NAME:
DOB:
MRN#:

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

Study Title: "*Clinical Pharmacology of Electronic Cigarettes"*

This is a research study about *the addictiveness and safety of electronic cigarettes*. The study researcher, **Dr. Neal Benowitz, MD** from the University of California, San Francisco Department of Medicine, is 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 a healthy smoker who smokes at least 5 cigarettes every day and uses an electronic cigarette device.

Why is this study being done?

The purpose of this study is to learn more about the addictiveness and safety of electronic cigarettes as nicotine delivery devices, assessing key pharmacological factors associated with the potential addictiveness of these products.

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

How many people will take part in this study?

About 36 people at UCSF 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 tobacco, alcohol, caffeine, and recreational drugs). In addition, there are several forms specifically about your 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 tests to confirm that you are a smoker.
- **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 not a 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 will be discarded.

If the screening exam shows that you can be in the main part of the study and you choose to continue, this is what will happen next:

Orientation Visit: Once your smoking status is confirmed from the screening visit saliva sample, if eligible, 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 **Study Block #1.**

- We will ask you **not to use any marijuana or other recreational drugs from the today until the study is completed.**
- You will be assigned to one of two products—e-cigarette only or tobacco cigarette only for the first week of the study (Block #1), then the alternate product for the following week (Block #2).
- We will purchase your normally used tobacco cigarette products, and your normally used electronic cigarette products if you use e-liquid concentration with a nicotine concentration of ≥ 6mg/mL. If you use an e-liquid with a nicotine concentration of <6mg/mL, we will provide you with an e-liquid similar to the one that you normally use, but with a nicotine

concentration of 6mg/mL. We will provide your first product (tobacco cigarettes or electronic cigarettes) for you to use for 4 days (outpatient days) prior to your admission to the research ward.

- You will also use a smartphone diary app to track your product use (number of disposable electronic cigarette devices, refill cartridges, volume of e-liquid used and tobacco cigarettes smoked per day) and will record each evening an assessment of urges to smoke and nicotine withdrawal symptoms experienced throughout the day. You will also be asked to return all electronic cigarette products and tobacco cigarette butts so that we may assess the amount of nicotine consumed and tobacco burned.
- **Urine Collection**: A sample of your urine will be collected for and tested for **nicotine breakdown by-products.**

Study Block #1 Outpatient Procedures:
You will be able to use your electronic cigarette device or tobacco cigarette product as you wish for **4 days**. We will ask that you use **only** the provided product during these outpatient days and that you keep track of your product usage with the study diary given to you at Orientation.

Study Block #1 Inpatient Procedures: You will be admitted to the SFGH Clinical Research Center (CRC) or UCSF Moffitt Hospital as an inpatient for **3 days**.

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 SFGH medical record*. If you wish, the results of your physical examination will be shared with you by the health care provider.

On **Day #5** of the study, the following will occur:

1. You will be asked to arrive at the research ward at **7am** to begin your inpatient study days. You will be given a light breakfast and, if you normally drink caffeinated beverages, you will be allowed a cup of your usual beverage (coffee or tea).
2. At approximately 8am, a plastic catheter (thin flexible tube) will be inserted into a vein on one of your forearms (this will be used to withdraw multiple blood samples and will be kept in place for about 10 hours).
3. At approximately 9:00am, you will be asked to smoke a commercial cigarette or e-cigarette device and to take puffs only at times signaled by the voice recorder.
4. After each puff, we will capture the smoke you breathe out by asking you to exhale into a sterile polypropylene mouthpiece which is connected to 3 gas traps. The gas traps are connected in series (i.e. in a line) and contain diluted hydrochloric acid or a solution containing citric acid, sodium phosphate, and ascorbic acid. A vacuum pump connected to the traps will suck your exhaled smoke into the traps. There will be NO contact between your mouth or your body with the diluted acidic solution in the gas traps. This step will allow us to compute the dose of nicotine taken in from the cigarette during the standardized session.
5. You will not be allowed to smoke again until 4 hours later, at which time you will be given one of your usual brand of cigarette or e-cigarette and allowed to smoke it in your usual way.
6. Blood samples, about one teaspoon each, will be withdrawn just before smoking, and

during the 4-hour abstinence period at 2, 5, 15, 30, 45, 60, 90, 120, 180, and 240 minutes.

7. You will be asked to fill out several *Questionnaires* about your smoking experience before and after smoking the cigarettes and during the 4 hours when you are not smoking.

On **Day #6** of the study, the following will occur:

1. You will be able to smoke your cigarettes or electronic cigarette device as you wish from 8am to 12am midnight.
2. The time of each cigarette or EC puff will be recorded using a mobile smartphone application and all cigarette butts and EC devices will be collected at the end of the day to determine product usage.
3. You will wear a 24-hour ambulatory blood pressure and heart rate recorder for *cardiovascular monitoring*.
4. You will be asked to fill out several *Questionnaires*.
5. There will also be 24-hour *urine collections*.

On **Day #7** of the study, the following will occur:

1. On the morning of Day #3, an intravenous catheter (like on Day #1) will be placed for blood collections every four hours starting at 8am until midnight, and at 8am the next day.
2. You will be asked to fill out several *Questionnaires*.
3. There will also be 24-hour *urine collections*.
4. You will be discharged on the morning of Study Block #2, Day #1 after your last blood draw and urine collection.

Study Block #2 Outpatient Procedures:

After being discharged from the research ward, you will be able to use your electronic cigarette device or tobacco cigarette product as you wish for **4 days**. We will ask that you **only** use the provided product during these outpatient days and that you keep track of your product usage with the smartphone study diary app.

Study Block #2 Inpatient Procedures:

Your second inpatient admission will follow the same structure as the first inpatient admission mentioned above, but instead you will be admitted for a period of **5 days** using the alternate product.

The first 3 days of your admission will follow the same procedure as your first admission, with an additional two day abstinence period in which you will be asked not to use any products. During the abstinence period, there will be one *blood draw*, 24-hour *urine collections*, 24-hour *cardiovascular monitoring,* and you will be asked to fill out several *Questionnaires*.

Study Block #1

Day #1 *Thursday* (Home)	Day #2 *Friday* (Home)	Day #3 *Saturday* (Home)	Day #4 *Sunday* (Home)	Day #5 *Monday* (SFGH/UCSF)	Day #6 *Tuesday* (SFGH/UCSF)	Day #7 *Wednesday* (SFGH/UCSF)
"Free Smoking" Period				Blood Draws	"Free Smoking" 24-hr CV monitoring 24-hr Urines	"Free Smoking" Blood Draws 24-hr Urines

Study Block #2

Day #1 *Thursday* (SFGH/UCSF/ Home)	Day #2 *Friday* (Home)	Day #3 *Saturday* (Home)	Day #4 *Sunday* (Home)	Day #5 *Monday* (SFGH/UCSF)	Day #6 *Tuesday* (SFGH/UCSF)	Day #7 *Wednesday* (SFGH/UCSF)	Day #8 *Thursday* (SFGH/UCSF)	Day #9 *Friday* (SFGH/UCSF)
Blood Draw Urine Collection Morning Discharge "Free Smoking" Period				Blood Draws	"Free Smoking" 24-hr CV monitoring 24-hr Urines	"Free Smoking" Blood Draws 24-hr Urines	Abstinence 24-hr CV monitoring 24-hr Urines	Abstinence 24-hr CV monitoring 24-hr Urines Blood Draw

- **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-CRC (5B Research Ward) at San Francisco General Hospital or at 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 hour), 8 outpatient days, 8 inpatient days for a total of **16 days**.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the Clinical Research Coordinator, your CTSI-CRC nurse, or the Study Nurse Practitioner if you are thinking about stopping or decided to stop.

The Clinical Research Coordinator, Study Nurse Practitioner or Study Physician 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?

You may have side effects while on the study. If you develop side effects, your participation in the study may be stopped, depending upon the severity.

You should talk to the Clinical Research Coordinator, the Study Nurse Practitioner, or the Study Physician about any side effects you experience while taking part in the study.

Risks 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 lose a total of about 1 cup of blood during the entire study. This amount of blood loss poses no risk to healthy individuals.
- The **Study Procedures** may be inconvenient and tedious (filling out forms, spending time in the hospital, providing specimens, etc.) and you may have trouble staying awake as required.
- 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.
- You may also feel uncomfortable when getting your **blood pressure** taken depending on the tightness of the cuff.

Are there benefits to taking part in the study?

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

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.

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 Committee on Human Research, the Study Sponsor (National Institutes of Health), and the Food and Drug Administration (FDA).

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. Two kinds of "charts" are created when you take part in one of our studies:

1. A medical record at 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 SFGH/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.

What are the costs of taking part in this study?

You will not be charged for any of the study activities.

Will I be paid for taking part in this study?

In return for your time and effort, you could be compensated a total of $2,030 if all parts of the study are completed. This includes the following:

- Screening Visit: $30
- Block #1 – 4 day Outpatient Procedures and 3 day Inpatient Procedures: $570
- Abstaining before first hospital admission: $30
- Block #2 – 4 day Outpatient Procedures and 5 day Inpatient Procedures: $870
- Abstaining before second hospital admission: $30
- Bonus for Completion of Study: $500

You will be compensated $30 for today's Screening Visit as long as your drug test is negative (marijuana is okay) and the saliva lab results indicate that you are a regular user of the Tobacco Cigarette and Electronic Cigarette products you reported.

You will be compensated $30 for abstaining before each hospital admission if your expired carbon monoxide is below 8 ppm, 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 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 *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 Clinical Research Coordinator (Annalise Davis at 415-608-4864), the Project Manager (Natalie Nardone, PhD at 415-514-1450), or the Study Physician (Neal Benowitz, MD at 415-206-8324) if you become sick or injured.

> **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 Committee on Human Research 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 and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get medical care from our institution.

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 (Annalise Davis at 415-608-4864), the Project Manager (Natalie Nardone, PhD at 415-514-1450), or the Study Physician (Neal Benowitz, MD at 415-206-8324) about questions or concerns you have about this study.

For questions about your rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's 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 on http://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 website at any time.

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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 participate or to withdraw from the study at any time 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. You may be withdrawn from the study without your consent if the researchers believe that it is in your best interest or if you fail to follow study procedures (for instance, failure to keep appointments or to provide specimens).

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 from you.

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, medical record number, laboratory results, and completed questionnaires) and to recontact 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 recontacted at any time by calling 415-476-3555.

_____ 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 recontacted for possible participation in future nicotine and smoking related studies for which I may be eligible.

_____	_____ / _____
Date	Participant's Signature for Consent Print
_____	_____
Date	Person Obtaining Consent