in this study is entirely your choice. If you do choose to take part, you can change your mind at any time. If you choose not to take part at this time, you may still have the opportunity to take part at a later date if the study is still ongoing. You are free to contact us at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Invitation to Participate and Description of Project

You are invited to take part in a research study designed to look at the involvement of the nicotinic acetylcholine system in electronic cigarette (e-cig) use and cigarette smoking. This study will help us further examine brain chemistry and factors that affect how e-cigs deliver nicotine.

You have been asked to take part because you are a healthy person who uses e-cigarettes. In total, about 20 subjects will participate in this part of the study. By agreeing to participate in this research, you may be asked to undergo one MRI scan session (about 1 hr of your time) and two or three PET scans (3.5 hrs each), during which you will participate in vaping/smoking challenges with e-cigs and/or regular cigarettes. These products will be provided to you. The study will take place at several locations at Yale University, Yale PET Center and the Yale Magnetic Resonance Research Center. To complete all parts of this study will require about two months. There will be up to 5 visits during this time period. Visits involving each PET scan will be approximately 2 weeks apart.

Also, you agree to not drink alcohol or use other medications or drugs (i.e. marijuana, cocaine, etc) that will affect your mind for one week prior to the PET study. If you do need to use any medications that are not part of your established medication regimen, please call us [203-737-6400] before taking the medication. You should not use any prescription or over the counter medications during this time unless the study physician has told you that it is safe to do so. If you do take anything you must tell us so that we can make a note of it in your records.

If you choose to participate you will be asked that you do not use nicotine gum, nicotine lozenges, nicotine patch or any other nicotine replacement products.

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.

Description of Procedures

If you agree to take part in this study, you may be asked to participate in the following procedures.

Appointment - Screening – All participants must complete this appointment

Prior to participating in the scanning part of the study, we will ask you to come for a screening Appointment. During the screening appointment you will participate in a physical, ECG, and blood work to make sure you are healthy to participate in PET scans. We will also ask you about your psychiatric and medication and drug use history. We will also ask you to complete a MR safety questionnaire to make sure there are no metals in your body. We may also ask you questions about your mood, memory, and attention. This appointment will take approximately 3 hours. If after this appointment you are found ineligible to participate in the PET study or you decide you do not want to participate, your information will be de-identified and discarded as appropriate under HIPAA guidelines.

Appointment – MRI/cognitive testing
You will be asked to go to the MRRC at The Anlyan Center for Medical Research & Education

(TAC, 300 Cedar Street) to have an MRI (Magnetic Resonance Imaging) scan of your brain. The purpose of the MRI is to help us identify the different regions of your brain on the PET scans. The MRI scan is a routine way to get pictures of the inside of the body. In the MRI Center, we will review whether you are carrying any metallic objects before you move toward the MRI system. These objects will be held for you in a locked cabinet in the MRI Center to avoid having these objects fly toward the magnet when you approach it. You will also be asked to walk through a metal detector. You will be asked to lie still in the MRI scanner for about 30 minutes. The scanner looks like a deep tunnel. You will be inside the tunnel from head to knees. You will not be able to see out of it, but you will be able to hear us and be heard if you wish to say anything. You will hear a drumming noise when the camera is taking pictures of your brain. If you feel uncomfortable during the scan, we can end the scan at any time you wish to do so. However, if you cannot complete the MRI scan, you will not be able to participate in any more of these studies.

We will also perform up to two sessions of testing of your memory, attention, and concentration. This will take approximately 1hr total. You will be given a break between these sessions. This may take place on the same day as the MRI scan, or on another day prior to PET scans if that works better with your and staff schedule.

During this visit, you may play a computer game called the Face Game. The goal of the Face Game is to win as much money as possible. You may earn money by quickly and correctly pressing one of two keys on the keyboard, each time you see a face on the screen. You will press one key if you think that the mouth on the face is long, and the other if you think it is short.

Cold Pressor Task

You may also be asked to participate in the cold pressor task during the study. In this task, we are investigating the body's physiological response to cold water. You will be asked to immerse your hand in a bucket of ice cold water maintained at 0-4°C. You will be told to raise your other hand when you begin to feel pain and to remove your hand from the water when you can no longer tolerate the pain. While your hand is immersed in water, you will also be asked to rate your pain on a scale from 0-100 and your heart rate and blood pressure will be monitored.

