NCT04449510

NAME:
DOB:
MRN#:

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: *"Short-Term Cardiovascular Effects of E-Cigarettes: Impact of E-Liquid pH"*

Principal Investigator:	Gideon St. Helen, PhD, Phone: 628-206-2687 Gideon.Sthelen@ucsf.edu

Clinical Research Coordinators:	Armando Barraza, Phone: 415-502-2465 Armando.Barraza@ucsf.edu

STUDY SUMMARY

Introduction: We are asking you to consider taking part in a research study conducted by Gideon St. Helen PhD at UCSF.

The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends and health care team.

Purpose of the study: The purpose of the study is to examine the effect of e-liquid pH on nicotine intake and the effects it will have on the body. We will have 3 different e-liquid pH levels to test.

Study Procedures: If you choose to be in this study, you will be given an e-cigarette with the e-liquid prepared that you will take at the hospital. In addition you must prepare to abstain from smoking 2 days before the study and the night before the visits. We will limit your caffeine intake to 1 cup of coffee or tea during the study day.

You will be in this study about 3 hours from screening, 7.5 hour study visits over the course of 3 days, and visit the research site approximately 5 times.

Possible Risks: There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

- Pain around venipuncture site
- Blood loss
- Trouble staying awake
- Coughing during sessions
- Headaches

There are also rare but serious risks of participation, like:

- Lung injury
- Burns and/or projectile injuries from e-cigarette device

We'll tell you about the other risks later in this consent form.

Possible Benefits: There will be no direct benefit to you from participating in this study.

Your Other Options: You do not have to participate in this study. Your other choices may include:

- Getting treatment or care for your condition without being in a study.
- Taking part in another study.
- Getting no treatment or receiving comfort care to relieve your symptoms and discomfort.

Please talk to your doctor about your choices before agreeing to participate in this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

DETAILED STUDY INFORMATION

This part of the consent form gives you more detailed information about what the study involves.

This is a research study about the impact of changes in e-liquid pH. The study researchers, Gideon St.Helen, PhD, Neal Benowitz, MD, and Peyton Jacob, PhD, from the University of California, San Francisco, Clinical Pharmacology Program of the Division of Cardiology, are conducting this study and the Clinical Research Coordinator will explain this to you.

Research studies include only people who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask the researchers.

You are being asked to take part in this study because you an exclusive user of e-cigarettes.

Why is this study being done?

The purpose of this study is to learn more about the effects e-liquid pH on nicotine exposure and how it could affect the heart and other cardiovascular outcomes.

This study is funded by the National Institutes of Health (NIH) and the Food and Drug Administration (FDA).

How many people will take part in this study?

About 21 people will take part in this study.

What will happen if I agree to donate my specimen?

If you agree to let researchers collect and store your specimens for future research, the following will happen:

- After all routine tests required for your care are finished, instead of discarding your leftover specimens we will save them in what is called a "tissue bank" for possible future research. We also will collect and save information from the study data collected during the study in which you have a non-identifiable form assigned to the data. This would mean we will not use your medical records with previous history to be used. This would be the non-identifiable study data from your written medical history during screening, involving vitals from nurses, vaping questionnaires, data from the e-cigarette device that detects number of puffs and the duration of puffs taken and data from the blood samples provided. We do not know for sure if your specimens or medical history will be used, but they might be used in research about heart disease or other cardiac diseases.
- We may give your specimens and certain medical information about you (for example, diagnosis, blood pressure, age if less than 85) to other scientists or companies not at UCSF, including to a controlled access government health research database, but we will not give them your name, address, phone number, or any other information that would identify you. Reports about any research will not be given to you or your doctor.
- Sometimes specimens are used for genetic research (about diseases that are passed on in families). Even if we use the specimen for genetic research, we will not put the results in your medical record. The research will not change the care you receive. Your specimen and any information about you will be kept until it is used up or destroyed. It may be used to develop new drugs, tests, treatments or products. In some instances these may have potential commercial value. Your personal health information cannot be used for additional research without additional approval from either you or a review committee.

