NAME:
DOB:
MRN#:

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

**Study Title:** *"Short-Term Cardiovascular Effects of E-Cigarettes: Influence of Device Power"*

This is a research study about the effects of the battery power in electronic cigarettes. The study researchers, Gideon St. Helen, PhD, Neal Benowitz, MD, and Peyton Jacob, PhD, from the University of California, San Francisco Department of Medicine, are conducting this study and the Clinical Research Coordinator will explain this study to you.

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

You are being asked to take part in this study because you are an exclusive user of e-cigarettes who vapes at least 25 days in the month.

## Why is this study being done?

The purpose of this study is to learn more about the impact of electronic cigarette device power on nicotine exposure and how it could affect the heart and other cardiovascular symptoms.

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 take part in this research study?

If you agree, the following procedures will occur:

Screening Visit: This is an approximately 2 hour 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 and ask any questions you wish. After reading the consent, 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, 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.
- **Expired Carbon Monoxide (Expired CO):** You will be asked to breathe into a machine that records how much carbon monoxide is present in your lungs, in order to confirm your smoking status. If the testing indicates that you are a regular user of tobacco products other than e-cigarettes (e.g., a tobacco cigarette smoker), you will be considered **ineligible and dismissed without payment**.
- **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 Testing** (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 sample will be discarded.

If the screening exam 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. Some of the things we may contact you about are visit reminders, clarifications of any medications you are taking, or questions about the products 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.

- 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 the night before** your admission date, starting at 10:00 P.M.

- You will be randomly assigned to a schedule of 3 different battery power levels. You will not know which level 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 liquid that we will provide
    - E-cigarette Device: The delivery device will be CUPTI™ made by KangerTech. It is a variable wattage all-in-one device with an operating wattage of 7.0–75.0 W.
    - E-liquid Selection: We will obtain the e-liquid from AVAIL, a leading premium e-liquid manufacturer and retail business which works with academic centers to provide research grade products.

Study In-patient Procedures: You will be admitted to **the Zuckerberg San Francisco General Hospital** (ZSFG) Clinical Research Center or the UCSF Moffitt Hospital as an inpatient for 3 separate study visits, for 2 nights each.

During the admission, you will have a pregnancy test (if female), medical history, and physical examination conducted by the Study Physician or a Nurse Practitioner. This is required for all hospital admissions and these documents will become part of your permanent ZSFG/UCSF medical record. If you wish, the results of your physical examination will be shared with you by the health care provider.

**Study Visits #1-3:**
On Day #1 of each of your in-patient stays, 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 CO will be measured. If your expired CO is beyond the required limit, you will be sent home.
2. You will be in a hospital-approved 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.
4. A light breakfast will be served.

*Standardized E-Cigarette Vaping Session*

5. At **9:00 AM**, you will vape the study-provided e-cigarette at your assigned power 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.
6. After each puff, you will exhale into a gas trap to determine the amount of nicotine exhaled.
7. After this session, you will begin a 4-hour abstinence period.

*4-Hour Abstinence*

8. Heart rate will be measured before and at 5, 10, 20, 25, and 30 minutes after the vaping session.
9. Blood samples will be drawn before and then at 2, 5, 15, 30, 45, 60, 90, 120, 180, and 240 minutes after the standardized vaping session.

10. You will fill out questionnaires immediately, 2 hours, and 4 hours after the vaping session.
11. At the end of the abstinence period, you will start the 90-minute *ad libitum*, or "free vaping", session where you will have access to the study-provided e-cigarette at the same assigned power level as during the standardized vaping session.

*90-minute ad libitum Session*

12. Blood samples will be collected before and every 15 minutes from the beginning of the session.
13. You will fill out questionnaires before and immediately after the session ends.
14. This "free vaping" session will be recorded to measure "vaping topography" (i.e., puff number and duration) using a frame-by-frame analysis.

On Day #2 of each of your in-patient stays, the following will occur:

1. You will wear a 24-hour ambulatory blood pressure and heart rate monitor to measure and record blood pressure and heart rate throughout the day (8:00 am – 8:00 am)
2. You will be free to vape with the study-provided e-cigarette with the assigned power level from 8:00 am to midnight.
    a. The time of each puff will be recorded by using a provided study diary (smartphone app or paper).
3. You will fill out questionnaires 4 times throughout the day:
    a. 8:00 am
    b. 12:00 pm (noon)
    c. 4:00 pm
    d. 8:00 pm
4. You will be collecting urine samples throughout the day.
5. Blood samples will be drawn every 4 hours from 8:00 am to midnight and once more at 8:00 am, the next morning.
6. You will be discharged in the morning after.

**Study Schedule:**

| **Study Visit #1: Assigned power level of 10, 35, or 70 watts (computer randomized)** | |
|---|---|
| **Day 1** | **Day 2** |
| **←---------- HOSPITAL ----------→** | |
| • **Standardized Session**<br>• **4-hr abstinence and blood draws**<br>• **Followed by 90 min Free use session w/ video monitoring** | • **Free use**<br>• **24-hr CV monitoring**<br>• **Circadian blood draws**<br>• **24-hr urine collection** |

| **Study Visit #2: Assigned 1 of the other 2 remaining power levels (computer randomized)** | |
|---|---|
| **Day 1** | **Day 2** |
| **←---------- HOSPITAL ----------→** | |
| • **Standardized Session**<br>• **4-hr abstinence and blood draws**<br>• **Followed by 90 min Free use session w/ video monitoring** | • **Free use**<br>• **24-hr CV monitoring**<br>• **Circadian blood draws**<br>• **24-hr urine collection** |

| **Study Visit #3: Assigned remaining power level (computer randomized)** | |
|---|---|
| **Day 1** | **Day 2** |
| **←---------- HOSPITAL ----------→** | |
| • **Standardized Session**<br>• **4-hr abstinence and blood draws** | • **Free use**<br>• **24-hr CV monitoring** |

| | |
|---|---|
| • **Followed by 90 min Free use session w/ video monitoring** | • **Circadian blood draws**<br>• **24-hr urine collection** |

- **Study locations:** The Screening and Orientation Visits will take place at the UCSF Tobacco Research Center (3130 20th Street, Suite 308) and the Inpatient Study Days will take place at the CTSI-CRS (5B Research Ward) at Zuckerberg San Francisco General Hospital (1001 Potrero Avenue, 5th floor) or at the UCSF Moffitt Hospital (505 Parnassus Avenue, 12th Floor).

## How long will I be in the study?

Participation in the study will consist of a screening visit (1-2 hours), Orientation visit (1-2 hours), and a total of 6 inpatient days for a total of **8 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.

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

You 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 10 hours. There is a small risk of pain, swelling, bruising, or infection.
- **Blood Loss:** You will give a total of about 1 cup 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-cigarette devices can explode and cause burns and projectile injuries (risk is 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.[1]
- **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 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. 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.

[1]http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx

## Will information about me be kept private?

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 include: the UCSF Institutional Review Board (IRB), the National Institutes 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 Institutes 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 study. 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 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 and sample testing results 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 on to ask that your samples be destroyed, and we cannot do this unless we know the link to your research study 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 this 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 tests 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 $1,830 if all parts of the study are completed. This includes the following:

- Screening Visit: $30
- Study Visit #1 (2 nights Inpatient): $440
    - Abstaining the night before hospital admission: $40
- Study Visit #2 (2 nights Inpatient): $440
    - Abstaining the night before hospital admission: $40
- Study Visit #3 (2 nights Inpatient): $440
    - Abstaining the night before hospital admission: $40
- Bonus for completion of study: $360

You will be compensated $40 for abstaining before each hospital admission if your expired carbon monoxide is below 5 ppm and if you also haven't used any e-cigarette and/or tobacco products, indicating overnight abstinence from 10pm to 7am hospital admission.

A check will be mailed to you after 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 *Ms. Patricia Winston* at 415-206-8326.

## 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 Coordinator, the Project Manager (Natalie Nardone, PhD at 415-514-1450), the Study Physician (Delia Dempsey, MD at 416-641-1465) or the Principal Investigator (Gideon St. Helen, PhD at 415-206-2687) 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, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University does 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 Project Manager (Natalie Nardone, PhD at 415-514-1450), the Study Physician (Delia Dempsey, MD at 416-641-1465), or the Principal Investigator (Gideon St. Helen, PhD at 415-206-2687) 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 Ms. Patricia Winston at 415-206-8326.*

**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.

***Re-contact for Future Studies:*** The researchers in the Division of Clinical Pharmacology and Experimental Therapeutics 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 agree to allow the researchers in the Division of Clinical Pharmacology and Experimental Therapeutics 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.

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## 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 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 |