VA Department of Veterans Affairs

# VA RESEARCH CONSENT FORM

**Subject Name:**_____ **Date:** _____
First Name MI Last Name

**Title of Study:** Nicotine Delivery Rate and Its Abuse Potential: Impact of Menthol

**Principal Investigator:** Mehmet Sofuoglu,M.D.,Ph.D. **VA:** VA Connecticut Healthcare System/689

(v.5.22.18) ID: 2000023289 NCT03580525

## SECTION I: THE PURPOSE OF THE STUDY AND HOW LONG IT WILL LAST.

You are invited to participate in a research study that will measure your response to nicotine following overnight abstinence from smoking. You have been invited to participate because you smoke cigarettes and are not currently seeking treatment to stop smoking. Your participation will include a screening and 5 Lab Sessions, spread out over approximately two and a half months.

Smoking is harmful to your health and well-being and we encourage you to get treatment to stop smoking. 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 judgment. This consent form gives you detailed information about the research study which a member of the research team will discuss with you. This discussion will 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.

## SECTION II: DESCRIPTION OF THE STUDY INCLUDING PROCEDURES TO BE USED.

Nicotine is found in cigarettes and contributes to tobacco addiction. Nicotine gum, lozenges, patches, nasal spray and inhalers are available over the counter, or by prescription, under the trade names Nicorette, Nicoderm and others, to help smokers quit smoking. In this study, we will use intravenous nicotine, which is an investigational drug and not approved by the FDA as a treatment for tobacco addiction. We plan to enroll about 100 participants in this study. If you agree to participate, a clinician will take a complete history and give you a physical examination to evaluate your general health, before entering the study. We will ask you detailed questions about your past hospitalizations, medical problems, and treatments you have received. We will also ask you questions related to your mental health and drug use history. An electrocardiogram (to examine the health of your heart) and routine blood and urine screening tests will be performed to aid the study physician in the decision as to whether it is safe for you to participate. Your urine will also be tested for drugs of abuse (for example: cocaine, marijuana and benzodiazepines), hormones that identify the possibility of pregnancy (for women), and for nicotine (quantitative cotinine levels). The screening will last 2-3 hours and it may take one week before we receive the test results. If your urine is positive for drugs, indicating recent use, or if you are pregnant, you will not be allowed to participate in the study. You will not be charged for these tests, and you will be paid $30 for participating in the screening. If you request, the results of these tests will be made available to you or to your medical doctor.

Based on the results of these tests, we will determine whether you are eligible to participate in the study. If you are eligible, you will then be scheduled for the next visit. If you agree to continue, you will come to the Biostudies Unit, located at the VA Connecticut Healthcare System (West Haven, CT) to participate in 5 Lab sessions over a 60-day period. Each Lab session will last about 5 hours. For all of the Lab sessions, we will ask you to come to the Biostudies Unit at 7:30 am. You will be asked not to smoke or drink alcohol after midnight before the Lab sessions. You must also not eat for four hours before each Lab session. You will have to go 10 hours without smoking. We will check and continue to make sure that you have not smoked by measuring your breath carbon monoxide levels. If the measurement indicates that you smoked recently, you will not be allowed to participate. In addition, before the start of Lab session we will measure breath alcohol levels (using a breathalyzer) and perform a drug screening. If the breathalyzer reading is over 0, indicating that you have recently used alcohol, or your urine drug screening indicates that you have used illicit drugs (with the exception of marijuana), you will be discharged from the study. If the study clinician determines that it is unsafe for you to leave the hospital, you may be taken to the Psychiatric Emergency Room. Since we will provide you a light meal at the end of each Lab session, we ask that you do not eat before coming to each Lab session.

**Lab SESSIONS**: In each Lab Session, you will have two IV catheters one in each arm. A small catheter placed into a vein in each arm by the Biostudies research nursing staff. In the event that IV catheter placements can't be obtained, the test day will be rescheduled. If one IV can be placed we will continue without blood draws. We will then measure your heart rate, blood pressure, and mood and perform a blood draw. We will then administer over 10 minutes an infusion of saline (salt water) or a dose of nicotine. You will then answer a series of questions about the effects of the infusion. You will also be asked to perform computerized testing of your attention in each lab session. You will then be asked to complete a Drug versus Money Multiple-Choice Procedure. You will not receive any additional nicotine or saline infusion nor will you pay or receive any money during this multiple choice procedure.

For each Lab Session (#1, #2, #3, #4 and #5) you will be assigned to receive saline or 1mg of nicotine (per 70kg body weight) infused at a slow, modest, moderate or rapid rate. The dose of nicotine will not exceed 1.2mg (this dose is approximately the same as smoking one cigarette). The order will be determined by random assignment, like flipping a coin (e.g. 1/5 chance of being assigned to the slow infusion rate condition for session #1). For example, if you receive the slow infusion rate of nicotine for Lab Session #1, you may be assigned the fast infusion rate of nicotine for Lab Session #2, moderate infusion rate of nicotine for Lab Session #3, saline for Lab Session #4 and the modest infusion rate of nicotine for Lab Session #5

All lab sessions will follow the same procedures. Each infusion will last 10 minutes. The lab sessions will be scheduled 1-15 days apart. Before discharge from the study, you will be given anti-smoking literature. We will talk to you about the harmful effects of smoking cigarettes and ask you about your interest in treatment for smoking cessation.

**SECTION III: DESCRIPTION OF ANY PROCEDURES THAT MAY RESULT IN DISCOMFORT OR INCONVENIENCE.**

Study procedures: During the Lab sessions, you may not leave the Biostudies Unit. You will not be able to smoke while you are in the test room. You must abstain from using any drugs or alcohol before each lab session. We will perform urine drug screenings prior to each session to ensure your compliance. For each of the Lab sessions, you will remain in the Biostudies Unit until we are satisfied that you are in good health.

During the study you will be asked questions related to your mental health and drug use history which may make you feel uncomfortable or sad. The psychological tests you will be given may also make you uncomfortable or stressed.

**SECTION IV: EXPECTED RISKS OF STUDY:**

There are potential risks, discomforts and inconveniences associated with participation in this study. These may be due to exposure to nicotine, blood draws, and confidentiality of information.

1) Nicotine can cause constriction of your blood vessels and increased blood pressure and heart rate. In addition, nicotine can cause nausea, vomiting, and abdominal pain. Toxic doses of nicotine may cause nausea, vomiting, abdominal pain, excessive salivation (drooling), diarrhea, dizziness, confusion, hearing and vision problems, fainting, seizures, low blood pressure, irregular pulse and death. However, these toxic effects occur at doses 10-20 times higher than the nicotine doses that will be used in our study and are unlikely to happen in our study.

2) Blood draws. Over the course of the study, you will have less than 300 ml (one and a quarter cups) of blood drawn. There will be blood draws in this study, one at screening and in each Lab Session. The IV placements and blood drawing may cause some pain, bruising or rarely infection.

3) For women of childbearing age: If you are pregnant, or become pregnant, this research may have a bad or unforeseen effect on a fetus and should not be done during pregnancy. To your knowledge, you are not pregnant at the present time, and agree to agree to avoid becoming pregnant. If you change your mind about becoming pregnant or regarding how you will avoid becoming pregnant, we ask you to notify us immediately.

You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study. If you change your mind about becoming pregnant or regarding how you will avoid becoming pregnant, we ask you to notify us immediately.

4) Confidentiality of Information: Participation in research may involve a loss of privacy. Your research records will be kept as confidential as possible. Only a code number will identify your research records. The code number will not be based on any information that could be used to identify you (for example, social security number, initials, birth date, etc.).
The master list linking names to code numbers will be kept separately from the research data. At this time all data will be kept in accordance with VHA guidelines.

All research information will be secured in locked files. Your identity will not be revealed in any reports or publications resulting from this study. Only authorized persons will have access to the information gathered in this study. Authorized persons may include regulatory agencies such as the Food and Drug Administration, (FDA), the Government Accounting Agency (GAO), or the Office for Human Research Protection (OHRP), Office of Research Oversight (ORO), as well as members of the Research Administrative staff of VA Connecticut. The Department of Veterans Affairs (VA) requires some information to be recorded in the VA electronic medical record for all veteran and non-veteran research subjects. Therefore, if you participate in this study, a medical record will be created if you do not already have one. Notes from your visits, procedures, and laboratory tests will be included in this record. In addition to the research team, and the VA staff who provide clinical services, other researchers may be granted approval to access this information in the future. Federal laws and regulation that protect privacy of medical records will apply to your VA record. Yale University Human Investigator Committee will also have access to your records and may inspect them at any time.

Genetics: We are interested in studying how genes might influence your response to nicotine in this study. To study this, we will take a blood sample during the screening visit. From this sample, your DNA will be kept in the laboratory indefinitely. DNA is the "blueprint" in your cells that makes you a unique individual.

The use of your blood for genetic testing raises special issues of confidentiality because it is conceivable that information about your genes could be used against you if this information became known to the wrong people. For example, an insurance company could try denying benefits, or an employer could try to deny employment if it became known that you carried certain genes. To reduce this possibility, the following specific measures will be taken to protect your confidentiality:

a) 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.

b) Genetic test results will not be made available to you, your doctors, your other clinicians, or any other clinical staff.

c) To protect the confidentiality of computer records related to you or your family members, information that could be used to identify you individually will be stored only on a separate protected VA server behind the VA firewall. Thus, even if a "hacker" breaks into the laboratory computer system, there will be no information stored there that can identify you as an individual. All paper records containing your identity will be stored in locked cabinets, and will be available only to authorized research staff.

d) Information about your genes will only be stored in the VA Connecticut Genetics Lab using procedures described above to protect your confidentiality, and is completely stripped of information that could identify you.

e) 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 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 VA could be compelled by a court or a law enforcement agency to produce such samples. In more than six years of collecting DNA samples here at VA Connecticut, in which many hundreds of samples have been collected, no outside agency has ever tried to gain access to any research participant's blood or DNA samples. Dr. Sofuoglu believes that the risk of this happening to your sample is extremely small. DNA will be extracted from your blood and used for genetic testing. Your DNA will be kept in the laboratory indefinitely (as long as possible) and may be used for many laboratory tests. The blood samples and the DNA will be labeled with a number only. Your name will not be attached to the samples in the laboratory. This measure is taken to protect your confidentiality.

Your participation in this study may be terminated any time during the study without your consent if, in the clinical judgment of the investigator, stopping your participation is in your best interest, if you do not follow study procedures, or if Human Studies Subcomittee/Human Investigator Committee withdraws approval of the study.

**SECTION V: EXPECTED BENEFITS OF STUDY.**
You will not personally be helped by taking part in this study, but your participation may lead to knowledge that will help others.

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time without a penalty or loss of benefits to which you are entitled. Your decision not to participate, or to withdraw, will not affect your relationship with the study doctors, or with the VA Healthcare System or Yale University School of Medicine.

The study may be stopped or your participation in the study may be ended without your consent. If this happens, it might be the result of a bad reaction you have to nicotine or because of new information that is learned about nicotine's safety. If any important new information is found during this study that may affect your desire to continue to be part of this study, you will be notified right away.

**SECTION VI: ALTERNATIVE THERAPY OR DIAGNOSTIC TEST.**
This is not a treatment study. Your alternative is not to participate.

**SECTION VII: USE OF RESEARCH RESULTS.**
You and your Clinician will be informed of any important discoveries made during this study which may affect you, your condition, or your willingness to participate in this study. If we have reason to believe that you intend to harm yourself or others, or if we identify other major clinical findings during clinical or research assessments, the study Clinician will be notified immediately. You may be held against your will until you are judged to no longer be considered a threat to yourself or to others.

These records will be kept in accordance to VHA guidelines. Only research staff will have access to your files. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent.
Your medical records will be maintained according to this medical center's requirements. However, there is a possibility that the Food and Drug Administration may inspect the records.

