Wake Forest®
School of Medicine

Informed Consent and HIPAA Authorization Form

The Impact of Cigarette Nicotine Content, E-Cigarette Nicotine Content and E-Cigarette Flavoring on Smoking Behavior

Researcher Team Contact Information:

For questions about research appointments, the research study, research results, or other concerns, call the study team at:

Researcher Name: Andrew Strasser, PhD Researcher Affiliation: University of Pennsylvania Phone Number: [redacted]	Study Coordinator: Valentina Souprountchouk Phone Number: [redacted]

Who is sponsoring this study?

This research is supported by National Institute of Drug Abuse. The study team has no financial interest in the outcome of this study.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you are an adult cigarette smoker who has also vaped on multiple occasions, and you are not interested in or currently seeking treatment for quitting.

What should I know about participating in a research study?

- Someone will explain this research study to you.
- Whether you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this study is to understand how nicotine content in cigarettes and nicotine content in vaping devices, along with e-liquid flavor choices, affect your tobacco use and health. This research may help inform decisions made by the Food and Drug Administration (FDA) with

the goal of improving public health in the future. This study is not a treatment program for smoking. If you would like to quit smoking, we can provide you with local smoking cessation resources.

The FDA regulates tobacco products. One of the ideas for reducing the harm caused by cigarettes is to reduce nicotine in cigarettes to levels below the point that they lead to addiction. If FDA were to reduce nicotine levels, cigarette smokers may use other products that deliver nicotine, like vaping devices. The amount of nicotine in and flavor of e-liquids might influence how smokers use both vaping devices and cigarettes.

The cigarettes used in this study are investigational and have been obtained from the National Institute on Drug Abuse. The FDA has not approved these cigarettes, but has given us permission to use these cigarettes after review of our study protocol and the potential effects of the study cigarettes.

How many people will take part in the study?

480 people at two research sites will take part in this study, including approximately 240 at the University of Pennsylvania.

How long will the research last?

We expect completing the study will take about 19 weeks. During this time, you will make 12 visits to our lab at the Center for Interdisciplinary Research on Nicotine Addiction. Some visits will be relatively brief (1 hour) while others may last several hours. The visits will be weekly for 7 weeks and then every other week for 2 months. Finally, you will attend a follow-up visit 1 month after you stop using the study cigarettes and vaping device.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

What happens if I say "Yes, I want to be in this research"?

Screening Procedures

If you agree to be in this study, we will find out if you are eligible to participate. To see if you are eligible, we will do the following screening steps. We will ask you to blow into a small machine that will tell us if you have been drinking alcohol recently. Then we will ask for a urine sample to test if you have recently used illegal drugs. If the tests show that you have been drinking or used illegal drugs (except for marijuana), we will stop the interview. If you have a prescription for the medication that caused you to fail the drug test, you may continue with the screening. If you fail the drug or alcohol tests, you can reschedule to come back at another time

if you would like to try again. If you test positive for alcohol or drugs at that visit, you will not be able to be in the study.

After passing the drug and alcohol screen, you will provide another breath sample for carbon monoxide (CO) that will tell us how much you have been smoking recently and we may check your urine to see if you are smoking enough to be in this study.

We will take your blood pressure, heart rate, and weight. You will be interviewed or asked to complete forms (pen and paper and on the computer) that ask personal questions about medical and emotional history, tobacco use history and dependence, smoking habits, motivation to quit, and use of alcohol and other recreational drugs. If you are a woman, we also will ask about your use of birth control. In addition, we will ask you to smoke your usual brand cigarette through a small, handheld device that measures how you smoke.

After you complete all of these measures, our medical staff will review the information to see if you are eligible. If you are eligible, you will be enrolled in the study and begin the study procedures.

Your participation in this screening interview is voluntary, which means that you can leave at any time.

Overall study design

The study will take about 19 weeks to complete, including 12 visits to the lab. We will also provide you with cigarettes and a vaping device.