- Your specimens will be kept until they have been used or are no longer needed. If you decide later that you do not want your specimens and information to be used for future research, you can notify the investigator in writing at tobaccocoord@ucsf.edu, and we will destroy any remaining identifiable specimens and information if they are no longer needed for your care. However, if any research has already been done using portions of your specimens, the data will be kept and analyzed as part of those research studies.

What risks are involved with donating specimens for research?

Confidentiality*:* Donating specimens may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically

secured. As with any use of electronic means to store data, there is a risk of breach of data security. Your name will not be used in any published reports from research performed using your specimen. Tobacco Biomarker Laboratory at ZSFG and select tissue bank staff members will have access to information attached to the non-identifiable number but they will not release any identifying information about you to researchers using your specimen. The UCSF Institutional Review Board and other University of California personnel also may see information about you to check on the tissue bank.

Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record.

Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk. Although your name will not be with the sample, it will have other facts about you such as given medical history from the written document during screening. These facts are important because they will help us learn if the factors that cause heart diseases to occur or get worse are the same or different based on these facts. Thus it is possible that study finding could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

What will happen if I take part in this research study?

If you agree, the following procedures will occur:

Screening Visit: This is an approximately 45-minute screening visit to see if you want to be in the study, and to see if you meet the qualifications to be in the study. You will first read this consent form and ask any questions you wish. After reading the consent form, you must sign it to continue the screening visit in order to be considered for participation in the study.

The following happens at the screening visit:

- **Forms:** You will be asked to fill out forms to provide information about yourself (including age, racial/ethnic background, medical and social history, use of prescription and over-the-counter medications, and the use of nicotine, tobacco, and alcohol, caffeine, and recreational drugs). In addition, there are several forms specifically about your vaping/smoking behavior, history, and dependence on nicotine.
- **Physical Data:** Your height, weight, heart rate, and blood pressure will be collected.
- **Saliva Sample:** You will be asked to give a saliva sample for laboratory test to confirm that you are a user of e-cigarettes.
    - If our tests of your saliva show that you **are not** a regular user of e-cigarettes, **you will not be** compensated for this screening visit.
- **Urine Sample:** A sample of your urine will be collected for:
    - **Drug Testing**
        - If the results are positive for substances other than marijuana or prescribed drugs, you **will not be eligible** to participate in the study. **You will be**

dismissed without compensation, and your urine will be discarded. However, if you would like to rescreen for the study at a later time (within 30 days) we will give you the option to schedule another screening visit. Results must be negative at that time for you to receive compensation for the visit and continue in the study if otherwise eligible.
    - If the results are positive for marijuana, you will continue to be evaluated for eligibility.
    - If the results are positive for prescribed drugs, you will continue to be evaluated for eligibility.
- **Pregnancy Test** (if applicable)
  If the results are positive for pregnancy, you **will not** be eligible to participate in the study. You will be compensated for the screening visit and your urine will be discarded.
- **E-Liquid Sample**: A sample of your regularly used e-liquid will be collected for:
    - Comparison of the e-liquid you regularly use and the e-liquid for the study. This will denote the baseline of habitual use.

If the screening visit shows that you are eligible to participate in the study and you choose to continue, this is what will happen next:

Throughout the study: We will keep in touch with you via your cell or home phone through calls or texts. Please note that text messages are not a secure form of communication; we will have backup contact methods should there be additional contact. Some of the things we may contact you about are visit reminders, clarifications of any medications you are taking, or questions about the products that you are using.

Orientation Visit: You will be asked to come back to the UCSF Tobacco Research Center for an Orientation Visit. At this visit, we will prepare you for the main study procedure at the hospital research ward. There will be no payment during this portion of the study.