Appointment - Nicotine Abstinence

Day 0: If you decide to participate in the study, you will be scheduled for a visit prior to your MRI. At this visit, you will talk with one of the research staff to discuss abstinence from nicotine-containing products including e-cigarettes and cigarettes, and the schedule of PET scan days and other appointments related to this research study. At this time, we may also administer questionnaires and measures that assess your memory. We may ask you to participate in some computer based cognitive tasks on this day and the day of your PET scan. This visit may be combined with the MRI.

One of these tasks measures impulsivity. You may be asked to play a game in which you will use a computer mouse to click a balloon pump that inflates a balloon on the screen. The objective of the task is to get the largest amount of the money possible while avoiding balloon

explosions. This assessment tests your impulsivity). You may be asked to play this game on the day of your PET scan too.

5-7 day Abstinence Period:

You will be asked to stop using nicotine-containing products (including e-cigarettes, cigarettes, and others) for approximately one week prior to each PET scan. You will be seen by research staff approximately once daily at a mutually convenient location from the time you stop smoking until the day of your PET scan (with e-cigarette or regular cigarette challenge). The appointments will be scheduled at a place convenient for you and staff members. During each appointment you will be asked to complete questionnaires regarding withdrawal and craving, and we will provide you with support to encourage continued abstinence. At this appointment we will also measure your breath carbon monoxide and obtain a urine sample from you to measure cotinine (a byproduct of nicotine) to confirm you have not been using nicotine. These appointments will take between 10-30 minutes. You will receive cash payments each day if you remain abstinent from using nicotine. If we determine that you have been using nicotine during this time, your study participation may be terminated. Following this first PET scan, you may go back to using nicotine as usual for at least 1 week. If you participate in another PET scan, you will be asked to stop using nicotine again one week prior to the next PET scan. After your last PET scan, you may decide to go back to using nicotine as usual, or to remain abstinent. We will provide you with referrals to other studies (with our group or others) as well as with long-term abstinence information.

Appointment – PET scan(s)

You will be asked to participate in one or more PET scanning session(s). The scans will be conducted at the Yale University Positron Emission Tomography (PET) Center, 801 Howard Avenue in New Haven. You may be asked to fast prior to the PET scan. At the PET Center, female subjects will have a urine pregnancy test and all subjects may have a urine drug screen. You cannot participate in this study if you are pregnant, planning to become pregnant, or nursing. In order to participate, you must use an acceptable form of birth control (birth control pills, diaphragm or condoms with spermicide) throughout the study period. You will also provide a urine sample to measure cotinine levels, which is a biomarker of tobacco smoking. If positive, your study participation may be cancelled.

A trained nurse or CNMT (Certified Nuclear Medicine Technologist) will place plastic catheters (tubes) in your arms (for the radiotracer injection, to take venous blood samples). On this day, an experienced physician may insert an arterial catheter in your wrist area. The arterial catheter is about 2 inches long, looks like a regular i.v. tube, but is inserted into an artery, not a vein. The blood flow in the arteries can tell us about your blood pressure. If an arterial catheter is in place, we can measure your blood pressure continuously. The other main reason to put in an arterial catheter is to be able to draw blood samples rapidly, repeatedly, and without causing you pain. Here is what happens when an arterial line is placed. First, the skin is cleaned with betadine solution (contains iodine) so that it is sterile and protected against infection. Second, the insertion area is numbed with a local anesthetic, so that you feel less pain when the catheter is inserted.

Third, the catheter will be flushed regularly during your scan with a salt solution, which prevents clogging of the catheter with a blood clot. Fourth, after the catheter is removed, local pressure is applied for a minimum of 15 minutes to prevent bleeding under the skin. A pressure dressing will then be applied and you will be asked not to lift heavy objects or to use the arm excessively over the next 24-48 hours.