Estimated timeline (may vary)	In person sessions	Cigarette provided	Vaping device provided
0 days	Screening		
7 days	Baseline	Usual brand	
14 days	Randomization	Study cigarettes	Study vape and e-liquid
21 days	Week 1	Study cigarettes	Study vape and e-liquid
28 days	Week 2	Study cigarettes	Study vape and e-liquid
35 days	Week 3	Study cigarettes	Study vape and e-liquid
42 days	Week 4	Study cigarettes	Study vape and e-liquid
56 days	Week 6	Study cigarettes	Study vape and e-liquid
70 days	Week 8	Study cigarettes	Study vape and e-liquid
84 days	Week 10	Study cigarettes	Study vape and e-liquid

98 days	Week 12		
128 days	30-day follow-up		

Study Cigarettes
The cigarettes used in this study were obtained from the National Institutes on Drug Abuse. These cigarettes are manufactured in the same way as your usual brand cigarette, but they contain genetically modified tobacco to reduce the level of nicotine. You may not share these cigarettes with anyone. The FDA has reviewed this protocol and the use of the study product is only for those individuals who have read and signed this consent form acknowledging the risks associated with smoking the study cigarettes.

Study Vape
The study vaping device and e-liquids are commercially available. You will be provided with a Halo Triton battery (3.7 V; 650 mAh) and Triton refillable tanks (2.4 ml, 2.2-2.4 ohm coil). All e-liquid used in the study are from Syndicate Distribution (previously known as Nicopure Labs) and your flavor options will depend on your experimental group. You may not share this device, any of its components, or the e-liquid with anyone else.

Study Procedures

If the study physician determines that you are eligible to participate in the study and you decide to participate, you will be required to come back to the lab for 11 additional visits that will take place over about three months, and then one additional visit one month after the study ends.

The Baseline Visit: During this visit, we will ask you questions about your health, smoking, and mood. You will smoke one of your usual brand cigarettes in the lab and complete some questions about that cigarette on the computer. You will complete questionnaires about social settings and other environments you smoke in, how you feel about the risk of different tobacco and nicotine products, and the usefulness of vaping. We will also ask you to provide us with two saliva samples while you are in the lab, which we will test for levels of nicotine and other chemicals that are in cigarettes. This visit should last approximately two hours. At the end of the baseline visit, we will provide you with a supply of your usual brand cigarette to smoke as you would like between the baseline and the Randomization Visit. You will return any unused cigarettes and any empty cigarette packs when you come to the lab for the Randomization Visit.

The urine and saliva samples we collect from you during this study will be sent to the University of Minnesota Masonic Cancer Center in Minneapolis, MN where they will be stored and analyzed. The urine and saliva samples may be used in future research to learn more about tobacco and nicotine exposure.

The Randomization Visit: This visit is longer, and likely going to last closer to four hours. We will ask you some of the same questions about your health, tobacco use, and mood that we have asked in previous visits. We will also require you to bring a urine sample from home, and to provide a urine sample while you are in the lab. We will test the urine samples for levels of nicotine and other chemicals that are in cigarettes and vaping devices and the effects these products have on your body. If you are a woman, we will ask you to provide us with a urine sample while you are in the laboratory. We will use this sample to perform a urine pregnancy test. If the tests show that you are pregnant, you will be withdrawn from the study.

At the Randomization Visit, you will be randomly placed into one of eight groups (see table below). The group you are assigned to is chosen by chance, like flipping a coin. Neither you nor the study staff will choose what group you get. You will be able to choose to receive menthol or non-menthol cigarettes. You and the study staff will not be aware of the nicotine content of your assigned study cigarette until after the study has been completed. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency. It is possible you will be smoking cigarettes that contain less nicotine than what is found in most brands. You could also be assigned to a cigarette that has levels of nicotine similar to cigarettes available in stores. Everyone will also receive a vaping device to use during the study. The amount of nicotine in the e-liquid will depend on your group assignment and will range from low nicotine (0.03% or 3 mg/ml) to moderate (1.8% nicotine or 18 mg/ml) levels of nicotine. At each visit to the lab, you will choose e-liquid flavors to use in your vaping device until the next visit. Depending on which group you are assigned to, you will either choose between different tobacco e-liquid flavors or between tobacco and non-tobacco e-liquid flavors.

