THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Informed Consent

INFORMED CONSENT/AUTHORIZATION FOR PARTICIPATION IN RESEARCH WITH OPTIONAL PROCEDURES

Evaluating Concomitant Use of Very Low Nicotine Content Cigarettes and E-cigarettes Among Daily and Non-Daily Smokers
2015-0638

Study Chair: Paul Cinciripini

_____ _____
Participant's Name Medical Record Number or Study ID

This is an informed consent and authorization form for a research study. It includes a summary about the study. A more detailed description of procedures and risks is provided after the summary.

This research has been reviewed and approved by an Institutional Review Board (IRB - a committee that reviews research studies).

STUDY SUMMARY

The goal of this research study is to learn more about the effects of different nicotine levels in cigarettes and electronic cigarettes (e-cigarettes). E-cigarettes use water vapor to deliver nicotine.

This is an investigational study.

This research may help inform the FDA how best to regulate e-cigarettes with the goal of improving public health.

Taking part in this study may help you find it easier to quit smoking completely. After you complete the study, the study staff will talk to you about the benefits of remaining smoke-free and will provide you with information about quitting smoking. There may be no benefits for you in this study.

Your participation is completely voluntary. Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including potential expenses, side effects, nicotine withdrawal, and time commitment.

You can read a list of potential risks below in the Possible Risks section of this consent.

You will have up to 5 in-person and/or virtual visits over 10-15 weeks. You will be taken off study if you develop serious medical problems, have intolerable side effects, are not able to follow the study directions, or become pregnant. Your participation may also be stopped by the study doctor at any time for any reason.

Your participation on this study will be over after the follow-up call (30 days after your last study visit).

There will be no cost for you to participate in this study.

You may choose not to take part in this study. You are not being offered treatment for smoking in this study. If you are seeking treatment for smoking, please let the study staff know and they will help you to find a treatment program.

Information about quitting smoking can be found by visiting the National Cancer Institute's website (www.smokefree.gov) or by calling their national Smoking Quitline: 1-877-44U-QUIT.

1. STUDY DETAILS

Screening Tests

Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the study staff decide if you are eligible:

- Your carbon monoxide (CO) levels may be measured. To measure your CO level, you will blow air through a CO-measuring device. CO is a gas that is found in higher levels among cigarette smokers.
- You will complete questionnaires about your demographics; your physical and emotional health; and your smoking behavior. These questionnaires should take about 30 minutes to complete. If you completed your questionnaires electronically before the visit, then the estimated time of completion for the remaining questionnaires is about 10 minutes.
- If you can become pregnant, urine may be collected for a pregnancy test at the study clinic, or you may be given a pregnancy test to complete at home. To take part in this study, you must not be pregnant or breastfeeding.

Tell the staff doctor about any medications you are currently taking as some of these medications may cause you to fail a drug test. In some cases, you may be allowed to proceed.

A member of the study staff will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. The study staff may decide after the screening that it is not in your best interest to take part in this study or if the principal investigator thinks you cannot take part, for example if you plan to be unavailable during the study, you may not be enrolled. If so, your next visit will be cancelled.

Up to 900 participants will be screened to take part in the study, but only up to 300 participants will be enrolled. All will take part at MD Anderson.

Smoking Schedule

There are 4 phases to this study. Phase 1 (Week 1), Phase 2 (Weeks 2-4), Phase 3 (Weeks 5-7), and Phase 4 (Weeks 8-10).

During **Week 1**, you will be asked to smoke your usual cigarette brand as you normally would.

During **Weeks 2-4**, you will be asked to smoke only the study cigarettes provided to you. You will receive a larger supply than you normally smoke because the study cigarettes have less nicotine, which may make you want to smoke more. You may choose to smoke either menthol or non-menthol study cigarettes.