After the arterial catheter is inserted, you will receive the radiotracer [18F]NCFHEB (a drug which is limited by Federal Law for investigational use only), during the PET scan. This radiotracer, which is a minimal amount of a drug that is labeled with a very small amount of a radioactive substance, binds to the receptors in the brain and can be detected by a special camera in the PET scanner. You may not feel anything as a result of its administration; however, you may briefly experience nausea shortly after the injection. As part of the PET scanning session, you will be asked to lie very still on a table. The radiotracer will then be injected into the tube in your vein. Following this injection, the PET scanner camera will detect the radiotracer present in the brain. This information will be used to create pictures of your brain. Blood samples during the PET scanning sessions will be used to measure the amount of radiotracer in your blood. We may also collect blood samples for measurement of cotinine/nicotine, about 4 tablespoons. Samples will be stored at the PET Center until analysis. The analysis of the samples will take place at Yale University laboratories. You will be asked to drink several glasses of water at the close of the PET scanning session to wash out the radiotracer. A light meal will be provided. After the PET scanning session you will be free to leave. You will be provided with a telephone number you can call anytime after the study if you need assistance for problems related to the study procedures.

You will also participate in cognitive testing on the PET scan day. This will take about 1-1.5hrs of your time.

E-Cig / Cigarette Challenge

Use of e-cig: We will ask you to use an e-cigarette during two of the PET scans. You will be given an e-cig (either the JUUL 5% or JUUL 3%) in randomized order. You will be instructed how often to puff on the e-cig. A mouthpiece to measure puff topography may be used.

Use of regular cigarette: If you smoke cigarettes daily, we may ask you to smoke a regular cigarette during a third PET scan. We will provide this cigarette for you. You will be instructed how often to puff on the cigarette. You may be asked to smoke via the puff device (CreSS from Plowshare Technologies, USA), which provides measures of depth of puff inhalation and volume.

Occasionally there are problems making the [18F]NCFHEB and there is not enough to perform the PET scan. If this happens, we would offer to reschedule your PET scan on another day within a few weeks. In the event that your PET scan day gets cancelled for reasons outside of your control (such as radiotracer synthesis failure), you will receive a minimum payment of $50 per cancelled scan, or a higher amount not to exceed the amount for a full scan day. This amount will be based on your length of participation on the scan day prior to cancellation, and will be up

to the discretion of the PI.

Risks and Inconveniences

Risks Associated with Radiation
This research study involves exposure to radiation from positron emission tomography (PET). Please note that this radiation exposure is **not** necessary for your medical care and is for research purposes only.

The total amount of radiation you will receive from participating in up to 3 PET scan sessions in this study is from up to 3 injections of [18F]NCFHEB and from transmission scans used to help obtain the PET images.

Although each organ will receive a different dose, the amount of radiation exposure you will receive from a ***single injection*** of [18F]NCFHEB is equal to a uniform whole-body exposure of 0.635 rem. If 2 scans are completed, the radiation dose will be 1.27 rem. If 3 scans are completed, the radiation dose will be 1.91 rem. The ***maximum*** amount of radiation exposure you will receive from this study is equal to a uniform whole-body exposure of **1.91** rem, which is the equivalent of approximately 6.37 years of natural environmental exposure from sources. This value is known as the "effective dose equivalent" and is used to relate the dose received by each organ to a single value. This amount of radiation exposure is below the annual limit of 5 rem set by the federal government for research subjects.

The effects of radiation exposure on humans have been studied for over 60 years. In fact, these studies are the most extensive ever done of any potentially harmful agent that could affect humans. In all these studies, no harmful effect to humans has been observed from the levels of radiation you will receive by taking part in this research study. However, scientists disagree on whether radiation doses at these levels are harmful. Even though no effects have been observed, some scientists believe that radiation can be harmful and may cause cancer at any dose- even low doses such as those received during this research.

Please tell your study doctor or other study personnel if you have taken part in other research studies at Yale or other places/hospitals that used radiation. This way we can make sure that you will not receive too much radiation. You should consider x-rays taken in radiology departments, cardiac catheterization, and fluoroscopy as well as nuclear medicine scans in which radioactive materials were injected into your body. Before you take part in any future studies that use radiation, you should also tell those study doctors about your participation in this study.
If you are pregnant or breast feeding, you may not participate in this research study. It is best to avoid radiation exposure to unborn or nursing children since they are more sensitive to radiation than adults. We will perform urine pregnancy tests prior to your participation on your PET scan day(s).

Risks Associated with MRI Scanning

Magnetic resonance (MR) is a technique that uses magnetism and radio waves, not x- rays, to take pictures and measure chemicals of different parts of the body. The United States Food and

Drug Administration (FDA) has set guidelines for magnet strength and exposure to radio waves, and we carefully observe those guidelines.