Groups:

	Very Low Nicotine Cigarettes		Normal Nicotine Cigarettes	
Range of Flavors	**LOW** nicotine e-liquid	**MODERATE** nicotine e-liquid	**LOW** nicotine e-liquid	**MODERATE** nicotine e-liquid
Tobacco Flavors	**LOW** nicotine e-liquid	**MODERATE** nicotine e-liquid	**LOW** nicotine e-liquid	**MODERATE** nicotine e-liquid

For the remainder of the study (through the Week 12 Visit), if you choose to smoke or vape, we ask that you only use the assigned study cigarettes and vaping device. This is very important for the study. We will give you more than enough cigarettes and e-liquids to use between visits to the lab. If you use any non-study nicotine or tobacco products, we ask that you inform us and we will work with you to try to avoid this in the future. We will also provide a monetary reward if the urine we collect from you while you are at the lab indicates you did not use other products (medications are ok). Additionally, we need to keep track of the cigarettes, vaping device, and e-liquid we give to you. Therefore, we would like you to keep all of your empty cigarette packs, unused cigarettes, unused e-liquid, and empty e-liquid tanks and bring them back to the lab each week. Failure to return unused study products may result in withdrawal from the study.

After you have been randomly assigned to a group, you will try both the cigarette and the vaping device in the lab and complete some assessments about them. You will be able to try the e-liquid of your choice. After trying both products, you will complete a task that involves choosing to take two puffs of the vaping device, two puffs of the cigarette, or not to take any puffs. You will make this choice ten times in a row.

Although this study is not a treatment program, if you choose to reduce the amount you smoke/vape or stop smoking/vaping entirely you are still able to participate in the study. If you decide to quit, we will provide you with information about stopping and referrals to local treatment programs. If you decide to quit, you can choose whether you want to take home your assigned study products. Having the product you want to quit in your possession during your quit attempt could make it difficult for you to stop.

While enrolled in the study, we ask that you refrain from consuming any grapefruit or grapefruit juice as this can affect the way your body metabolizes nicotine.

Weekly and biweekly lab visits (also called "experimental phase"): Once you are assigned to a group, you will visit the lab weekly between Week 1 and Week 4, then bi-weekly (every other week) between Week 6 and Week 12, and once more for the 30-day follow up. These visits will last approximately 2 hours or less.

At most of the lab visits, the following procedures will be carried out:

- Providing a first void urine. You will bring in a first void urine to every lab visit. This urine sample is from the first time you urinate in the morning after waking up. This urine sample will be tested for nicotine, cancer-causing agents and other chemicals that are in tobacco and their breakdown products.
- Providing breath alcohol level to show you have not been drinking before the appointment.

- Providing breath carbon monoxide level to measure your amount of smoking.
- Completing several forms asking about tobacco use, withdrawal symptoms, urges to smoke, mood, reaction to the products, current medication use and your health.
- Measuring blood pressure, heart rate, and weight.
- Receiving supportive counseling to help you follow the study instructions.
- Reviewing the amount of study cigarettes and e-liquid you have used since the previous visit.
- Returning your study cigarette packs (full, empty or partial packs) and review how many you have smoked since last visit. These cigarettes are owned by the government and we are required to keep careful track of them. You will need to keep track of all the study cigarettes we give to you.
- Returning your unused study e-liquids and empty e-liquid bottles.
- Providing you with an adequate supply of your assigned cigarettes, and chosen e-liquid flavors
- Providing a spot urine sample. One of these samples will be randomly picked to confirm you are not using non-study cigarettes. If you are a woman who could get pregnant, we will also test your urine sample for pregnancy at some visits. If you become pregnant while you are smoking the study cigarettes or using any tobacco products, you will not be eligible to continue in the study.