During **Weeks 5-10**, you will be asked to smoke only the cigarettes and e-cigarettes provided to you. You will smoke either low- or high-nicotine content e-cigarettes for the first 3 weeks (Phase 3) and then switch to whichever one you have not yet received for the remaining 3 weeks (Phase 4). Neither you nor the study staff will know the order in which you are receiving the high- and low-nicotine content e-cigarettes. However, if needed for your safety, the study staff will be able to find out what you are receiving.

Study Visits

At your second visit, you will be given a smartphone to use during the study. If you lose the smartphone, we ask that you file a police report since the phone is the property of MD Anderson. However, you will not be financially responsible due to the loss of the smartphone and this will not affect your compensation. You will be asked to return the smartphone when your participation on the study is complete. You will receive instructions on how to use it to answer a questionnaire about your nicotine cravings and mood, and to log your daily smoking activity every day for up to 63 days. The questionnaire link will be sent either by text or email to the study phone. Please note that if you need to speak to the study staff, do not reply back to the text or email sent to the study phone as the inboxes are not monitored. Please refer to the staff call sheet and call directly. It should take about 10-15 minutes each day to complete the questionnaire. If study reports show that you have not completed any questions for at least 2 days in a row, study staff may call you to see if there is a problem. You will be asked to return the smartphone when your participation on the study is complete.

At **Visits 1, 2, 3, and 4**:

- Your CO level may be measured.
- A cheek swab and mouthwash sample will be collected to measure e-cigarette exposure. You may be asked to go to the study clinic at the University of Texas MD Anderson Cancer Center, or to an alternate collection site, to provide your sample under the supervision of lab staff.
- You will complete questionnaires about mood, nicotine withdrawal symptoms, and smoking behavior. These questionnaires will take about 30 minutes to complete.
- You will complete a questionnaire about respiratory symptoms including coughing, wheezing, phlegm production, and shortness of breath.

- You will complete an electronic survey about your opinion of the study cigarettes. This survey should take about 1 hour to complete.
- You may be able to complete your questionnaires electronically prior to the visit. You will be emailed a link to the questionnaires and by filling them out before the visit you can reduce your clinic time.
- Urine may be collected for testing for substances that are related to tobacco at the study clinic at MD Anderson or at an alternate collection site, or you may be asked to collect and mail back your urine sample in a prepaid collection kit.
- If you can become pregnant, urine will be collected for a pregnancy test at the collection site, or you may be given a pregnancy test to complete at home. To take part in this study, you must not be pregnant or breastfeeding.
- At Week 1 you will choose the e-cigarette flavor that you will use during the study.
- Around 3 days after Visit 1 and Visit 2, staff may contact you to make sure you are not having any problems with the study products.
- You may be asked to pick up the study cigarettes and e-cigarettes in person at the study clinic at MD Anderson, or at an alternate collection site.

If you need to have any at-home tests (like the pregnancy test or urine collection) or you need to go to a place different than MD Anderson, the study team will discuss this with you.

At your **first** and **last** visits, you may be asked to complete a lung function test to check your respiratory health. For this test, you will blow air through a tube into a measuring device.

Follow-Up Visit

About 30 days after your last study visit, you will be called by a member of the study staff to ask about how you are doing. This call should last about 10 minutes.

Other Information

- The study staff may contact you by text message and/or unencrypted email to remind you about study visits and procedures
- You should smoke only the cigarettes assigned to you for 9 weeks (weeks 2-10). You should also only vape the e-cigarette assigned to you for 6 weeks (weeks 5-10). If you smoke other cigarettes during the study, vape other e-cigarettes, or use other nicotine products like nicotine gum, you can still be in the study. However, it is important that you tell the study staff about any non-study cigarettes, tobacco, or nicotine products that you use.
- This study is not a treatment program, however if you want to reduce the amount you smoke or stop smoking entirely, you may still take part in the study. If you decide to quit during or after the study, the study staff will refer you to the MD Anderson smoking cessation program. In this program, you will be provided with up to 8 weeks of free smoking cessation treatment, including nicotine replacement therapy and smoking cessation counseling. Alternatively, the staff can provide you with information about stopping smoking and referrals to local treatment programs. If you decide to quit, you can choose whether you want to take home your assigned study cigarettes. However, having cigarettes or e-cigarettes in your

possession during your quit attempt could make it difficult for you to refrain from smoking or vaping.