- We will ask that you do not use any marijuana or other recreational drugs from the Orientation Visit until the study is completed.
- We will ask that you **abstain from using any e-cigarettes or tobacco products the night before** your admission date, starting at 10:00 P.M.
- You will be randomly assigned to a schedule of 3 different e-liquid pH levels. You will not know which pH condition you are assigned to for each study visit.
- During the main study procedures at the hospital, you will be using a study e-cigarette device and e-liquid that we will provide.

Study Out-patient Procedures: You will be admitted to the **Zuckerberg San Francisco General Hospital** (ZSFG) Clinical Research Center or the UCSF Moffitt Hospital as an outpatient for 3 study visits. All out-patient study visits will be conducted from around 7 AM - 4 PM.

Upon admission, you will have a pregnancy test (if female), medical history, and brief vital assessment conducted by the nurses during intake. This is required for all hospital admissions and these documents will become part of your permanent ZSFG/UCSF medical record.

- (if female) Pregnancy testing: If the results are positive for pregnancy, you will no longer be eligible to participate. You will be compensated for travel and dismissed.

Study Visits #1-3:
The devices you will use during these study visits will be Paranormal DNA 250C Mod and Joytech Cubis Pro Tank.

On each day of your out-patient stay, the following will occur:

You will be admitted to the hospital research ward at **7:00 AM** after an overnight abstinence from e-cigarettes starting at 10:00 PM.

1. At the time of admission to the hospital ward, expired carbon monoxide (CO) will be measured. If your expired CO is beyond the required limit, you will be given the option to delay procedure until your levels decrease or you will be sent home without pay.
2. You will be in a hospital-approved smoking/vaping room with negative pressure and a fan ventilating to the outside.
3. At about **8:00 AM**, an intravenous catheter will be placed in one of your forearms for blood drawing during the study.

Standardized E-Cigarette Vaping Session

4. At **9:00 AM**, you will vape the study-provided e-cigarette at your assigned e-liquid pH level in a standardized protocol:
    a. One 4-second puff every 30 seconds for a total of 10 puffs.
    b. A voice recording will guide you through the session.
5. After this session, you will begin a 4-hour abstinence period.
6. Heart rate will be measured before vaping and at 5, 10, 20, 25, and 30 minutes after the vaping session.
7. Blood drawing (venipuncture): Blood nicotine samples will be drawn before vaping and then at 2, 5, 15, 30, 45, 60, 90, 120, 180, and 240 minutes after the standardized vaping session. Each sample will be approximately a teaspoon.
8. Blood drawing (venipuncture): Blood catecholamine samples will be drawn before vaping and then at 5 minutes after the standardized vaping session. Each sample will be less than a teaspoon.
9. There will be a total of 13 blood draws for this session and a total of 39 for the whole study.
10. Skin blood flow will be measured with a handheld laser instrument on your right foot at 10 minutes before and 5 and 30 minutes after vaping.
11. You will fill out questionnaires immediately, 2 hours, and 4 hours after the vaping session.

90-minute ad libitum Session

12. At the end of the abstinence period, you will start the 90-minute *ad libitum*, or "free use vaping", session where you will have access to the study-provided e-cigarette at the same assigned e-liquid pH as during the standardized vaping session.
13. Blood drawing (venipuncture): Blood samples will be collected before and every 15 minutes from the beginning of the session. There will be a total of 6 blood draws for this session and a total of 18 for the whole study.

14. You will fill out questionnaires before and immediately after the session ends.
15. This "free vaping" session will be video recorded with audio to measure "vaping topography" (i.e., puff number and duration) using a frame-by-frame analysis.
16. You will be discharged after the *90-minute ad libitum Session*

Study Schedule:

Study Arm #1: e-liquid pH level 5.7, 7.4, or 8.7
← ---------- **Day 1**---------- →
❖ **Standardized Session for pH measurement** ❖ **4 hour abstinence and blood draws** ❖ **Followed by 90 minute Free use session w/ video monitoring**

Study Arm #2: 1 of the other 2 remaining e-liquid pH levels
← ---------- **Day 2** ---------- →
❖ **Standardized Session for pH measurement** ❖ **4 hour abstinence and blood draws** ❖ **Followed by 90 minute Free use session w/ video monitoring**