You will be watched closely throughout the MR study. Some people may feel uncomfortable or anxious. If this happens to you, you may ask to stop the study at any time and we will take you out of the MR scanner. On rare occasions, some people might feel dizzy, get an upset stomach, have a metallic taste or feel tingling sensations or muscle twitches. These sensations usually go away quickly but please tell the research staff if you have them.

There are some risks with an MR study for certain people. If you have a pacemaker or some metal objects inside your body, you may not be in this study because the strong magnets in the MR scanner might harm you. Another risk is the possibility of metal objects being pulled into the magnet and hitting you. To lower this risk, all people involved with the study must remove all metal from their clothing and all metal objects from their pockets. We also ask all people involved with the study to walk through a detector designed to detect metal objects. It is important to know that no metal can be brought into the magnet room at any time. Also, once you are in the magnet, the door to the room will be closed so that no one from outside accidentally goes near the magnet.

We want you to read and answer very carefully the questions on the MR Safety Questionnaire related to your personal safety. Take a moment now to be sure that you have read the MR Safety Questionnaire and be sure to tell us any information you think might be important.

This MR study is for research purposes only and is not in any way a complete health care imaging examination. The scans performed in this study are not designed to find abnormalities. The principal investigator, the lab, the MR technologist, and the Magnetic Resonance Research Center are not qualified to interpret the MR scans and are not responsible for providing a health care evaluation of the images. If a worrisome finding is seen on your scan, a radiologist or another physician will be asked to review the relevant images. Based on his or her recommendation (if any), the principal investigator or consulting physician will contact you, inform you and your parents of the finding, and recommend that you seek medical advice as a precautionary measure. The decision for additional examination or treatment would lie only with you and your physician. The investigators, the consulting physician, the Magnetic Resonance Research Center, and Yale University are not responsible for any examination or treatment that you receive based on these findings. The images collected in this study are not a health care MR exam and for that reason, they will not be made available for health care purposes.

Risks Associated with Use of an Arterial Line.

Putting in the plastic tube into the artery in the wrist area may cause bruising, and potentially infection. The arterial puncture may also cause spasm or clotting of the artery with a temporary decrease in blood flow, hematoma (a solid swelling of blood within the tissues), bleeding, or inflammation. If this occurs, signs and symptoms will dissipate over time, usually 24 to 72 hours after the event. In rare instances blocking of the artery, poor healing, infection, at the catheter insertion site may occur. Insertion of arterial catheters for giving drugs or sampling blood may be associated with mild-to-moderate pain or bruising at the puncture site. To minimize these risks,

an experienced physician will insert the arterial line and a trained nurse will oversee subject care. You may experience a rare allergic reaction to the medicine used to numb your skin prior to placement of the arterial catheter. If you have had a bad reaction to lidocaine or other anesthetic agents used to numb the skin in the past, please tell us about this experience before you go through the arterial line placement. Severe allergic reactions can be life threatening.
You will be also asked to abstain from using aspirin and other anti-inflammatory drugs (such as Motrin or Aleve) for 7-10 days prior to A-line insertion and 7-10 days following the arterial line removal. Important: If you have a history of a bleeding disorder or are taking medication to thin your blood, you will not be allowed to participate in this study.

Risks Associated with Blood Drawing and IV Line Insertion
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 8 weeks after the study. The total volume of blood collected during this study will be up to 32 tablespoons, including screening laboratories and blood drawn from your vein and/or artery during your PET scan day(s). This amount of blood is safe for healthy persons.

Risks Associated with E-Cigarette Use

The physiologic effects of EC use have been evaluated in human subjects in several studies. The following physiologic effects were associated with acute exposure to EC aerosols:
-Mouth and throat irritation and dry cough at initial use (which decreased in severity with continued use)
-No immediate change in the following biomarkers: complete blood count (CBC), lung function, cardiac function, inflammatory markers, carbon monoxide (CO) level
-Variable effects on plasma nicotine level and heart rate
-Reduced fractional exhaled nitric oxide (FeNO) and increase in airways resistance

Signs of acute nicotine toxicity from e-cigarettes include nausea, increased heartrate or palpitations, headache, dizziness, tremor, or seizures.