- Quitting smoking can greatly improve your health. However, changes in your smoking can lead to changes in the levels of drugs you are taking. Please make sure to tell the study staff about all the drugs you take. Quitting smoking may alter the way in which your body metabolizes certain medications. If you quit smoking and are taking certain medications regularly (e.g., medications to treat asthma or diabetes) discuss this with your regular doctor to determine if a change in these medications is warranted.
- The amount of nicotine in the study cigarettes and e-cigarettes provided to you may be lower/higher than your normal brand of cigarettes.
- You must not share the study e-cigarette or e-cigarette cartridges with anyone. You should not give or lend the e-cigarette and cartridges to other people. You should store them in a safe location outside the reach of children.
- Once your participation in the study is complete, you must return to study staff (in-person or mailed back using a prepaid collection kit) the e-cigarette device and all used and unused e-cigarette cartridges that were assigned to you.
- You must not engage in study procedures (such as completing a survey) or interact/meet with study staff while operating a vehicle or heavy equipment/machinery.

2. POSSIBLE RISKS

While on this study, you are at risk for side effects. You should discuss these with the study doctor. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after the study procedures are stopped, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Side effects will vary from person to person, and some may occur after you have stopped taking part in the study. Tell the study staff about any side effects you may have, even if you do not think they are related to the study procedures.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaires, you are encouraged to contact your doctor or the study chair. The only risk of these questionnaires is your loss of privacy if other people find out the results.

Smoking cigarettes can lead to the following medical problems:

- **Cardiovascular Disease**: heart disease, heart attack, stroke, heart and/or blood vessel disease, reduced blood flow, weakness in the walls of arteries (possible serious bleeding)
- **Respiratory Diseases**: Emphysema, lung inflammation, and difficulty breathing due to lung damage

- **Cancers:** Lung cancer, bladder, cervical, esophageal, kidney, larynx, mouth, pancreatic, throat, stomach cancers, and acute myeloid leukemia
- **Other Health Risks:** Infertility, early delivery, stillbirth, low birth weight, sudden infant death syndrome (SIDS), lower bone density in postmenopausal women, and increased risk for hip fracture in women
- **Death**

Smoking and nicotine can affect the cardiovascular system which may result in changes in blood pressure and/or heart rate. Smoking and nicotine can affect a person's mood and emotions and are associated with psychiatric disorders including major depressive disorder, general anxiety disorder, bipolar disorder, and eating disorders.

Smoking during pregnancy can lead to miscarriage, preterm delivery, stillbirth, low birth weight, problems with the placenta, birth defects such as cleft palate, sudden infant death syndrome (SIDS), and early childhood behavioral problems. If you are pregnant, you will not be able to take part in this study.

For more information about the harmful effects of smoking and the benefits of quitting, please visit the Centers for Disease Control and Prevention (CDC) website: http://www.cdc.gov/tobacco/, the National Cancer Institute's website: www.smokefree.gov or call the National Cancer Institute's Smoking Quitline: 1-877-44U-QUIT.

In a previous study, there was no evidence that smoking the study cigarettes increased withdrawal symptoms. Due to changes in nicotine levels, there could be changes in how frequently you use cigarettes, including the way you inhale the smoke. You may also experience increases in levels of carbon monoxide, a gas from smoke.

The study cigarettes have been obtained through the National Institute on Drug Abuse and the Food and Drug Administration has reviewed the study protocol. These cigarettes are manufactured in the same way as your usual brand of cigarettes, but they contain tobacco that has been genetically modified to lower the levels of nicotine.

A full study of the possible side effects of the products of these genetically modified nicotine plants has not been conducted, so the effects of inhaling this product is unknown.

Smoking **withdrawal symptoms** can include anger, irritability, frustration, anxiousness, nervousness, depressed mood or sadness, desire or craving for a cigarette, difficulty concentrating, increased appetite, hunger, weight gain, insomnia, sleep problems, awakening at night, restlessness, impatience, constipation, dizziness, coughing, daydreaming or nightmares, nausea, and sore throat.

It is possible that if you return to smoking your usual brand of cigarette at the end of the study you may experience mild nausea, dizziness, and lightheadedness.

e-Cigarette Side Effects

The short and long-term risks of using e-cigarettes are currently unknown. However, the following side effects have been seen in people using e-cigarettes:

• chest pain • fever • fatigue/tiredness • dizziness • headache • seizures • nausea/vomiting	• diarrhea • taste changes • dehydration • increased mucus in the throat/sinuses • dry mouth • sore throat	• mouth blisters/sores • difficulty breathing • shortness of breath • dry cough • dependence on nicotine

If stored improperly (in a pocket or where the device can turn on accidentally), overheating of the device may occur, which presents a minor burn risk.

The **lung function test** requires that you blow into a tube connected to a machine called a spirometer. This may cause you to feel dizzy or light-headed. It may raise your blood pressure for a short time. In rare cases, the test can cause fainting or loss of consciousness. If you have any of these side effects, the test will be paused until you feel better.

Although every effort will be made to keep **study data** safe, there is a chance that your personal health information could be lost or stolen. All study data will be stored in password-protected computers and/or locked file cabinets.

The National Institute of Drug Abuse has received a Certificate of Confidentiality from the federal government, which will help them protect the privacy of research participants. The Certificate protects against the involuntary release of information about participants collected during the course of covered studies. The researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the participant or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the participant or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review National Institute of Drug Abuse records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act. The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.

This study may involve unpredictable risks to the participants.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active.

Birth Control Specifications: If you are able to become pregnant, you must use birth control while on the study. Acceptable forms of birth control include hormonal methods (such as birth control pills, patches, implants, injections, or vaginal ring); barrier methods (such as condoms, diaphragms, sponge, or cervical cap with spermicide); or intrauterine devices (IUDs).

Females: If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

3. COSTS AND COMPENSATION

If you suffer injury as a direct result of taking part in this study, MD Anderson health providers will provide medical care. However, this medical care will be billed to your insurance provider or you in the ordinary manner. You will not be reimbursed for expenses or compensated financially by MD Anderson or National Institute on Drug Abuse for this injury. You may also contact the Chair of MD Anderson's IRB at 713-792-2933 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

Unless otherwise stated in this consent form, all of the costs linked with this study, which are not covered by other payers (health maintenance organization [HMO], health insurance company, etc.), will be your responsibility.

Samples that are collected from you in this study may be used for the development of treatments, devices, new drugs, or patentable procedures that may result in commercial profit.

There are no plans to compensate you for any patents or discoveries that may result from your participation in this research.

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All protocol procedures and tests will be paid for by the study.

The total amount of compensation that you could earn for this study is up to $988. You may receive:

$40 for completing each in-person or virtual visit (up to $200);
$10/visit for completing questionnaires electronically prior to an in-person visit (up to $50);

$10/phase for returning home-collected urine samples (up to $40);
$10/phase for providing saliva/cheek swab samples (up to $40) during virtual study participation;
$2/instance for completing daily diaries (up to $126); and
$3/instance for completing smartphone assessments (up to $252)

You may also receive additional compensation as an incentive to follow study procedures.

You may receive:
a $100 incentive per Phases 2, 3, and/or 4 if you use only the very low nicotine content cigarettes and e-cigarettes in the given phase (up to $300 bonus) OR
a $10 incentive per Phases 2, 3, and/or 4 for honest reporting of smoking your usual brand or other tobacco products in the given phase (up to $30 bonus).
$30 for returning your study phone in working order (including the accessories that were issued with the phone like charger, cord, case and screen protector, etc).

You will receive your study compensation on a reloadable Bank of America Card. If you lose your card, you will have to pay a $5.00 replacement fee.

You will also receive parking vouchers or a metro card, or alternatively, a $10 transportation reimbursement per visit to collection site, if needed.

Payments that you receive from MD Anderson Cancer Center for participating in a research study are considered taxable income per IRS regulations. If the total amount you receive from MD Anderson Cancer Center reaches or exceeds $600 in a calendar year, you will be issued a Form 1099. Because the total possible compensation you may receive in this study is greater than $600, you will be asked to provide your Social Security Number on a W-9 document for this purpose.

Additional Information

4. You may ask the study chair (Dr. Paul Cinciripini, at 713-792-0919) any questions you have about this study. You may also contact the Chair of MD Anderson's Institutional Review Board (IRB - a committee that reviews research studies) at 713-792-6477 with any questions that have to do with this study or your rights as a study participant.

5. You may choose not to take part in this study without any penalty or loss of benefits to which you are otherwise entitled. You may also withdraw from participation in this study at any time without any penalty or loss of benefits. If you withdraw from this study, you can still choose to be treated at MD Anderson.

6. This study or your participation in it may be changed or stopped at any time by the study chair, National Institute on Drug Abuse, or the IRB of MD Anderson.

7. You will be informed of any new findings or information that might affect your willingness to continue taking part in the study and you may be asked to sign

another informed consent and authorization form stating your continued willingness to participate in this study.

8. MD Anderson may benefit from your participation and/or what is learned in this study.

9. This study is sponsored and/or supported by: National Institute on Drug Abuse.

Future Research

Data

Your personal information is being collected as part of this study. These data may be used by researchers at MD Anderson and National Institute on Drug Abuse and/or shared with other researchers and/or institutions for use in future research.

Samples

Samples (such as blood and/or tissue) are being collected from you as part of this study. Researchers at MD Anderson may use any leftover samples that are stored at MD Anderson in future research. Leftover samples stored by National Institute on Drug Abuse may be used in future research.

Before being used or shared for future research, every effort will be made to remove your identifying information from any data and/or research samples. If all identifying information is removed, you will not be asked for additional permission before future research is performed.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the Institutional Review Board (IRB) of MD Anderson before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. The IRB is a committee of doctors, researchers, and community members that is responsible for protecting study participants and making sure all research is safe and ethical.

If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

Genetic Research

Research samples collected from you as part of this study may be used for genetic research, which may include whole genome sequencing. Whole genome sequencing is a type of testing in which researchers study your entire genetic makeup (DNA). This may help researchers learn how changes in the ordering of genes may affect a disease or response to treatment. If genetic research is done with your samples, those who have access to those samples may be able to identify you. The results of this research may also be able to be linked to you.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson may be collecting and using your PHI. For legal, ethical, research, and safety-related reasons, the research team may share your PHI with:
   - The OHRP
   - The IRB and officials of MD Anderson
   - National Institute on Drug Abuse, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study
   - Federal Drug Administration (FDA)
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it

   The University of Minnesota may receive your urine and saliva samples to process for cotinine and other nicotine metabolites.

   Your study data will be labeled with a special code instead of your name or other identifying information. Only the researchers working on this study will have access to the list that can link you to your code. This information will be stored on a password-protected computer during the study and for 7 years after the end of the study.

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study if you do not agree and sign.

C. MD Anderson will keep your PHI confidential when possible according to state and federal law. However, in some situations, health authorities could be required to reveal the names of participants.

   Once disclosed outside of MD Anderson, federal privacy laws may no longer protect your PHI.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer of MD Anderson at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and included in data analysis. However, no further information about you will be collected.

E. 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.

CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT