Title: Assessment of Two New Electronic Cigarettes in Cigarette Smokers

NCT #: NCT03435562

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ID: HM20012013 View: SF - Study Identification

HM20012013 - Alison Breland
Assessment of Two New Electronic Cigarettes in Cigarette Smokers

Study Identification

1. * **Select the Principal Investigator:**
   Alison Breland

2. * **Study Title:**
   Assessment of Two New Electronic Cigarettes in Cigarette Smokers

3. * **Is this a student or trainee project in which activities will be carried out by that individual under your supervision (for example, dissertation or degree-required projects):**
   - ○ Yes
   - ● **No**

4. * **Please select the primary department or center that this study is being conducted under:**
   Psychology

5. **If this is associated with other VCU IRB protocols or a resubmission of a withdrawn/closed protocol, select the VCU IRB numbers assigned to those studies:**

ID	Title	PI
HM20002567	CSTP Overall Screening and Registry	Alison Breland

6. **Select all individuals who are permitted to edit the IRB protocol and should be copied on communications (study staff will be entered later). These individuals will be referred to as protocol editors:**

Last Name	First Name	E-Mail	Phone	Mobile
[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]		

7. * **Select one of the following that applies to the project (selection will branch to new pages):**

   Note: VCU IRB offers guidance for many types of studies, including secondary data analysis studies, internet research, registries, EFIC, HUD, and Emergency Use protocols. See https://research.vcu.edu/human_research/guidance.htm

   - ● **Research Project or Clinical Investigation [*most exempt, expedited, and full board research studies]**
   - ○ Exception from Informed Consent (EFIC) for Planned Emergency Research
   - ○ Humanitarian Use of Device for Treatment or Diagnosis
   - ○ Humanitarian Use of Device for Clinical Investigation
   - ○ Emergency Use of Investigational Drug, Biologic or Device
   - ○ Treatment Use (Expanded Access to Investigational Product for Treatment Use)
   - ○ Center or Institute Administrative Grant Review
   - ○ Request for Not Human Subject Research Determination (i.e. request a letter confirming that IRB review is not required)

ID: HM20012013 View: SF2 - Federal Regulations

Federal Regulations

1. * **Is this a FDA regulated study?**

   FDA regulated research includes all clinical investigations involving a test article and a human subject(s) that has been submitted for approval to the FDA or may be submitted in the future. Check Yes if the study involves an IND/IDE, abbreviated IDE, IND/IDE exemption, HUD, expanded access, or is otherwise subject to 21 CFR 56. Also check Yes if the study does not involve a test article but intends to provide safety or efficacy data to the FDA about an FDA regulated product.

   ○ Yes ● **No**

2. * **Is this study supported by the Department of Defense (DoD):**

- ○ Yes
- ● **No**

3. * **Check if any of the following funding sources apply to this research (including Direct and/or Indirect funding):**

- ☐ Department of Education
- ☐ Department of Justice
- ☐ Environmental Protection Agency
- ☑ **None of the above**

ID: HM20012013 View: SF2 - IRB Panel Setup

IRB Panel Setup

1. * **To which IRB is this study being submitted for review?**

- ● **VCU IRB**
- ○ Western IRB
- ○ NCI Central IRB
- ○ Other IRB

2. * **Does this protocol already have a VCU IRB study number (HM number) and is being submitted as a new study in order to transition to review by another IRB?**

- ○ Yes - transitioning from VCU IRB to an external IRB (WIRB, CIRB, Other)
- ○ Yes - transitioning from an external IRB (WIRB, CIRB, Other) to VCU IRB
- ○ No or not applicable

ID: HM20012013 View: SF2 - Review Setup

Review Setup

1. * **Select which study type best describes the majority of the study. Your response will help determine which IRB panel should review this.**

- ○ Bio-Medical Research
- ● **Social/Behavioral/Education (SBE) Research**

2. * **Does this study involve greater than minimal risk:**

Does this study involve greater than minimal risk:

- ○ Yes
- ● **No**

3. * **Review type requested: (subject to IRB approval):**

- ○ Full Board
- ● **Expedited**
- ○ Exempt

The IRB has determined that the selected Exempt and/or Expedited categories apply to this study.

The below information is read-only to investigators, and the categories are set by the IRB during review. All categories will appear blank until the IRB has made a determination. If a category is not checked, it does not apply to this study.

4. **For Expedited Studies:**

Category 2	Collection of Blood	Involves only the collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from individuals where the amount of blood does not exceed allowable amounts (see help).
Category 3	Specimen Collection	Involves prospective collection of biological specimens for research purposes by noninvasive means.
Category 4	Noninvasive Procedures	Involves the collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding x-rays or microwaves.
Category 5	Nonresearch Data Collection	Involves materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes including medical treatment or diagnosis.
Category 7	Behavioral	Is research that will be performed on individual or group characteristics or behavior OR will employ a survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

ID: HM20012013 View: SF2 - Initial Setup Complete

Initial Setup Complete

Protocol Progress:
● **INITIAL SETUP**
② BACKGROUND, RATIONALE & GOALS
③ RESEARCH PLAN
④ CONSENT PLAN
⑤ RISKS, PRIVACY & CONFIDENTIALITY
⑥ POPULATIONS WITH SPECIAL CONSIDERATIONS
⑦ INSTITUTIONAL REQUIREMENTS
⑧ DOCUMENTS

Click Continue below to go to the next section

ID: HM20012013 View: SF2 - Background, Rationale and Goals

Background, Rationale and Goals

1. * **Describe the study's background and significance, including citations, or upload a citation list in document upload. Use lay language whenever possible.**

Today's electronic cigarette (ECIG) was patented in 2003 (1) and the product is intended to aerosolize a nicotine-containing liquid for inhalation. To the extent that the nicotine in the liquid is plant-derived and the product is not marketed with therapeutic intent, ECIGs are considered tobacco products under US law. (2) This legal determination, coupled with the fact that ECIGs and other alternative products have recently not been under the authority of FDA's Center for Tobacco Products, means that many diverse tobacco products have come to the market that have significantly different design features. One unanswered question is: How do design features influence emissions?

Most ECIGs consist of a battery, an electrical heater, and a liquid that is aerosolized for users to inhale. The name "electronic cigarette" actually encompasses a variety of design types, from products that look like a cigarette (sometimes called "first generation devices" or "cigalikes"), to products that can be much larger than a cigarette and may use a "cartridge" or "tank" to hold the liquid, and that generally have a battery that is separate from the cartridge or tank. Because most cigalikes are "closed" in that they are not intended to be refilled with liquid nor their battery or atomizer replaced by the user and many cartridge- or tank-based systems are "open" in that they are intended to be refilled and often allow users to select and replace some components, we refer to these products as "closed" and "open" ECIGs. ECIGs also have a variety of names, such as "vapes," "mods," "e-hookahs," and "vape pens".

Aside from appearance, ECIGs can differ based on a variety of features, including, but not limited to, voltage and resistance (which together determine device power output). The liquids are usually (but not always) composed of nicotine, as well as at least one solvent (usually propylene glycol and/or vegetable glycerin), and flavorants (tobacco, menthol, candy- or beverage-themed, and more). These features combine with user puffing behavior to influence the toxicant content (or "yield") of the aerosol that emerges from the ECIG.

JUUL is a closed ECIG product that has been available on the market for several years that uses liquid containing nicotine salts, but little is known about the physiological and subjective effects associated with using this ECIG device. The use of nicotine salts (vs. freebase nicotine that is typically used in ECIG liquids) and the unique device design relative to other ECIG devices warrants investigation.

In addition to ECIGs becoming increasingly popular, heat-not-burn products have started to appear on the market. Heat-not-burn tobacco products are devices that use some type of a heating element to heat tobacco to a temperature below combustion with the purpose of delivering nicotine to the user while reducing exposure to chemical compounds generated in combustion. Clinical laboratory methods have been used to evaluate other heat-not-burn tobacco products (i.e., Pax Ploom) (5), but these products use heated loose-leaf tobacco and may often be used for cannabis smoking.

IQOS is a new heat-not-burn device that using an electrically heated metal skewer to heat a tobacco stick that is inserted onto the stick. Phillip Morris, the makers of IQOS, report similar claims to other heat-not-burn products regarding reduced exposure to chemicals generated from combustible tobacco use, however, little is known about user physiological and subjective effects associated with IQOS use.