Study Arm #3: 1 of the other 2 remaining e-liquid pH levels
← ---------- **Day 3** ---------- →
❖ **Standardized Session for pH measurement** ❖ **4 hour abstinence and blood draws** ❖ **Followed by 90 minute Free use session w/ video monitoring**

- **Study locations:** The Screening and Orientation Visits will take place at the UCSF Tobacco Research Center (Building 100, Room 261) and the Outpatient Study days will

take place at the CTSI-CRS (5B Research Ward, 5th Floor) at Zuckerberg San Francisco General Hospital (1001 Potrero Avenue).

How long will I be in the study?

Participation in the study will consist of a Screening Visit (~45 minutes), Orientation Visit (1 hour), and a total of 3 outpatient days (7.5 hours) over a total of **5 days**.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell the Clinical Research Coordinator, your CTSI-CRS nurse, the Study Physician, or the Principal Investigator right away if you are thinking about stopping or wish to stop being in the study.

The Clinical Research Coordinator, Study Physician, or the Principal Investigator may stop you from taking part in this study at any time if he or she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

In rare cases, people are unable to give blood even if a catheter is placed correctly. If this happens while you are on the study, the Study Physician may stop you from continuing the study. You would be compensated for that study day and withdrawn from the study.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

Everyone taking part may have side-effects while on the study. If you develop side-effects, your participation in the study may be stopped, depending on the severity.

You should talk to the Clinical Research Coordinator, your CTSI-CRS nurse, or the Study Physician about any side-effects you experience while taking part in the study.

Risk and side-effects related to the study procedures include:

- **Venipuncture and Catheterization:** A catheter (small plastic tube) will be placed in a vein in one forearm in order to make it easier to take the multiple blood samples. The

catheter will remain in place for about 7 hours. **Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.**

- Blood Loss: You will give a total of about less than 2 cups of blood during the study. This amount of blood loss poses no risk to healthy individuals.
- Inconvenience: The study procedures may be inconvenient and tedious (filling out forms, spending time in the hospital, providing samples, etc.) and you may have trouble staying awake as required.
- Withdrawal Symptoms: During abstinence, you may feel uncomfortable, irritable, restless, or have difficulty concentrating due to possible nicotine withdrawal. This may result in headaches, nausea, fatigue, or changes in mood.
- Blood Pressure and Heart Rate Measurement(s): You may also feel uncomfortable when getting your blood pressure taken depending on the tightness of the cuff. In obtaining your blood pressure and heart rate we may find that you have an abnormal blood pressure and/or heart rate.
- Electronic Cigarettes (i.e., e-cigarettes, vaporizers, etc.): Although long-term consequences or effects are uncertain, a 2018 report from the National Academies of Sciences show that use of e-cigarettes could increase dependence on e-cigarettes; cause increased levels of blood pressure and heart rate; increase coughing and wheezing; exacerbate asthma symptoms; increase risk of ever using combustible tobacco cigarettes among youth and young adults; increase exposure to e-cigarette aerosols that can increase risk of cancer and adverse reproductive outcomes. Additionally, e-cigarettes devices can explode and cause burns and projectile injuries (risk if significantly increased when batteries are of poor quality, stored improperly, or are being modified by users). Intentional or accidental exposure to e-liquids (from drinking, eye contact, or skin contact) can result in adverse health effects including, but not limited to seizures, anoxic brain injury, vomiting, and lactic acidosis; intentionally or unintentionally drinking or injecting e-liquids can be fatal.
- Lung Injury: As of February 25, 2020 the CDC, FDA and state health have identified the cause of e-cigarette or vaping product use associated lung injury, EVALI. Most of these cases have occurred while vaping informal THC products with vitamin e acetate from friends, family in-person and online dealers. Some may have occurred while vaping nicotine with insufficient evidence to rule out other chemicals of concern. Per CDC guidelines the risks of lung damage from vaping e-liquids from reputable retailers such as AVAIL, where we purchased the e-liquids used in this study, are thought to be low.
- Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important to understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Pregnancy testing will be required the day of screening and the morning of the study visit.
- Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.
- Video Recording: Participants will be video-recorded with audio during the 90 minute free use vaping portion of the study. This portion of the study is not optional. Recordings

are immediately stored on an encrypted hard drive and then removed from the video recording device.

- **Survey Questionnaires:** You will be asked to answer personal and private questions during this study, including about your medical history, drug and alcohol use, breath sample measurements, urine tests of drug use and pregnancy, and questionnaires about your mood. Answering these personal questions could make you feel uncomfortable.
- **Breach of Confidentiality:** The only risk of this interview is your loss of privacy if other people find out about your results. All efforts are made to keep your information confidential, but confidentiality is not absolute.

For more information about risks and side-effects, ask one of the researchers.

Are there benefits to taking part in the study?
There will be no direct benefit to you from participating in this study. However, the information that you provide will contribute to the novel data that may help health professionals better understand the health consequences of e-cigarette use.

What other choices do I have if I do not take part in this study?
You are free to choose not to participate in the study. You may also choose to take part in another study. If you decide not to take part in this study, there will be no penalty to you. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

Will information about me be kept private?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. If you do not have a UCSF medical record, one will be created for you. Your signed consent form and some of your research tests will be added to your UCSF medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records but will not be added to your medical record. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

We will do our best to make sure that the personal information gathered for this study is kept private. However, we cannot guarantee total privacy. Your personal information may be given

out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your research records for research, quality assurance, and data analysis included: the University of California (UCSF), the National Institute of Health (NIH), and the Food and Drug Administration (FDA).

Certificate of Confidentiality: To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institute of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings

Exceptions: A Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information about you, without your consent. For example, we will voluntarily disclose information about incidents such as child abuse, and intent to hurt yourself or others. In addition, 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 an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. Finally, the Certificate may not be used to withhold information from the Federal government needed for auditing or evaluating federally funded projects or information needed by the FDA.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other health care providers may see your test results and become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

Two kinds of "charts are created when you take part in one of our studies:

1. A medical record at *Zuckerberg San Francisco General Hospital* or the *UCSF Moffitt Hospital* will be created because of your participation in this stud. Your consent form, hospital nursing forms, and some of your hospital laboratory test results will be included in this record. Therefore, other health care providers may see your test results and become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially. The forms you will fill out during your screening visit, many of the forms filled out during the study, the generic testing results, and the results of assays on the biological specimens collected on the study will not become part of your hospital records.
2. We make a "research chart" specifically to hold the forms, sample testing results, and video-recording that do not appear in the ZSFG medical record. You will be given a unique study identification number that will be used in this research chart and on your study samples. This number is different from your medical record number. While the study is in process. We keep some identifying information in this chart, so that we are able to contact you, process payments, etc. Once the study is completed, identifying information is removed from the chart and stored separately where it is only available to research personnel who need access to it. Charts and samples are always kept in locked

rooms. We keep the link between your identity and your study number and your samples (if you allow us to keep them) for several reasons. We may want to contact you (with your agreement) to see if you want to participate in additional studies. We also need to keep track of when a subject participates in more than one study so that certain tests are not repeated. Or you may want to contact us later to ask that your samples be destroyed, and we cannot do this unless we know the link to your research number.

Are there any costs to me for taking part in this study?

No. The sponsor has agreed to pay for all items associated with this research study; you or your insurer will not be billed.

Will I be paid for taking part in this study?

In return for your time today, you will be paid $30 to be screened for this study, however you **MAY NOT RECEIVE payment for the visit if:**

- You ARE NOT interested in consenting, screening for this visit, or completing the study
- If there are discrepancies between your email/phone screen responses and your responses today
- If our test show that you ARE NOT an exclusive user of e-cigarettes

In return for your time and effort in study participation, you will be compensated a total of $1,430 if all parts of the study are completed. This includes the following:

- Screening Visit: $30
- Study Visit #1 (1 day Outpatient): $350
- Study Visit #2 (1 day Outpatient): $350
- Study Visit #3 (1 day Outpatient): $350
- Bonus for completion of study: $350

Your expired carbon monoxide must be below 5 ppm on the day of your admission and you must abstain from using e-cigarette and/or other tobacco and nicotine products from 10PM to 7AM the night before your hospital admission and you must have a 48 hour abstinence from tobacco products.

A check will be mailed to you after your completion of each portion of the study and it may take up to 4-6 weeks for you to receive your check. You should be aware that the income you receive from being in the study may need to be reported to the IRS on your income tax return. If you receive more than $600 in a calendar year, the income will be reported to the IRS and an IRS

Form 1099 will be sent to you. You will need to provide your home address and social security number for reporting purposes and to receive payment.

If your *payment checks are not received by the end of 6 weeks* from the last day of your study visit for that portion of the study, please contact *Lisa Lawrence* at 415-502-2465.

What happens if I am injured because I took part in this study?

It is important that you tell the study personnel if you become sick or injured. You may directly tell the Clinical Research Coordinators, the Clinical Research Supervisor (Sundos Yassin at 628-206-8955), the Study Physician (Neal Benowitz at 628-206-8324), or the Principal Investigator (Gideon St. Helen, PhD at 628-206-2687) if you feel that you have been injured because of taking part in this study.

> **Treatment and Compensation for Injury:** If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor National Institutes of Health, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make. There will be no penalty to you in any way. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to the Clinical Research Coordinator, the Clinical Research Supervisor (Sundos Yassin at 628-206-8955), the Study Physician (Neal Benowitz at 628-206-8324), or the Principal Investigator (Gideon St. Helen, PhD at 628-206-2687) about any questions, concerns, or

complaints you have about this study. *If your payment check is not received by the end of 6 weeks from the last day of your study, please contact your study coordinator.*

For questions about your rights while taking part in this study, you may call the Office of the Institutional Review Board (a group of people who review the research to protect your rights) at **415-476-1814.**

A description of this clinical trial will be available at http://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 website at any time.

OPTIONAL RESEARCH

Please note: This section is optional and these choices will not affect your participation in this study.

Re-contact for Future Studies: The researchers in the Clinical Pharmacology Program of the Division of Cardiology at UCSF would like to know if you are interested in participating in future studies for which you may be eligible. By initialing this section of the form, you are giving them permission to keep a file of your information (name, contact information, date of birth, laboratory results, and completed questionnaires) and to re-contact you. You will be under no obligation to actually participate in any new study, and whether or not you initial this section will have no effect on your participation in the current study. You may withdraw permission to be re-contacted at any time by calling the research coordinator or emailing research staff at tobaccocoord@ucsf.edu.

_____I ***DO*** agree to allow the researchers in the Clinical Pharmacology Program of the Division of Cardiology at UCSF to keep my information on file as described above so that I may be re-contacted for possible participation in future nicotine and/or smoking related studies for which I may be eligible.

_____I ***DO NOT*** agree to allow the researchers in the Clinical Pharmacology Program of the Division of Cardiology at UCSF to keep my information on file as described above so that I may be re-contacted for possible participation in future nicotine and/or smoking related studies for which I may be eligible.

Specimen Storage: Your agreement to allow your leftover blood and urine samples to be used in any future research is voluntary, and if you choose not to participate it will in no way affect your participation in the current study. These samples may be used for other research not related to this study. These samples will be retained in non-identifiable form, meaning that there will be no information associated with the blood or urine samples that will allow anyone to know your identity. The samples will be stored at the Tobacco Biomarker Laboratory at ZSFG and they will be kept until they are used up or no longer needed. Only UCSF researchers or other academic institutions working in collaboration with the study investigators will be allowed to access to the samples and data. The samples may be used in the development of tests, products, or discoveries that may have potential commercial value, you will not share in any financial benefits. You may at any time ask to have your samples withdrawn from research use by emailing research staff at tobaccocoord@ucsf.edu, and any non-identifiable samples and associated data still in their possession will be destroyed. Please indicate whether you are willing to allow your samples to be saved and used for future research by initialing one of the lines below:

_____ ***Yes,*** the researchers may keep my blood and urine samples for future related research.

_____ ***No,*** I do not want my blood and urine samples used for any research tests other than those needed for the main research study.

Research results: There may be times when researchers using your information and/or specimens may learn new information. The researchers may or may not share these results with you, depending on a number of factors.

Methods of Contact: Throughout the study the clinical research coordinator will keep in contact with you about visit reminders, questions, concerns, or clarification. Please indicate the preferred method of communication below. Number 1 – 3 with 1 being the preferred method and 3 being the least. Note that texting is not a secure form of communication. If any of these change during the study inform the clinical research coordinator. This portion is not optional.

_____ Phone Number for Texting:_____ _____ _____ _____

_____ Phone Number for Calling: _____ _____ _____ _____

_____ Email: _____ _____ _____ _____ _____ _____

****

CONSENT

You have been given a copy of this consent form and the Experimental Subject's Bill of Rights to keep.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled. If you are a student or employee of the University, refusal or withdrawal will not affect your grades or your employment status.

If you wish to participate in this study, you should sign below. In addition, you will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent

- Blood Loss: You will give a total of about less than 2 cups of blood during the study. This amount of blood loss poses no risk to healthy individuals.
- Inconvenience: The study procedures may be inconvenient and tedious (filling out forms, spending time in the hospital, providing samples, etc.) and you may have trouble staying awake as required.
- Withdrawal Symptoms: During abstinence, you may feel uncomfortable, irritable, restless, or have difficulty concentrating due to possible nicotine withdrawal. This may result in headaches, nausea, fatigue, or changes in mood.
- Blood Pressure and Heart Rate Measurement(s): You may also feel uncomfortable when getting your blood pressure taken depending on the tightness of the cuff. In obtaining your blood pressure and heart rate we may find that you have an abnormal blood pressure and/or heart rate.
- Electronic Cigarettes (i.e., e-cigarettes, vaporizers, etc.): Although long-term consequences or effects are uncertain, a 2018 report from the National Academies of Sciences show that use of e-cigarettes could increase dependence on e-cigarettes; cause increased levels of blood pressure and heart rate; increase coughing and wheezing; exacerbate asthma symptoms; increase risk of ever using combustible tobacco cigarettes among youth and young adults; increase exposure to e-cigarette aerosols that can increase risk of cancer and adverse reproductive outcomes. Additionally, e-cigarettes devices can explode and cause burns and projectile injuries (risk if significantly increased when batteries are of poor quality, stored improperly, or are being modified by users). Intentional or accidental exposure to e-liquids (from drinking, eye contact, or skin contact) can result in adverse health effects including, but not limited to seizures, anoxic brain injury, vomiting, and lactic acidosis; intentionally or unintentionally drinking or injecting e-liquids can be fatal.
- Lung Injury: As of February 25, 2020 the CDC, FDA and state health have identified the cause of e-cigarette or vaping product use associated lung injury, EVALI. Most of these cases have occurred while vaping informal THC products with vitamin e acetate from friends, family in-person and online dealers. Some may have occurred while vaping nicotine with insufficient evidence to rule out other chemicals of concern. Per CDC guidelines the risks of lung damage from vaping e-liquids from reputable retailers such as AVAIL, where we purchased the e-liquids used in this study, are thought to be low.
- Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important to understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Pregnancy testing will be required the day of screening and the morning of the study visit.
- Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.
- Video Recording: Participants will be video-recorded with audio during the 90 minute free use vaping portion of the study. This portion of the study is not optional. Recordings