COMPOUND AUTHORIZATION AND CONSENT FOR PARTICIPATION IN A RESEARCH STUDY

YALE UNIVERSITY SCHOOL OF MEDICINE

Study Title: Effects of E-cigarette Flavors on Young Adults

Principal Investigator (the person who is responsible for this research):
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Research Study Summary:

- We are asking you to join a research study.
- The purpose of this research study is to examine the effects of different e-cigarette flavors on how much people like/dislike e-cigarettes.
- Study procedures will include one intake visit to complete questionnaires to see if you are eligible for the study and one lab visit. During the lab visit, participants will sample two flavors of an e-cigarette that contains nicotine. They will also fill out questionnaires and complete some other measures, like blood pressure. We will also conduct a follow up phone call one month after completing the study.
- During the lab session, we will ask you to wear a silicone smartband, similar to a smartwatch or fitbit. You will wear this on the same arm that you use to vape the e-cigarette. The smartband is used to monitor movement to track e-cigarette puffing behavior.
- 2 visits are required; one intake visit to see if you are eligible and one visit.
- The intake and lab visit will each take about 2 hours.
- There are some risks from participating in this study including the risks of vaping an e-cigarette that contains nicotine, withdrawal from nicotine before your lab appointment, collecting urine and saliva during the study, completing questionnaires and assessments, and potential risks to confidential information. We'll go over these risks in detail in this consent document.
- The study may have no benefits to you but will help inform public health by helping us understand how flavors in e-cigarettes affect use.
- Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You can also change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.
- If you are interested in learning more about the study, please continue reading, or have someone read to you, the rest of this document. Take as much time as you need before you make your decision. Ask the study staff questions about anything you do not understand. Once you understand the study, we will ask you if you wish to participate; if so, you will have to sign this form.

Why is this study being offered to me?

We are asking you to take part in a research study because you are a young adult between 18-20 years old and report using e-cigarettes that contain nicotine. We are looking for 40 participants to be part of this research study.

Who is paying for the study?

This study is funded by the Food & Drug Administration's Center for Tobacco Products and the National Institute on Drug Abuse.

What is the study about?
The purpose of this study is to examine the how different types of flavors in nicotine e-cigarettes can influence how much an e-cigarette is liked and used by young adults.

What are you asking me to do and how long will it take?
If you agree to take part in this study, this is what will happen:

- **Intake visit:** Study participants will first be asked to complete an intake visit to determine if they are eligible. You will come to the CT Mental Health Center at 34 Park Street, New Haven or SATU at 1 Long Wharf Dr., New Haven for this appointment. We will read you this consent form and if you agree to participate, you will sign it. During this appointment, you will provide personal information, including your medical history and your history and current use of nicotine and tobacco products. Information will be collected by you filling out questionnaires via a website and the researcher administering questionnaires. You will also have a brief clinical evaluation in which you will meet with a licensed clinical psychologist, a licensed social worker, or team member supervised by a licensed clinical psychologist on the research team to review your psychological history. We will also collect a urine sample to detect cotinine (a byproduct of nicotine), which will help us understand more about your current use of nicotine products.

  We will also use the urine sample to verify that you are not currently using other drugs or are currently pregnant. Pregnant females will not be allowed to participate. If you test positive for any drugs aside from marijuana at the intake appointment, you will not be paid for the visit, but will have the opportunity to reschedule this appointment one time. Additionally, we will collect blood pressure, heart rate, spirometry (a measure of lung function), and pulse oximetry, which measures how well oxygen is being sent through the body. This is measured using a clip-like device on your finger and is quick and painless. For appointments, we ask that you do not bring any weapons to any appointments you have with us. We ask that you do not drink any alcoholic beverages for 12 hours prior to your appointment time. If we suspect that you may be intoxicated, we may do a breathalyzer, ask you to remain in the clinic until it is safe to leave, and may reschedule your appointment. ***If participants would like, we can complete consent and questionnaires remotely (using Zoom or Facetime) and then can set up a time to collect the measures that would need to be in person, such as a urine sample and a blood pressure reading.***

- **COVID-19 Related Procedures:** You must be fully vaccinated against COVID-19 (as defined by CDC guidelines). Before you decide whether to participate in this study, talk to your study doctor or tour research team about anything you do not understand or any concerns you may have. For all in person visits, we will ask that you fill out a COVID symptom online questionnaire beforehand. This questionnaire will be sent to you via an online link to your cell phone or email (depending on your preference). Depending on symptoms, we may need to call you to follow up on your symptoms. You will not be allowed to attend in-person visits until your COVID symptom questionnaires are completed. If you are not able to fill out the online questionnaire, study staff can administer the questionnaire via phone. Additionally, at all appointments, you will be asked to wear mask and study staff will also wear masks and gloves. If you do not have a mask, one will be provided to you by study staff. You will be asked about COVID symptoms. A temperature check will be conducted. If you report symptoms, have a temperature of >100, you will be escorted out of

the building and asked to reschedule your visit. You will be instructed to immediately contact their primary health care provide or call the Campus COVID Resource line (203-432-6604).