At some weekly and bi-weekly visits, there will be other measures that may take additional time to complete:

- Weeks 1 and 10: We will ask you to smoke a cigarette and vape through a device that measures how you smoke.
- Weeks 4, 8, 12: You will complete questionnaires about drug use, alcohol use, dependence, and changes in mood.
- Week 12 only: You will complete questionnaires about your smoking, mood, dependence and other measures to capture your thoughts about the study and the study products. You will also be asked to think about how much you would be willing to spend on your study cigarettes and vaping product. Lastly, you will be asked to complete several questionnaires similar to those filled out at the baseline visit about smoking settings, and the usefulness of vaping. In addition to a spot urine sample collected during the visit at the lab, we will also request you bring a first void urine on the day of you Week 12 Visit.

At the Week 12 Visit, you will need to turn in all study cigarettes, vaping device equipment and liquids.

Due to your participation in this study, you may find it easier to quit smoking completely. Therefore, throughout the study we ask you whether you are interested in or already trying to quit. If you are, we can provide you with information and resources that may help.

Daily Phone Calls

Every day throughout the study, from baseline to your Week 12 Visit, you will report the number of cigarettes you smoke and any other tobacco or nicotine products you use to an automated message system. You will make this report using your home phone or a cell phone. We will give you instructions on how to complete the daily calls. You will complete the daily telephone calls every morning for the first 12 weeks you are in the study. These phone calls will take less than 3 minutes. To be enrolled in this telephone system, we will be providing the vendor's website with some identifiable information (your telephone number only). This information will be used for website enrollment only; the data analysis group will not have access to identifying information nor will it be shared with anyone outside of this study. You will be unenrolled from this system at the Week 12 Visit. The vendor we will be using for this study is MicroAutomation.

30-day Follow-Up

About 30 days after your Week 12 Visit you will return to the lab. During this visit you will discuss tobacco product use since the study ended, complete questionnaires related to dependence and craving and we will obtain some physiological measures such as breath alcohol concentration, a carbon monoxide reading, weight, blood pressure and heart rate. We will ask you to provide a first-void urine sample that you bring into the lab, and will also collect a spot urine sample during your follow-up visit.

As part of this study, you will be asked questions about your mental health and suicide. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for completing the procedures described above including attending visits, keeping track of tobacco and nicotine use through daily calls, and keeping track of the study cigarettes, vaping device and e-liquids you receive.

What are the risks of being in this study?

This research may hurt you in the following ways and you should be aware of these before deciding to be part of the study:

Smoking Any Cigarettes

All cigarettes are harmful to a person's health and can lead to the following medical problems:

a) Heart and blood vessel disease: Heart disease, heart attack, stroke, peripheral vascular disease (PVD), reduced blood circulation, abdominal aortic aneurysm;
b) Lung disease: Emphysema, asthma, bronchitis, tuberculosis and chronic airway obstruction (COPD);

c) Cancer: Lung, bladder, liver, colon, cervical, esophageal, kidney, larynx, mouth, pancreatic, throat, stomach cancers and acute myeloid leukemia;
d) Diabetes;
e) Abnormal immune function, rheumatoid arthritis;
f) Other health risks: Infertility, tubal pregnancy, sudden infant death syndrome (SIDS), birth defects, lower bone density in postmenopausal women, and increased risk for hip fracture in women, male sexual dysfunction, vision problems and age-related macular degeneration;
g) Smoking and nicotine can affect your heart and blood vessels which may result in changes in blood pressure and/or heart rate;
h) Death.