To help keep information about you confidential ,we have received a Certificate of Confidentiality from the Department of Health and Human Services. The Certificate of Confidentiality is intended to protect you by preventing the researchers from being forced to release information that could identify you in various types of civil and criminal proceedings.

However, this protection is not absolute. There are six circumstances in which information identifying you might be released:

1) The researchers will report certain communicable diseases as required by State regulations. These types of reports will be made without your knowledge.

2) The researchers will report current cases of physical or sexual abuse (including child abuse and elder abuse).

3) The researchers may disclose medical information without your permission in the event of an emergency. If you indicate you are in imminent danger of hurting yourself or others, the researchers may need to reveal this in order to protect you or someone else.

4) The researcher may be required by VA regulations or by federal law to disclose information from research records.

5) The researchers are required to allow access to research records when requested by regulatory agencies such as the Food and Drug Administration (FDA) for the purpose of program evaluation or audit.

6) Also, The Certificate of Confidentiality does not protect you in the event that you, someone in your family, or someone you know, voluntarily releases information about you.

**SECTION VIII: SPECIAL CIRCUMSTANCES.**

You will be paid cash; $30 for participating in the screening visit and $150 for each of the 5 lab sessions. You must abstain from nicotine and alcohol before each session. In addition, to help offset transportation costs, you will be paid $20 for each of the 5 lab sessions. If you are asked to return in addition to these visits for any reason, you will be paid an additional $20 for travel. If you decide to stop the study at any time during the lab session, you receive full payment for that day. If a session is terminated early for medical reasons or safety concerns, you will receive full payment for that day. If you become ineligible to continue in the study for noncompliance with study procedures, you will only be paid for the portions of the study in which you have participated. You may be paid up to $880 for your study participation. Payment may exceed $880 if you are asked to return in addition to the screening visit and the 5 lab sessions for any reason.

Payment schedule

| Visits | Amount paid | Total |
|---|---|---|
| Screening Visit | $30.00 | 30.00 |
| Lab session | $150 each lab session | Five lab sessions $750 |
| Travel to each lab session | 20.00 each lab session | Travel for 5 session $100 |
| | Max total | $880.00 |
| If subject is asked to return for additional testing or visit | $20 for travel | $20.00 |

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 are a Veteran who receiving care at VAMC, There will be no charge for your care received as part of your participation in this study. However, some Veterans are required to pay a co-payment for medical and other services provided by the VA Connecticut Healthcare system that are not part of this study. These co-pay requirements will continue to apply to medical care and services provided by VA that are not part of this study.

If you are injured as a direct result of your participation in this research study, VA will provide necessary medical treatment at no cost to you. There are no plans to provide compensation for disability or other losses occurring over the long term or if an injury becomes apparent after your participation in the study has ended. However, by agreeing to participate in this research study, you are not waiving or giving up any legal rights to seek compensation. If you have any questions about your right as a participant, you may contact the Chairman of the Human Studies Subcommittee at 203-932-5711, extension 3350. If you have any questions about compensation for injury you may contact the Research Office at 203-937-3830.

**RESEARCH SUBJECTS' RIGHTS**

I have read or have had read to me all of the above, and I voluntarily consent to participate in this study. The study has been explained to me and my questions have been answered. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled. I will receive a signed copy of this consent form.

The results of this study may be published, but my records will not be revealed unless required by law.

In case there are medical problems or questions, I have been told I can call Dr. Mehmet Sofuoglu, M.D.,Ph.D. at 203-937-4809 during the day, and the Psychiatric Emergency Room at the VA Connecticut Healthcare System and ask for the Substance Abuse Research Psychiatrist at (203) 932-5711, extension 4472 after hours or during the weekends.

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|---|---|
| Signature of Participant | Date |

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| Signature of Person Obtaining Consent | Name of Person Obtaining Consent (Print) | Date |

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|---|---|
| Signature of Principal Investigator | Date |

HSS Approval Stamp
APPROVED
MAY 25 2018
Human Studies Subcommittee