- **Lab Session (1 Total):** For this study, you will complete one lab visit that will be approximately 2 hours long. Laboratory sessions are conducted on weekdays at the J.B. Pierce Laboratory, 290 Congress Ave in New Haven, CT or at the West Campus Research Unit (WCRU), 500 West Campus Dr, West Haven, CT.

  At the beginning of the lab session, we will collect blood pressure, spirometry (a measure of lung function), heart rate, and pulse oximetry. We will also collect a saliva and urine sample and have you fill out some general health questionnaires. If you are female, we will also conduct a pregnancy test prior to the vaping session.

  After this, we will familiarize you with the e-cigarette and rating scales we will be using to make sure you understand how to complete them. During this practice, an e-cigarette without nicotine or any flavors will be used.

  During the lab session, you will sample two e-cigarette flavors. For each flavor, you will inhale from the e-cigarette ten times taking a three-second-long puff each time you inhale. Then you will complete questionnaires about the e-cigarette experience and give a saliva sample. After waiting 30 minutes, you will do the same procedure with a second flavor. During that 30-minute period you can drink water but should not eat or drink anything else. The e-cigarettes will contain nicotine and only you will be using the e-cigarettes you are given (they will not be used by others). If you feel any uncomfortable side effects during lab sessions (e.g., nausea, vomiting), you will be told that you can discontinue the puffing bout at any time. After using both e-cigarettes, you will complete a brief interview about the e-cigarette flavors you tried. You will not be told the flavors or nicotine concentration the e-cigarettes are. We will note that the level of nicotine in these products is like commercial e-cigarettes.

  During the lab session, we will ask you to wear a silicone smartband, similar to a smartwatch or fitbit. You will wear this on the same arm that you use to vape the e-cigarette. The smartband is used to monitor movement to track e-cigarette puffing behavior.

  For your safety, the lab session will take place in a private environmentally controlled room that utilizes continuous floor-to-ceiling airflow to limit exposure. The rooms have plexiglass dividers to adhere to social distancing guidelines when in-person interactions are necessary. Other times, instructions and communication will occur remotely using a 2-way audio system. Hand sanitizer will be available, and you will be asked to wear a mask when possible, during the session and gloves for the duration of the lab session.

- **Assessment and Educational Materials:** At the end of the lab session, you will discuss the similarities between the e-cigarette you used in the experiment and your own e-cigarettes, including your perceptions about use and risk of e-cigarettes. You will be provided with educational information about the potential risk of continued e-cigarette use as well as quitting resources. This should last approximately 10 minutes.

- **Follow Up Appointment:** You will be asked to complete a brief, paid follow up phone call one month after study completion to fill out some questionnaires regarding your health and current e-cigarette use and preference of flavored tobacco products.

What are the risks and discomforts of participating?

1) **COVID and Tobacco Product Use:** Although the science on the relationship between COVID and tobacco use such as e-cigarettes is still not clear, you should remember that using tobacco products like e-cigarettes could lead to respiratory conditions. Although scientific evidence is incomplete, some studies have suggested that use of e-cigarettes may add to your risk of getting COVID-19 and may contribute to the severity of illness if you do get the virus. We recommend you follow the CDC guidelines for the most up to date information about ways to reduce your risk for exposure to COVID-19. https://www.cdc.gov/coronavirus/2019-ncov/index.html

   If you develop symptoms for COVID-19 (fever, cough, shortness of breath, difficulty breathing, muscle aches, sore throat, congestion or runny nose, nausea or vomiting, diarrhea, new loss of taste or smell) or have known or suspected exposure, please self-isolate and contact your healthcare provider to discuss obtaining a test for COVID-19. Please inform research staff if you develop any of these symptoms or have known/suspected exposure to COVID-19. If you become infected with COVID-19, we recommend you stop using all tobacco products.

   The potential risks in this study are related to 1) Use of e-cigarette and flavors 2) Nicotine administration, 3) Urine and saliva collections, 4) Tobacco use and Drug use 5) Limits to Confidentiality and 6) Rating scales and assessments

2) **Use of e-cigarette and flavors:** You were asked to participate because you have experience with e-cigarettes, therefore reducing the risk to experience any kind of adverse reaction to an e-cigarette. As a current e-cigarette user, you are already self-administering nicotine (as indicated by cotinine levels at Intake) and already have experience with various e-cigarette flavors. The lab session will be conducted by trained research staff sensitive to tobacco users and trained to monitor any potential adverse effects. We will also include a debriefing/motivational intervention after the last session and offer you referral sources to quit tobacco use if you are interested.

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

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

- CDC and FDA recommend that people not use THC-containing e-cigarette, or vaping, products, particularly from informal sources like friends, family, or in-person or online dealers.

- Vitamin E acetate should not be added to any e-cigarette, or vaping, products. Additionally, people should not add any other substances not intended by the manufacturer to products, including products purchased through retail establishments.
- Adults using nicotine-containing e-cigarette, or vaping, products as an alternative to cigarettes should not go back to smoking; they should weigh all available information and consider using FDA-approved smoking cessation medications. If they choose to use e-cigarettes as an alternative to cigarettes, they should completely switch from cigarettes to e-cigarettes and not partake in an extended period of dual use of both products that delays quitting smoking completely. They should contact their healthcare professional if they need help quitting tobacco products, including e-cigarettes, as well as if they have concerns about EVALI.
- E-cigarette, or vaping, products (nicotine- or THC-containing) should never be used by youths, young adults, or women who are pregnant.
- Adults who do not currently use tobacco products should not start using e-cigarette, or vaping, products.
- THC use has been associated with a wide range of health effects, particularly with prolonged frequent use. The best way to avoid potentially harmful effects is to not use THC-containing e-cigarette, or vaping, products.
- Persons engaging in ongoing cannabis use that leads to significant impairment or distress should seek evidence-based treatment by a healthcare professional.
- The e-cigarettes and e-liquid pods that we use in the current study are purchased only from a licensed retailer and do not contain CBD, THC, or Vitamin E Acetate. The pods we are giving you contain nicotine, solvents, and flavorings. At this time, we do not know what the risks associated with the use of the e-cigarettes and e-liquids, flavors, etc. that we use in this study are, and who might develop symptoms. However, despite these safety measures, it is possible you could still be affected.

  Although there is much research devoted to EVALI, the exact cause of this lung injury remains unknown. Therefore, we ask you to abstain from using tobacco and THC-containing products from unknown sources, as they may not comply with standards set by Good Manufacturing Practices and could contain contaminants. The symptoms of EVALI can include cough, shortness of breath, chest pain, nausea, vomiting, stomach pain, diarrhea, fever, chills, or weight loss. If you feel sick or experience any of these symptoms, contact the study team as soon as possible.

  We will assess your health at the intake to make sure you are healthy prior to participating and will continue to monitor your health closely during the study. If you experience any symptoms (such as abdominal pain, nausea, vomiting, diarrhea, cough, shortness of breath, chest pain) or have other concerns, please let us know and let your doctor know right away. Go to the emergency room right away if your symptoms are severe or increase rapidly. It is possible that the hospital may report cases of illness after using e-cigarettes to the State Health Department and the CDC. The report could contain the name and address of the person who is ill.

  In addition, e-cigarettes contain other chemicals besides nicotine including propylene glycol/vegetable glycol/vegetable glycerin. At this time, we do not know the risks associated with the propylene glycol/vegetable glycerin that may in the fillers in the liquids used in this study.

  It is important to note that there may be unforeseen risks (such as allergic reactions). Some people are allergic to propylene glycol. You should not participate if you are allergic to

propylene glycol. We will be using e-liquids that are made to be identical to e-cigarettes that are currently available commercially. Some research has indicated that in large doses propylene glycol and vegetable glycerin can be harmful. All levels of e-liquids administered in this research study are below any potentially harmful levels. You may experience burning or irritation when using the e-cigarettes. Research staff will monitor e-cigarette use during the lab session. If you feel any discomfort or need to stop for any reason, please let the researcher know. You can stop the session at any point.

Use of flavors: Currently, there is little known about the short and long-term effects of inhaling flavorants. There may be unforeseen risks (such as allergic reactions). We will be using e-liquids that are made to be identical to e-cigarettes that are currently available commercially with flavors doses like current commercial products. If you experience any side effects, you can stop the session at any point. Research staff will monitor e-cigarette use during the lab session. If you feel any discomfort or need to stop for any reason, please let the researcher know.