Smoking Study Cigarettes

The study cigarettes are made in the same way as your usual cigarettes. But in order for the study cigarettes to be lower in nicotine, they are made from genetically modified tobacco plants (GMO). As with other tobacco products made by tobacco companies, this tobacco has not been tested for safety. Long-term effects of inhaling the study cigarettes are unknown. Smoking the study cigarette is not any less risky than your usual brand of cigarette and could pose increased health risks.

There is a potential for a change in your use of cigarettes due to the lower nicotine levels including how you inhale the smoke or smoking more cigarettes per day. This increased rate of smoking may continue after completing the study. You may experience an increase in exposure to carbon monoxide, a gas from smoke, due to altered smoking habits.

Nicotine Withdrawal or Too Much Nicotine

You may experience symptoms of nicotine withdrawal if you are assigned to the very low nicotine content cigarettes. These symptoms may include: craving tobacco, irritability, frustration or anger, anxiety, restlessness, sleep problems, dreaming or nightmares, trouble with concentration, depressed or sad mood, constipation, dizziness, coughing, nausea, sore throat and increased appetite or weight gain. These feelings can be uncomfortable, but are of low risk.

The use of the nicotine replacement products (gum, lozenges or patch) and use of other tobacco or nicotine products in addition to smoking cigarettes may cause some symptoms of too much nicotine. Symptoms of too much nicotine may include headache, dizziness, shakiness, nausea, vomiting or diarrhea, weakness and fast heartbeat. You will be monitored for any of these side effects to make sure you are safe. If serious side effects occur we may stop the use of the study products. Use of both cigarettes and other nicotine/tobacco products may result in an increase in the level of nicotine and other things in your body.

Worsening of Mental Health Symptoms

Smoking and nicotine can affect a person's mood and emotions and are associated with mental health problems including major depressive disorder, general anxiety disorder, bipolar disorder and eating disorders. Any changes in nicotine or tobacco consumption could have a negative effect on mental health conditions.

Interaction of Study Cigarettes with Medications

Quitting smoking can greatly benefit your health. However, changes in your smoking can lead to changes in the levels of your medications. Please make sure to tell us about all the medications you take. We also recommend you discuss any planned or actual changes in how much you are smoking with your doctor, especially if you are taking medications for mental health, heart or blood vessel problems, or other serious diseases.

Interaction of Study Cigarettes with Oral Contraceptives in Women

Women who smoke and are over the age of 35 should not take oral contraceptives that contain estrogen without consulting their physician. Smoking while using oral contraceptives can increase the risk of having a cardiovascular event such as a heart attack or stroke. Additionally, there is a potential risk of thrombosis associated with hormonal therapy (including contraceptives) and smoking.

Vaping devices

Long term health effects of the vaping devices are not known since little research has been done on these products. There is a notice from the FDA regarding the safety of this product that says they do not know whether e-cigarettes are safe for their intended use, how much nicotine or other potentially harmful chemicals are being inhaled during use, or if there are any benefits associated with using these products. Some of the samples tested have low but detectable levels of toxic chemicals. The most common side effects are changes in taste, mucus in throat/sinus, dry mouth, dry cough, throat irritation, sore throat, mouth ulcers, dizziness, headache, seizures, and nausea.. If you experience loss of consciousness, memory lapse, change in mental status, confusion, tremor, shaking, or seizure, please stop use of e-cigarette (or other nicotine products) and promptly notify study staff. Although uncommon, there have been rare occasions where the batteries in vaping devices have exploded and injured users. While not harmless water vapor, vaping devices generally contain fewer toxins than smoked tobacco products. Vaping devices can overheat and present a burn risk if the device is turned on repeatedly. Be careful if storing the device in a place where the button might be accidentally pressed often, like your pocket. Defective cartridges, tanks or devices may leak e-liquid. If this should happen, wash the exposed area to remove the e-liquid immediately. On rare occasions, allergic reactions have occurred after using vaping devices.