Early nicotine exposure through e-cigarettes has been shown to lead to dependence. The long-term effects of chronic EC use are unknown and could pose future health risks that have not yet been identified.

There have been recent reported cases of severe lung (pulmonary) illness linked to “vaping” or e-cigarette use. These cases included symptoms such as coughing, shortness of breath, chest pain, fever, fatigue, nausea, vomiting, diarrhea, and/or abdominal pain. Some patients reported symptoms to have occurred over a few days and some reported to have occurred over a few weeks. Vaping-related disorders have ranged from mild to severe with hospitalization, intensive care with breathing machines and in some cases death. In most cases, but not all, people experiencing these symptoms were using cannabidiol (CBD) or marijuana (THC) e-liquids, and/or were using e-cigarette devices and e-liquids that were mixed at home or purchased off market (such as purchasing an e-liquid or device on the street, not from a licensed retailer).

CDC warnings

The Center for Disease Control (www.cdc.gov) has issued the following information on vaping:

- **The CDC has warned against using vaping e-cigarettes**
- The use of e-cigarettes is unsafe for kids, teens, and young adults. *
- Most e-cigarettes contain nicotine. Nicotine is highly addictive and can harm adolescent brain development, which continues into the early to mid-20s.*
- E-cigarettes can contain other harmful substances besides nicotine.
- Young people who use e-cigarettes may be more likely to smoke cigarettes in the future. *
- Adults who do not currently use tobacco products should not start using e-cigarettes.
- If you do use e-cigarette products, you should not buy these products off the street (for example, e-cigarette or vaping products with THC or other cannabinoids).
- You should not modify e-cigarette products or add any substances to these products that are not intended by the manufacturer.
- Adult smokers who are attempting to quit should use evidence-based treatments, including counseling and FDA-approved medications. If you need help quitting tobacco products, including e-cigarettes, contact your doctor or other medical provider.

The e-cigarettes and e-liquid pods that we use in the current study are purchased only from a licensed retailer and do not contain CBD or THC. The pods we are giving you contain nicotine, solvents, and flavorings. At this time, we don't know what the risks associated with the use of the e-cigarettes and e-liquids, flavors, etc. that we use in this study are, and who might develop symptoms. If you agree to be in this study, it is mandatory, for your safety, that you only use the e-cigarette pods provided and do not attempt to hack or modify the e-cigarette device in any way.

E-cigarettes contain other chemicals besides nicotine including propylene glycol/vegetable glycol/vegetable glycerin. At this time, we do not know the risks associated with the propylene glycol/ vegetable glycerin that may in the fillers in the liquids used in this study.
It is important to note that there may be unforeseen risks (such as allergic reactions). We will be using e-liquids that are freely available for purchase and the propylene glycol/vegetable glycerin doses will be what is available in these e-liquids. Some research has indicated that in large doses propylene glycol and vegetable glycerin can be harmful. All levels of e-liquids administered in this research study are below any potentially harmful levels. However, if you experience any side effects, you can stop the session at any point. Research staff will monitor e-cigarette use during the lab session. If you feel any discomfort or need to stop for any reason, please let the researcher know.

We will assess your health at the intake to make sure you are healthy prior to participating and will continue to monitor your health closely during the study. If you experience any symptoms (such as abdominal pain, nausea, vomiting, diarrhea, cough, shortness of breath, chest pin) or other concerns, please let us know and let your doctor know promptly. (right away). Go to the emergency room promptly if your symptoms increase. You can stop the study at any point. If you feel any discomfort or need to stop for any reason, please let the research team know. The CDC requires the hospital to report to the State Health Department and the CDC cases of illness after using e-cigarettes. The report will contain the name and address of the person who is ill.

Risks associated with smoking abstinence

Smokers that abstain from smoking may experience symptoms of nicotine withdrawal such as craving cigarettes, mild anxiety, restlessness, irritability, difficulty concentrating, loss of energy, and excessive hunger. These are typical symptoms that people experience when they stop smoking and they can be uncomfortable but they are not life threatening.

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

Benefits

The research is not intended to benefit you directly. However, what we learn may help us better understand e-cigs and possibly develop treatments for smoking addiction. Any significant new clinically relevant research findings will be provided to you.

Economic Considerations

You will be paid $550 for participation in each PET scan session and $50 for each arterial line placement, $50 for each MRI. You will also be reimbursed $40 for cognitive testing at baseline and may earn up to $100 additionally during impulsivity task. If you play the Face Game, you may be compensated for how much you win during the task up to $50. You may receive $10 each time you participate in the Cold Pressor Task. You are free to stop the study at any time; however, if you choose to withdraw, you will be paid only for the parts of the study that you completed. These payments may be provided to you in a form of check, cash, or a prepaid credit card. In addition, you may be provided with a light lunch on the days of your PET scans, and reimbursed for reasonable transportation costs. Receipts must be submitted. Please contact the study coordinator prior to your study date to discuss your transportation plans and confirm that they will be appropriate for reimbursement.

During abstinence, you will be paid each time you provide a breath carbon monoxide reading indicating that you have not smoked. You will be paid $10 at each appointment that your CO level is less than 11ppm and your urine cotinine is negative or lower than the previous day. There are three instances in which you will not be paid: 1) if your CO level is greater than 11, 2) if your urine cotinine level is positive (positive means that cotinine is detected in your urine, which means that you have smoked a cigarette), or 3) if your urine cotinine level is the same or

greater than the one obtained on the previous day.

Other than time, there are no direct costs to subjects for participation.

Cancellations: In the event that your PET scan day gets cancelled for reasons outside of your control (such as radiotracer synthesis failure), you will receive a minimum payment of $50 per cancelled scan, or a higher amount not to exceed the amount for a full scan day. This amount will be based on your length of participation on the scan day prior to cancellation, and will be up to the discretion of the PI.

According to the rules of the Internal Revenue Service (IRS), payments that are made to you as a result of your participation in a study may be considered taxable income.

Treatment Alternatives/Alternatives

The alternative to participation in this research protocol is to not participate. You are free to choose not to participate and you are free to withdraw from the study at any time during its course. Should you choose not to participate or if you withdraw, it will not adversely affect your relationship with the University, research staff, or your doctors. If you desire more help to quit smoking, we can provide you with information for smoking cessation programs.

Confidentiality and Privacy

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute on Drug Abuse (NIDA), which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

Identifiers might be removed from the identifiable private information or identifiable biospecimens and after such removal, the information or biospecimens could be used for future

research studies or distributed to another investigator for future research studies without additional informed consent

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. 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.

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.

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 date of birth and address. 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. Additionally, all data is securely stored in locked filing cabinets or on a password-protected computer server. De-identified PET subject data will be kept for a minimum of 7 years.
The information about you that will be collected in this study includes the following, all of which will be coded with a unique code and will not have your name on it.

- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during and regarding this research
- Questionnaires

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 insuring 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 (Stephen Baldassarri, MD) and appropriate research staff
- Yale University PET Center where your PET scans will occur.

- Yale University Magnetic Resonance Center where your MRI/MRS scans will occur.
- FDA;
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, according to the study plan

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.

All health care providers subject to HIPAA (Health Insurance Portability and Accountability Act) are required to protect the privacy of your information. The research staff at the Yale School of Medicine and Yale New Haven Hospital are required to comply with HIPAA and to ensure the confidentiality of your information. 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.

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to Stephen Baldassarri, 300 Cedar St, TAC 455-S at the Yale University, New Haven, CT 06520

You have the right to review and copy your health information in your medical record in accordance with institutional medical records policies.

In Case of Injury

If you are injured while on study, seek treatment and contact the study doctor as soon as you are able. Yale School of Medicine and Yale PET Center do not provide funds for the treatment of research-related 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 any of 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 sign this authorization, you may change your mind at any time, but the researchers may continue to use information collected before you changed your mind to complete the research

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 (if applicable).

The researchers may withdraw you from participating in the research if necessary. The conditions in which you may be withdrawn from participating include a positive pregnancy test for women or your non-compliance with the research study

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

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:
Stephen Baldassarri
Yale University School of Medicine
300 Cedar St, TAC 455-S
New Haven CT 06520

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.

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 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 you have further questions about this project or if you have a research-related problem, you may contact the Principal Investigator Stephen Baldassarri, MD 203-785-3627

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. If after you have signed this form you have any questions about your privacy rights, please contact the Yale Privacy Officer at 203/436-3650