We will provide you with referral sources to quit e-cigarette use if you are interested.

3) **Nicotine administration:** Common side effects of nicotine include nausea, vomiting, heartburn, and elevated heart rate and blood pressure. You will be offered light snacks to reduce the incidence of nausea from nicotine administration that may be heightened by administration of nicotine on an empty stomach. Toxic doses of nicotine may cause abdominal pain, hyper salivation, diarrhea, dizziness, confusion, hearing and vision problems, fainting, seizures, hypotension (low blood pressure), irregular pulse, and death. However, these toxic effects occur at doses 40 to 50 times higher than those that will be used in this study. Also, since you are an e-cigarette user, it is not likely that you will experience side effects. Again, if you experience any side effects or feel uncomfortable, you can stop the session at any point.

4) **Urine and saliva collections:** Urine collections will be done at your intake appointment and lab session to measure the amount of cotinine in your body. Saliva samples will be collected during the lab sessions to determine nicotine and cotinine levels. This is done by chewing on a cotton salivette (swab) around in your mouth for thirty seconds. Urine and saliva sample collection is not risky.

5) **Tobacco Use and Drug use**: You will be asked about current and past use of illicit "street" drugs at the intake to rule out substance abuse. If you are currently using certain drugs, you may not be eligible to participate.

6) **Limits to confidentiality**: We do not reveal any personal information collected as part of the research procedures, including your reported tobacco use and other substance use history. However, there is always the possibility that if you participate in the study, others, including friends, may become aware of your tobacco use status. If you do not feel comfortable with this, you should not participate in the project.

7) **Rating scales and assessments:** These are all noninvasive and should add no risk. The major disadvantages are the time taken to complete them, and possible breach of confidentiality. You can choose not to answer any questions that may make you feel uncomfortable.

How will I know about new risks or important information about the study?

We will tell you if we learn any new information that could change your mind about taking part in this study.

How can the study possibly benefit me?
In this study we monitor for the symptoms of EVALI, which is a direct benefit for those who may be at risk for developing this condition. There are no other direct benefits of this study.

How can the study possibly benefit other people?
We expect that the results of the study, however, will benefit science and others through increasing our knowledge of how e-cigarette flavors alter vaping behavior.

Are there any costs to participation?
You will not have to pay for taking part in this study. The only costs include transportation and your time coming to the study visits.

Will I be paid for participation?
You will be paid for taking part in this study. You will be compensated $50 for the intake appointment and $100 for the lab session. Both payments will be cash. For the follow up phone call, you will be paid $25 in the form on an Amazon gift card or cash. You will be compensated $20/day for travel to in person appointments (up to a total of $40) if not utilizing travel services provided by the study (i.e., you will not receive travel payment if the study arranges a cab service to take you to your appointment. You are responsible for paying state, federal, or other taxes for the payments you receive for being in this study. Taxes are not withheld from your payments.

You may also earn a $25 referral bonus for each friend that you refer to participate in this study. To receive this bonus, your friend(s) must complete the intake appointment.

What are my choices if I decide not to take part in this study?
Instead of participating in this study, you can choose not to participate in this study.

How will you keep my data safe and private?
We will keep information we collect about you confidential. We will share it with others if you agree to it or when we must do it because U.S. or State law requires it. For example, we will tell somebody if we learn that you are hurting a child or an older person.

We understand that information about you obtained in connection with your health is personal, and we are committed to protecting the privacy of that information. If you decide to be in this study, the researcher will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and demographic information. This information will be de-identified at the earliest reasonable time after we receive it, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, and this link will be kept secure and available only to the PI or selected members of the research team. Any information that can identify you will remain confidential. The research team will only give this coded information to others to carry out this research study. The link to your personal information will be kept for 7 years after the conclusion of the study, after which time the link will be destroyed and the data will become anonymous. The data will be kept in this anonymous form indefinitely.
If you decide that you will be in this study, and you will be visiting the Connecticut Mental Health Center (CMHC) as part of your study procedures, some information about your

participation in this research study will become part of your CMHC medical record that identifies you. If you do not already have a medical record at CMHC, one will be made for your visit. This chart will say you are/were a research participant and had an EKG and lab work at the CMHC.

If you complete the laboratory portion of this study at the WCRU, a Yale New Haven Hospital medical record will also be created for you if you do not already have one. The information that will be entered into your YNHH medical record will include the following: name, contact information, social security number, and that you are participating in a research study. This record will be confidential.