The Centers for Disease Control and Prevention (CDC) and FDA are investigating recent reports of serious lung disease associated with use of vaping devices. Many of the incidences are related to vaping cannabis oil. FDA has advised consumers to avoid buying vaping products on the street and refrain from using THC oil or modifying/adding any substance to products purchased at stores. If you use e-cigarette/vaping products and experience any symptoms such as cough, shortness of breath or chest pain, nausea, vomiting or diarrhea seek prompt medical attention.

The liquid in vaping devices (often called e-liquid or e-juice) can contain nicotine that can cause harm and possible death if the e-liquid or the refill cartridges containing e-liquid are eaten.

Keep all e-liquid and cartridges away from pets and children.

If ingested (e.g., if you or someone else drinks the liquid): call [redacted] immediately and contact study staff. For skin exposure: wash well with soap and water for 10-15 minutes.

Continued use of vaping device

As part of this study, you will try a vaping device on multiple occasions and can use a vaping device as much as you like over the 12-week period. This product may contain nicotine, an addictive chemical. It is possible that this experience could lead to long-term use of vaping devices after the trial is over.

Returning to regular smoking

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

Survey Questions

You will be asked questions about your medical history, drug and alcohol use and mood. Answering these kinds of questions may make some people feel uncomfortable.

Abnormal Vital Signs or Other Health Findings

You will have your vital signs (heart rate and blood pressure) taken every visit. You may find out that your blood pressure or heart rate is out of the normal range. You may tell us about health problems during the study (things like chest pain, numbness or shortness of breath) that our medical staff feels should be examined more closely. If this should happen, we will ask you to follow up with your primary care doctor and may require you to do so to stay in the study.

Breach of Confidentiality

There is a risk of loss of privacy if other people find out about your participation. This would include the alcohol and drug testing results. All efforts are made to keep your information confidential, but confidentiality cannot be guaranteed.

Other

In addition to these risks, this research may hurt you in ways that are unknown. These risks may be a minor inconvenience or may be so severe as to cause death. At each visit, we will ask you how you feel, and if we think that being in this study is putting your health at risk, we will stop your participation.

If any of these side effects mentioned above occur, please notify the research staff [redacted] or in emergency situations after hours: [redacted]). If these side effects are serious, discontinue the use of the study products.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

Risk of Smoking While Pregnant

Smoking any cigarette is a risk for pre-mature birth, stillbirth, and low birth weight. To avoid these risks, it is important that you are not pregnant during this study or while using any tobacco products. Avoiding sexual activity is the only certain method to prevent pregnancy unless you are at an age where your periods have stopped for more than 2 years or you have had a hysterectomy. However, if you are sexually active and able to become pregnant, you should use an appropriate "double barrier" method of birth control (such as using a diaphragm, intrauterine device (IUD), or contraceptive sponge, in addition to your partner's use of a condom). You should be aware, pregnancy could still result even with the use of these birth control methods. While use of prescribed "birth control" pills, injections, or implants is an acceptable method of birth control to be in this study, you should be aware that use of this type of birth control is not recommended for women who smoke. Smoking greatly increases the chance of serious heart or blood vessel side effects from oral contraceptive (birth control pills) use. The risk increases with age and with heavy smoking (about 15 or more cigarettes per day) especially in women over 35 years of age. It is unclear whether smoking while using birth control injections or implants increases the risks of heart attack and stroke, so it is recommended that women who use injections or implants do not smoke.

You should not be or become pregnant or breastfeed while participating in this research study. Pregnancy tests will be done at the beginning (baseline) and every month while you are smoking study cigarettes. If you become pregnant while participating in this research study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study. We will follow up with you after you have had your baby to follow pregnancy outcomes in the event of a pregnancy.

Will being in this study help me in any way?

There is no direct benefit for you from taking part in this study. However, this information will help inform the FDA about what happens when nicotine levels in cigarettes are reduced.

This is not a quit smoking treatment program. If you decide to quit smoking or vaping during the study you may continue in the study. **You will not be required to smoke the study cigarettes or vape if you choose to quit smoking during the study.**

What happens if I do not want to be in this research?

This is a research study and you can choose whether or not you want to participate. You can also leave the research study at any time. Leaving will not be held against you. If you decide to leave the research study, contact the study staff so that we can schedule an exit visit and you can bring back study products.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Meaning, your choice not to be in this study will not negatively affect your right to any present or future medical treatment, your academic standing as a student, or your present or future employment.

If you stop being in the research, already collected information about you will not be removed from the study database.

What other treatments are available?

This study is not a treatment for quitting smoking. If you are seeking treatment for smoking, please let us know and we 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: [redacted]. The alternative is not to participate.

Will it cost me anything to participate in this research study?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

Will my research records be confidential?

In addition to the investigator listed on the first page of this consent form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

- Collaborating investigators at the University of Minnesota and Wake Forest University
- Authorized representatives of the Wake Forest University Research Conduct and Compliance Office and the Office of Clinical Research at the University of Pennsylvania may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study.

- Authorized representatives of the sponsor of this research study, the National Institute on Drug Abuse, may review and/or obtain identifiable information related to your participation in this research study for the purpose of monitoring the accuracy and completeness of the research data and for performing required scientific analyses of the research data. While the study sponsor understands the importance of maintaining the confidentiality of your identifiable research information, the UPMC, Wake Forest University and the University of Pennsylvania cannot guarantee the confidentiality of this information after it has been obtained by the study sponsor.
- Additionally, authorized representatives from any federal, state or local governmental agency that regulates the study may also have access to your identifiable information. Agencies include the Food and Drug Administration (FDA), the U.S. Department of Health and Human Services (DHHS) and Office for Human Research Protections (OHRP).
- Employees at MicroAutomation will have access to your telephone number. They will not be provided with any other identifiable information such as your full name, address or social security number.

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Information on your participation in this study will be shared, as needed, with the other researchers at Wake Forest University School of Medicine. This includes information about the type and duration of study, your health information and tobacco use status. The information is shared to make sure you are only in one study at a time, meet the eligibility criteria to participate and to maintain your safety.

In this study, you will be asked about illegal activities or highly personal behavior. We have obtained a **Certificate of Confidentiality** from the federal government. This means in most cases the information you share is protected and will not be released to authorities upon request. However, we may still be required under certain circumstances to release your information. The Certificate cannot be used to resist a demand for information from personnel of the United States federal or state government agency sponsoring the project and that will be used for auditing or program evaluation of agency funded projects 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 or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you provide your written consent to receive research information, then the researchers will not use the Certificate to withhold that information. The Certificate of Confidentiality will not be used to prevent disclosure of certain information to

state or local authorities. If we learn about current or ongoing child or elder abuse or neglect, we may be required by law or policy to report this information to authorities. In addition, if we learn that you intend to harm yourself or others, we may be required to report this information.

What about my health information?

Protected Health Information

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. We will make every effort to keep this information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. We cannot promise complete privacy.

Your personal health information and information that identifies you may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital, representatives of the University of Pennsylvania; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement office, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire.

You can tell Dr. Andrew Strasser that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Andrew Strasser

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

What information about me may be collected, used or shared with others?
Provide a description of the information to be used or disclosed for the research project. This may include, for example, information in the medical record, results of physical examinations, medical history, lab tests, or protected health information such as name, address or social security number, e.g.,

- Name, address, telephone number, date of birth, email address
- Social Security number (for compensation purposes)
- Personal medical history
- Results from tests or procedures
- Infromation on tobacco related biomarkers

Why is my information being used?
Your information is used by the research team to contact you during the study. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- to evaluate and manage research functions.

Who may use and share information about me?
The following individuals may use or share your information for this research study:

- The investigator for the study and the study team
- Other authorized personnel at Penn, including offices that support research operations
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

Who will have access to identifiable information related to my participation in this research study?
In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following entities will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:
The Food and Drug Administration
The Office of Human Research Protections
University of Minnesota
Wake Forest University
MicroAutomation

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

How long may the School of Medicine use or disclose my personal health information? Your authorization for use of your personal health information for this specific study does not expire.

Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information? Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Clinical Trial Participation

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time

What happens if I experience an injury or illness as a result of participating this study?

We will offer you the car needed to treat injuries directly resulting from taking part in this research. WE may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed in the consent form.

What are my rights as a research participant?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any additional information we become aware of that would affect your willingness to continue to participate in the study.

Who do I contact if I have questions, concerns or feedback about my experience?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Andrew Strasser at [redacted].
If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the

Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling [redacted].

You will be given a copy of this signed consent form.

Will I be compensated for my participation?

If you agree to take part in this research study, we will give you up to $1070 for your time and effort.

You will receive $30 for attending the Screening Visit, $20 for each shorter visit you complete (Baseline, Visit 01 through 03, Visit 06, Visit 10, and 30-day Follow-up), $40 for each longer visit you complete (Visit 04, 08, 12), and $60 for completing the longer Randomization visit. You will also receive $10 to cover transportation costs for each visit ($120).

You will receive $1 for each completed daily call (up to $10 per week). An additional bonus of $5 will be awarded for missing no calls between visits (up to $50).

There are additional incentives you can earn for good attendance and not using non-study cigarettes or other vaping/tobacco products.

- If you miss no more than two visits between the Week 1 Visit and Week 8 Visit, and attend both Weeks 10 and 12, you will receive a $100 bonus for good attendance.
- At each visit during the experimental phase, you will provide a spot urine sample. This sample will be analyzed to help us determine whether you have only been using your assigned study cigarettes and vaping device/study e-liquids and not other cigarettes or vaping/tobacco products. At the end of the study we will randomly select one of your urines, and if it shows you were compliant, you will receive a $300 bonus. If you miss a Visit during the experimental phase, that week will count as “non-compliant” should that urine sample be drawn.

The schedule below shows the amount you receive if you complete all study activities.

Visit	Transportation Compensation **(given at each visit)**	Study Visits Compensation **(given at each visit)**	Daily Calls $1/call, $5 for missing 0 between visits **(given total IVR compensation at Week 12 Visit)**
Informational Session	$10	n/a	n/a
Screening Visit	$10	$30	n/a
Baseline Measures Visit	$10	$20	Up to $15
Randomization Visit	$10	$60	Up to $15
Week 1	$10	$20	Up to $15
Week 2	$10	$20	Up to $15
Week 3	$10	$20	Up to $15

Week 4	$10	$40	Up to $15
Week 6	$10	$20	Up to $25
Week 8	$10	$40	Up to $25
Week 10	$10	$20	Up to $25
Week 12	$10	$40	Up to $25
30-day Follow-up Visit	$10	$20	n/a
Total: **up to $670**	**$130**	**$350**	**Up to $190**

The table below shows the breakdown of additional money you can earn for attending all sessions, compliance and honesty:

Attendance Bonus (Can miss two Visits between Week 1 and Week 8 and still receive this bonus.) This bonus will be received at the Week 12 Visit.	$100
Compliance Bonus (Only using your assigned study cigarettes and study vape/e-liquids and not other cigarettes or vaping/tobacco products, as measured in randomly selected urine sample.) This bonus will be given at the 30-day Follow-Up Visit.	$300
Total:	**$400**

You should be aware that the income you receive from being in the study may be considered taxable income and need to be reported to the IRS on your income tax return. You will be mailed a 1099. To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

Please Note: In order to be compensated for your participation in this study, you must provide your Social Security Number. Additionally, please note that the University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that total $600 or more in a calendar year.

Study Results

After the study is fully completed, the data has been analyzed and the results written up, you will receive a letter informing you of the results.

Record of Consent

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

I have read this informed consent and HIPPAA authorization form and have decided to volunteer.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm