NCT# 02955329

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

Study Title: "*Vaping THC from Electronic Cigarettes: a Novel Evaluation of Intake and Pharmacokinetics"*

This is a research study about the intake and effect of cannabis when vaped alone, and in combination with tobacco. The study researchers Neal Benowitz, MD and co-investigators, Gideon St. Helen, PhD and Peyton Jacob III, PhD from the Department of Medicine, University of California San Francisco and Zuckerberg San Francisco General Hospital (ZSFG), are conducting this research. 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 a healthy adult who smokes tobacco cigarettes and uses cannabis.

Why is this study being done?

The purpose of this study is to learn more about the safety of orally vaping cannabis (THC) and nicotine. This study will provide more information about the health effects of THC alone, as well as when combined with nicotine, by observing key markers in your blood and urine.

This study is funded by the National Institutes of Health (NIH).

How many people will take part in this study?

About 14 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 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 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 use of nicotine products, alcohol, caffeine and recreational drugs). In addition, there are several forms specifically about your tobacco cigarette use and cannabis use, smoking behavior, and history and dependence on nicotine and cannabis.
- **Physical Data**: Your height, weight, heart rate, and blood pressure will be measured.
- **Saliva Sample:** You will be asked to give a saliva sample for laboratory testing to confirm that you use cigarettes.
- **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, which will help determine your smoking status.
- **Urine Sample:** A sample of your urine will be collected for:
    - **Drug Testing**
        - If the results show that you have used substances other than cannabis or prescribed drugs, you **will not be eligible** to participate in the study. **You will be dismissed without payment,** 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 one re-screening visit.
        - If the results show that you have not used cannabis, you **will not be eligible** to complete the study. **You will be dismissed without compensation, and your urine will be discarded**.
    - **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.
- **Tobacco Cigarettes:** You have been asked to bring your usual tobacco cigarettes so that we can correctly identify the type you use regularly. We will take photographs of the product.
- **Cannabis Product:** You have been asked to bring your usual cannabis products so that we can correctly identify the type of product that you typically use. We will take photographs of the product.

Orientation Visit: If eligible, once our lab analyzes your saliva sample and confirms that you are a regular user of tobacco cigarettes, you will be asked to come back to the UCSF Tobacco Research Center for an Orientation Visit. The Orientation Visit will be conducted at least 48 hours before Study Day 1. The following will occur at your Orientation Visit:

- **Drug Testing**
    - If the results are positive for substances other than cannabis or prescribed drugs, you **will not be eligible** to participate in the study. **You will be dismissed without payment,** and your urine will be discarded.
- We will review study procedures with you, and do a practice session to prepare you for the gas trap procedure.

- We will ask you to provide a baseline urine sample.
- We will ask you to **not use cannabis or cannabis-containing products from 6pm the night before each hospital admission.**
- We will ask you to **not use any nicotine products from 6pm the night before each hospital admission.**
- We will ask you to **not use any cigars, cigarillos or blunts from products from 6pm the night before each hospital admission.**
- We will ask you to **not use any recreational drugs from today until the study is completed.**

Outpatient Study Visits:

- All outpatient study visits will be conducted at ZSFG from 7am-3pm.
- Upon admission, you will have a drug test, 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 medical record.
    - **Drug testing:** If the results show that you have used substances other than cannabis or prescribed drugs, **you will be dismissed without payment,** and your urine will be discarded.
    - **(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.
- At each visit, you will vape cannabis leaves and/or tobacco using the PAX loose-leaf vaporizing device (or "vape pen").
    - Following a predetermined order, you will be vaping cannabis leaves alone, tobacco leaves alone, and cannabis leaves combined with tobacco leaves. We will not tell you which study product you are using.
    - We will provide the PAX vape pen, cannabis, and tobacco leaves for you to use during your outpatient study visits. You will return all study products to us before you are discharged each day.
    - Although the PAX vaporizer device is commercially available, this device has not been reviewed or approved by the FDA. The potential risks of the PAX vaporizer are unknown.
- This outpatient study visits will last approximately 8 hours.

Outpatient Hospital Admissions

Upon arriving at the research ward, the following will occur:

1. You will be asked to arrive to the research ward at 7am.
2. Nurses will ask you when you last smoked or used THC. **If you used any nicotine or cannabis products less than 12 hours before either admission, you will be dismissed from the study.**
3. You will be asked to breathe into a machine to see when you have last smoked. **If your CO reading is greater than 5 ppm, you will be dismissed from the study**.

4. A pregnancy test will be administered to female participants. **If the pregnancy test is positive, you will be dismissed from the study**.
5. A drug test will be administered. If the results show that you have used substances other than cannabis or prescribed drugs, **you will be dismissed without payment.**
6. At the time you are admitted, any nicotine and cannabis products you possess will be taken away, stored by study staff, and returned after discharge.

Outpatient Hospital Procedures

1. You will be given a light breakfast, and you may drink decaffeinated beverages such as coffee or tea. You will also be given liquids (water) in preparation for a urine sample.
2. At about 8:20 AM a plastic catheter will be inserted into a forearm vein for blood sampling. A blood sample, urine sample, your heart rate, and your skin temperature will be taken and you will fill out a questionnaire packet.
3. At approximately 8:40 AM you will begin your standardized vaping session where you use the PAX to vape either cannabis leaves alone, cannabis and tobacco leaves, or tobacco leaves alone.
    - You will take puffs out of the PAX at regular intervals. During the vaping session, the amount of THC and nicotine you inhale will not exceed 1 mg, each. Upon finishing the vaping session, the PAX device will be returned to study staff.
4. On select study days, you will be asked to blow into the "gas trap" during your vaping standardized session. On these study days, you will exhale into a sterile mouthpiece which will trap the exhaled aerosol into a bottle of solution.
5. Following the vaping session, the following will samples and data will be collected:
    - 6mL blood samples will be taken at regular time points (2, 5, 15, 30, 45, 60, 90, 120, 180, and 360 minutes after vaping)
    - Your heart rate will also be measured at these time points
    - Your skin temperature will be measured at 5, 15, 30, 60, 90, 120, 180, and 360 minutes after vaping
    - A urine sample will be taken 360 minutes after vaping
    - Questionnaire packets will be given at 2 minutes, 5 minutes, 10 minutes, 15 minutes, 20 minutes, 25 minutes, 55 minutes, 85 minutes and 360-minutes after vaping
6. After the vaping session, you will not vape for the duration of the study day until you leave.
7. A light lunch will be served at about noon.
8. You will not be allowed to doze or sleep for the duration of the study.
9. You will be discharged from the hospital and allowed to go at about 3:00 PM.

The other two outpatient study days will follow the same structure and procedures as the first outpatient admission.

All visits will be separated by 48 hours from your first admission (example: Monday, Wednesday, and Friday).

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. Your mobile or landline provider's standard rates for sending/receiving text messages or calls will apply.

- **Study location:** The screening visit will take place at the UCSF Tobacco Research Center [redacted] and the three outpatient study days will be done at the Clinical & Translational Science Institute (CTSI)-CRC [redacted] at the Zuckerberg San Francisco General Hospital or UCSF Moffitt Hospital [redacted].

How long will I be in the study?

Participation in the study will consist of a screening visit (45 minute), orientation visit (30 minute), and 3 outpatient days (8 hours each) for a total of about 25 hours.

Can I stop being in the study?

Yes. You can decide to stop at any time. Just tell any member of the research personnel right away if you are thinking about stopping or wish to stop being in the study.

Also, research personnel 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
- 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.

In unlikely cases, people experience feelings of paranoia after using cannabis. If this happens while you are on the study, the CRC, Study Physician, or PI may stop you from continuing on the study. You will stay at the research ward in a private, non-threatening room until the paranoia resolves.

In these cases, 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 study coordinator, the CTSI-CRC nurse, or the study doctor 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 8 hours. There is a small risk of pain, swelling, bruising, or infection.
- **Paranoia:** Some people experience feelings of paranoia after using cannabis, typically in the form of unfounded or excessive fear that someone is trying to harm them.
- **Pulmonary disease:** Severe pulmonary disease has been reported with vaping cannabis oil products, although the types of products used are unknown. Since you will be vaping small doses of cannabis leaf material, we believe the risk of a pulmonary problem in the present study is low, if any.
- **Blood Loss:** You will give a total of about 198 mL (<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.
- **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.
- **Undiscovered Drug Toxicity:** There may be undiscovered drug toxicity associated with the use of cannabis that can put you at risk for unknown effects.
- **Long-term effects:** There may be long-term effects associated with the use of cannabis that are currently unknown to the scientific community.
- **Drug Use and Pregnancy:** Use of cannabis or nicotine during pregnancy poses risk to the fetus. A pregnancy test will be conducted at your screening visit and prior to each hospital admission, but the earliest this test can detect pregnancy is around 2 weeks of gestation, depending on the sensitivity of the test.

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

Are there benefits to taking part in the study?

The drugs you will use during this study are not intended to be therapeutic, and there will be no direct benefit to you from participating in this study. However, the information that you provide may help the Tobacco Research Center and other health professionals better understand/learn

more about the safety and addictiveness of tobacco cigarettes as cannabis and nicotine delivery devices.

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.

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.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the National Institutes of Health
- Representatives of the University of California
- Representatives of 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. Additionally, your records may be inspected by the Research Advisory Panel of California.

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 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/UCSF Moffitt 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, effort, and travel expenses you will be paid **$450** if all portions of the study are completed, which includes:

- $30 for the screening visit ($20 compensation+$10 for transportation)
- $100 for each study day, totaling $300
- $40 bonus for complying with study procedures prior to and during your three outpatient hospital visits, for up to $120 in bonus compensation

You will receive $30 for today's screening visit, as long as you meet the following requirements:

- Your drug test is positive for cannabis, and negative for all other drugs
- Your saliva lab results indicate that you are a regular user of tobacco cigarettes

- A check of $30 will be mailed to you, and you will receive it approximately 4-6 weeks after participation in the screening visit.

You will need to provide your home address and social security number 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 [redacted].

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

It is important that you tell the Clinical Research Coordinator, the Project Manager [redacted], the Study Physician [redacted], or the co-investigator [redacted] if you become sick or injured.

> **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, 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 [redacted] the Study Physician/Principal Investigator [redacted], or the co-investigator [redacted] 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* [redacted]

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

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

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 [redacted]

_____ 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.

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 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 [redacted] and any 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 current study.

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.

I have read this information, which is printed in English. This is a language that I read and understand.

Date	Participant's Signature for Consent
Date	Person Obtaining Consent