When we publish the results of the research or talk about it in conferences, we will not use your name. If we want to use your name, we will ask you for your permission.

We may also share information about study results with other researchers for future research, but we will not use your name or other identifiers. This includes information like study urine or saliva samples, which will not have identifiable information on them. We will not ask you for any additional permission.

What Information Will You Collect About Me in this Study?

The information we are asking to use, and share is called “Protected Health Information.” It is protected by a federal law called the Privacy Rule of the Health Insurance Portability and Accountability Act (HIPAA). In general, we cannot use or share your health information for research without your permission. If you want, we can give you more information about the Privacy Rule. Also, if you have any questions about the Privacy Rule and your rights, you can speak to Yale Privacy Officer at 203-432-5919.

The specific information about you and your health that we will collect, use, and share includes:

- Research study records
- Medical and laboratory records of only those services provided in connection with this study.
- Records about phone calls made as part of this research
- Records about your study visits
- Information obtained during this research regarding
    - Assessments and questionnaires
    - The diagnosis and treatment of medical and/or mental health conditions
    - Use of illegal drugs or the study of illegal behavior
    - Records about any study e-cigarette you received

How will you use and share my information?

We will use your information to conduct the study described in this consent form.
We may share your information with:

- The U.S. Department of Health and Human Services (DHHS) agencies
- Representatives from Yale University, the Yale Human Research Protection Program and the Institutional Review Board (the committee that reviews, approves, and monitors research on human participants), who are responsible for ensuring research compliance. These individuals are required to keep all information confidential.
- The U.S. Food and Drug Administration (FDA) This is done so that the FDA can review information about e-cigarettes involved in this research. The information may also be used to meet the reporting requirements of drug regulatory agencies.
- The study sponsor
- Principal Investigator of the study

- Study Coordinator and Members of the Research Team
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study

We will do our best to make sure your information stays private. But, if we share information with people who do not have to follow the Privacy Rule, your information will no longer be protected by the Privacy Rule. Let us know if you have questions about this. However, to better protect your health information, agreements are in place with these individuals and/or companies that require that they keep your information confidential.

Why must I sign this document?

By signing this form, you will allow researchers to use and disclose your information described above for this research study. This is to ensure that the information related to this research is available to all parties who may need it for research purposes. You always have the right to review and copy your health information in your medical record. However, this is a double blinded study and if you sign this permission form, you will not be allowed to look at or copy your study related information until after the research is completed.

What if I change my mind?

The authorization to use and disclose your health information collected during your participation in this study will never expire. However, you may withdraw or take away your permission at any time. You may withdraw your permission by telling the study staff or by writing to Suchitra Krishnan-Sarin, PhD at the 34 Park Street, New Haven, CT 06511.

If you withdraw your permission, you will not be able to stay in this study but the care you get from your doctor outside this study will not change. No new health information identifying you will be gathered after the date you withdraw. Information that has already been collected may still be used and given to others until the end of the research study to ensure the integrity of the study and/or study oversight.

Who will pay for treatment if I am injured or become ill due to participation in the study?

You or your insurance carrier will be expected to pay the costs of this treatment. No additional financial compensation for injury or lost wages is available. You do not give up any of your legal rights by signing this consent form.

What if I want to refuse or end participation before the study is over?

Taking part in this study is your choice. You can choose to take part, or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

We would still treat you with standard therapy or, at your request, refer you to a clinic or doctor who can offer this treatment. Not participating or withdrawing later will not harm your relationship with your own doctors or with this institution.

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

The researchers may withdraw you from participating in the research if necessary. Examples of reasons the researchers might withdraw you includes:

- You do not follow directions of the study team
- The study team decides the study is not in your best interest

- You become pregnant, intend to become pregnant, or are nursing a child during this study.

What will happen with my data if I stop participating?

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

If you withdraw from the study, biological samples (for example, urine samples) that have been collected from you can be withdrawn if they have not yet been analyzed or destroyed. If you want your samples withdrawn, you must tell the study team before or at the time you leave the study.

Who should I contact if I have questions?

Please feel free to ask about anything you don't understand.

If you have questions later or if you have a research-related problem, you can call the Principal Investigator at 203-974-7595.

If you have questions about your rights as a research participant, or you have complaints about this research, you call the Yale Institutional Review Boards at (203) 785-4688 or email hrpp@yale.edu.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law (NCT03634839). 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.

Authorization and Permission

Your signature below indicates that you have read this consent document and that you agree to be in this study.

We will give you a copy of this form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date