References

1. Hon, L., Inventor. 2003. Patent No. 2518174 A1.
2. Sottera, Inc v. FDA, 627 F.3d 891 (D.C. Cir. 2010)
3. Talih, S., Z. Balhas, T. Eissenberg, R., et al. 2015a. Effects of User Puff Topography, Device Voltage, and Liquid Nicotine Concentration on Electronic Cigarette Nicotine Yield: Measurements and Model Predictions. Nicotine & Tobacco Research 17(2): 150-157.
4. Wagener T, Floyd EL, Stephanov I, Driskills LM, Frank SG, Meier E, Leavens EL, Tackett NM, Quelmado L. (2017). Have combustible cigarettes met their match? The nicotine delivery profiles and harmful constituent exposures of second-generation and third-generation electronic cigarette users. Tobacco Control e1: e23-e28.
5. Lopez, Alexa A.; Hiler, Marzena; Maloney, Sarah; Eissenberg, Thomas; Breland, Alison B. (2016). Expanding clinical laboratory tobacco product evaluation methods to loose-leaf tobacco vaporizers. Drug and Alcohol Dependence. 169: 33–40.

2. * **Describe the study hypothesis and/or research questions. Use lay language whenever possible.**
The purpose of this study is to determine differences in nicotine delivery, user behavior, subjective effects, and physiological effects, when cigarette smokers use an two new electronic cigarette devices (JUUL and IQOS) relative to their using their own brand of cigarettes.

3. * **Describe the study's specific aims or goals. Use lay language whenever possible.**
The aims of this study are to better understand how two new electronic cigarette devices with different technology (JUUL - electronic cigarette with nicotine salts, and IQOS - a "heat-not-burn" product) affect a variety of measures.

4. * **Describe the scientific benefit or importance of the knowledge to be gained:**

The benefits of this research are of a scientific nature, which should in the long-term benefit society at large. In particular, the use of ECIGs and heat-not-burn tobacco products has become increasingly popular. There is a lack of information about these products and their effects. The results of this study will inform future work regarding the physiological and subjective effects of ECIG use and heat-not-burn tobacco product use in cigarette smokers.

5. * **Describe any potential for direct benefits to participants in this study:**
None.

6. **Upload a supporting citation list if applicable:**

Study Population

1. * **Provide the maximum number of individuals that**

   1. May participate in any study interaction or intervention (including screening, consenting, and study activities)
   AND/OR
   2. You obtain any data/specimens about (regardless of identifiability)

   at VCU and at other sites under the VCU IRB's oversight. See the help text for additional guidance.
   75

2. **If this is a multi-Center Project, what is the maximum anticipated number of subjects across all sites?**

3. * **Provide justification for the sample size by explaining how you arrived at the expected number of participants and why this number is adequate for answering the research questions:**
   A total of 30 participants will give us the statistical power to examine differences in the physiological and subjective effects of the products. We may consent up to 75 participants in order to obtain 30 participants who complete the entire study.

[redacted]

6. * **Will individuals with limited English proficiency be included in or excluded from this research?**
   - ○ Included
   - ○ Excluded - safety concerns if participants are unable to communicate with the study team
   - ○ Excluded - instruments/measures only validated in English
   - ○ Excluded - no prospect of direct benefit to individual participants
   - ● **Excluded - minimal risk study**
   - ○ Excluded - lack of budget/resources for translation and interpretation [provide an explanation in next question]
   - ○ Excluded - other reason [provide an explanation in next question]

7. **Justify the inclusion and exclusion criteria if you are either targeting, or excluding, a particular segment of the population / community. Provide a description of the group/organization/community and provide a rationale.**

Background, Rationale & Goals Section Complete

Protocol Progress:
● **INITIAL SETUP**
● **BACKGROUND, RATIONALE & GOALS**
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Click Continue below to go to the next section

Study Procedures

1. * **Describe the study hypothesis and/or research questions. Use lay language whenever possible.**
The purpose of this study is to determine differences in nicotine delivery, user behavior, subjective effects, and physiological effects, when cigarette smokers use an two new electronic cigarette devices (JUUL and IQOS) relative to their using their own brand of cigarettes.

2. * **Describe the study's specific aims or goals. Use lay language whenever possible.**
The aims of this study are to better understand how two new electronic cigarette devices with different technology (JUUL - electronic cigarette with nicotine salts, and IQOS - a "heat-not-burn" product) affect a variety of measures.

3. * **Will the investigator obtain information or biospecimens for the purpose of screening, recruiting or determining the eligibility of prospective subjects?**
- (●) **The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative.**
- ( ) The investigator will obtain identifiable private information by accessing records.
- ( ) The investigator will obtain identifiable biospecimens by accessing stored identifiable biospecimens.
- ( ) None of the above

4. * **Choose all types of recruitment materials that may be used:**
- [ ] E-mail invitations
- [ ] Phone Solicitation scripts
- [x] **Flyers, Mailed Letters or Newspaper/TV/Radio Ads**
- [ ] TelegRAM announcements
- [x] **Website text**
- [ ] Study-specific web sites (design and text)
- [ ] Social Media
- [ ] Psychology Research Participant Pool (SONA) study descriptions
- [ ] Scripts for announcements made to groups
- [ ] Other recruitment material
- [ ] No recruitment materials

5. * **Provide a description of**
1. How potential participants or secondary data/specimens of interest will be identified and
2. All procedures that will be followed to carry out recruitment and screening activities (if applicable).

Include details (as applicable) about:
- How secondary data/specimens that meet the study's eligibility criteria will be identified (i.e. what database(s) will be queried and the search terms that will be used)
- How potential participants will be identified and their contact information obtained
- The timing and frequency of recruitment activities
- Where and how recruitment procedures will be completed
- Who will recruit or respond to potential participants
- What and how written or verbal recruitment materials and reminders (if any) will be used
- What screening activities will occur and how these procedures will be performed
See the help text for additional guidance.
Participants will be recruited via word-of-mouth and advertisements that will be posted as flyers around the community, in newspapers, on Craigslist, and on internet forums. Any postings on internet sites will use exactly the same information that is presented in those previously approved flyers (we will use advertisements that are already approved as part of the CSTP registry: HM20002567). Potential participants will make the initial contact via telephone by calling the phone number provided on the advertisements, or by going to the website provided on the advertisements. Please note that for the initial screening, we will use a multi-study screening process/registry described in HM 20002567. Participants who appear eligible based on the initial screening questionnaire (in HM20002567 and attached) are then contacted (either via phone or e-mail), told about this study using only language from the approved consent form, and if interested, participants are invited for an in-person screening, where consent for this study will be obtained.

Individuals who are participants in other, ongoing CBPL/CSTP studies (participants with whom we have a pre-existing relationship) may be verbally referred to this study, and directed to either call the laboratory or visit the website indicated on the advertisements/flyers, if they are interested.

6. * **Is a separate protocol document being uploaded that contains a detailed description of the study's methodology and procedures?**
- ( ) Yes
- (●) **No**

7. * **If a separate protocol document is NOT uploaded, describe the proposed research using language understandable to those IRB committee members whose expertise is not scientific. The description must include:**

1. A statement explaining the study design
2. A detailed description of all the procedures that will be followed to carry out the study, preferably in sequential order, and in sufficient detail that the study's methods could be replicated
3. A description of all research measures/tests/interventions that will be used (if applicable)
4. A detailed description or list of all secondary data elements and/or secondary specimens that will be obtained and how they will be used (if applicable)
See the help text for additional guidance
Participants will first be screened via phone or online, via a multi-study screening process/registry described in HM 20002567 (see attachment "Registry consent form and questions"). Participants can tell study staff if they are interested in screening for a particular study only. All screening data collected from participants who choose to join the registry will be used in this study. Participants who appear eligible will then be scheduled for an in-person screening visit where they will provide informed consent if they choose to participate and complete other forms (see in-person screening forms: ICF, Health Information Form, Penn State Cigarette Dependence Index, and FTND. These will be completed on paper forms or via RedCap). Participants will also be able to view other questionnaires (Direct Effects of Product Questionnaire, Direct Effects of Nicotine Questionnaire, Tiffany-Drobes QSU, Hughes-Hatsukami Questionnaire - listed as Subjectives - 1-4 in documents), via computer, and the study equipment. Women will be excluded if they are breast-feeding or test positive for pregnancy (by urinalysis) at screening. After screening and informed consent, eligible participants will enroll in this study, which is modeled on our previous work (e.g., Spindle et al., 2016). A total of 30 participants are needed to complete the study.

Once enrolled, participants will attend the lab for three additional experimental sessions where they will use the JUUL, IQOS, and own brand cigarettes. Participants will use each of the three products, using one product during a single session. For example, a participant may use the JUUL for the first session, own brand cigarettes for the second session, and the IQOS for the last session. Order of the products used in each session will be assigned using Latin-

square order procedure, which is similar to random assignment of order. The flavor chosen for the JUUL and IQOS sessions will match their usual brand of cigarettes (tobacco-flavored or menthol-flavored). Participants who enroll in the study at the in-person screening will schedule all of their visits with study staff. These visits may change based on participant and researcher/lab availability, but will follow a schedule described below. Research staff will contact participants over the phone to remind them of upcoming visits and reschedule if necessary.

The sessions will occur no more than 2 days per week and will be separated by at least 48 hours. The approximate total time that participants will be in the laboratory is 12.5 hours (30 minutes for screening and 12 hours for sessions). This does not include the 12 hours before each session that we ask participants to abstain from smoking.

During each session, participants will first complete a 10-puff product use bout, and then a 90-minute ad lib product use bout (each session will be approximately 3 hours). Sessions will be preceded by 12 hours tobacco/nicotine abstinence and an in-person 1-hour waiting period (to help ensure nicotine abstinence) to measure the extent to which each device suppresses nicotine/tobacco abstinence symptoms; and session order will be ordered by Latin-square. Other outcomes include plasma nicotine, carbon monoxide levels, cardiovascular response, and subjective effects (direct effects of the product and nicotine, abstinence symptoms, acceptability, as in Blank et al., 2009).

More specifically, upon arrival at the laboratory for each session, participants' breath CO will be measured to ensure compliance with the overnight abstinence criteria (i.e. CO < 10 ppm; see Breland et al., 2006). The session will then begin with a 1-hour waiting period (to help ensure nicotine abstinence). After this waiting period, an IV catheter will be inserted into a forearm vein of the participant, physiological monitoring equipment will be attached (arm blood pressure cuff, pulse oximotor placed on finger), and the session will begin. A detailed timeline of the sessions is described below. Please note that because catheter insertion can be difficult, we will attempt to insert a catheter no more than three times in one day, and if all three attempts are unsuccessful, the session will be discontinued, with payment as outlined in the consent and compensation section.

The subjective questionnaires administered at each time point are as follows: Direct Effects of Product Questionnaire, Direct Effects of Nicotine Questionnaire, Tiffany-Drobes QSU, and the Hughes-Hatsukami Questionnaire. All of these questionnaires will be administered via RedCap or paper and pen.

Experimental session timeline (times approximate):

Participant arrives, CO test to confirm tobacco abstinence,

1-hour waiting period, then the rest of the session will begin, as described below.

0 Hr 0 min - Attach physio equipment, insert catheter administer Subjectives -1

0 Hr 30 min Blood draw #1 and record Carbon Monoxide

0 Hr 35 min 10 puffs from product (30s inter-puff interval)

0 Hr 40 min Blood draw #2

0 Hr 45 min Record Carbon Monoxide, Subjectives - 2

1 Hr 05 min Blood draw #3, record Carbon Monoxide, Subjectives - 3, ad lib use period begins

2 Hr 35 min Blood draw #4 (ad lib period ends)

2 Hr 40 min Record Carbon Monoxide, Subjectives - 4

2 Hr 45 min Remove Catheter, Stop Physio Monitoring

Payment

Release

8. * **The IRB only reviews research procedures, so differentiate which of the study procedures are:**

   a. Being performed exclusively for research purposes (i.e. they would not otherwise be done apart from this study).
   b. Alterations of routine procedures (e.g. the study is altering the timing, frequency, method, location, amount, etc.).
   c. Being done for other purposes and whose data/results will be used secondarily in the study (e.g. standard medical or psychological tests, routine education practices, quality improvement initiatives, etc.).
   All procedures are performed exclusively for research purposes.

9. **If applicable, describe alternatives (research or non-research) that are available to potential participants if they choose not to participate in this study:**

10. **Upload any supporting tables or documents (e.g. protocol documents, figures/tables, data collection forms, study communications/reminders):**

    Upload ALL instruments/guides that will be used or that participants will experience (i.e. see, hear, complete), including measures, scripts/questions to guide interviews, surveys, questionnaires, observational guides, etc,:

    Upload ALL recruitment and screening materials, including such as ads, flyers, telephone or in-person scripts, letters, email invitations, TelegRAM announcements, and postcard reminders, screening scripts, screening forms, and screening measures:

Project Details

1. * **Select all of the following types of interventions that apply to this study (selections will branch):**
   - [x] **Social/Behavioral Interventions or experimentation / Tasks / Environmental manipulations**
   - [ ] Deception ((misleading participants through false or incomplete information)
   - [ ] Drug(s) / Biologics / Supplement(s) / Other Compounds (investigational products or products whose administration is dictated by the study protocol and not per the physician's clinical judgment)
   - [ ] Placebos
   - [ ] Safety and/or effectiveness evaluation of Bio-Medical Device(s), including in-vitro diagnostic devices/assays, mobile medical apps, and HUDs used in clinical investigations
   - [ ] Washout Periods
   - [ ] Expanded Access - Treatment Use of an Investigational Product

- [x] **Medical or Surgical Procedures (eg: physical exam, clinical procedures, scans, etc)**
- [x] **Specimen/biological sample collection**
- [ ] None of the Above

2. * **Select all of the following types of interactions that apply to this study (selections will branch):**
   - [ ] Passive Internet data collection (i.e. passively observing online behavior)
   - [x] **Active Internet data collection (i.e. using the Internet to interact or intervene directly with research participants)**
   - [ ] Audio / Video recording or photographing participants
   - [ ] Observations
   - [ ] Educational Settings/Assessments/Procedures
   - [ ] Interviews / Focus Groups / Verbal responses to questions
   - [x] **Surveys / Questionnaires /Written responses to questions (including data entry)**
   - [ ] None of the Above
3. * **Select all types of secondary information and/or specimens that apply to this study (selections will branch): See the help text for definitions.**
   - [ ] Protected Health Information (PHI)
   - [ ] Secondary data/specimens NOT from a research registry or repository
   - [x] **Information/specimens from a research registry or repository (Usage Protocol)**
   - [x] **Information/specimens originally collected for a previous research study**
   - [ ] Publicly available information/specimens
   - [ ] Government-generated or collected information that was or will be obtained for nonresearch activities [only applicable to research conducted by or on behalf of a Federal department or agency]
   - [ ] No secondary data/specimens will be used

ID: HM20012013 View: SF2 - Behavioral Intervention Details

Behavioral Intervention Details

1. * **Describe the duration of the social/behavioral intervention:**
   The duration of the intervention is approximately 12 hours. There are three visits of approximately four hours each.
2. * **Describe any potential harms or discomforts that participants could experience during the intervention:**
   From the consent form:

   "You may experience some discomfort during abstinence from cigarettes and nicotine before the session or while using tobacco products/electronic cigarettes during the session. Side effects from tobacco/nicotine abstinence can include irritability, anxiety and restlessness, excessive hunger, difficulty concentrating, and sleep disturbance. These are common abstinence symptoms in cigarette smokers. Though uncomfortable, these feelings are not medically dangerous. Side effects from products that contain nicotine can include sweating, lightheadedness, dizziness, nausea, vomiting, and nervousness. These effects are unlikely in individuals who use nicotine-containing products regularly. In addition, some people who use e-cigarettes experience seizures."
3. * **Will the intervention be physically invasive or painful?**
   - ○ Yes
   - ● **No**
4. * **Describe the impact the intervention will have on participants, including the nature and duration of any impact(s):**
   Participants may experience the effects stated above from using an e-cigarette or other tobacco product, although these are unlikely in regular ECIG/tobacco users. The duration of any impacts is the duration of each session (approximately four hours).
5. * **In the investigator's opinion, is there any reason to think that the participants will find the intervention offensive or embarrassing? Explain why or why not.**
   No.

ID: HM20012013 View: SF2 - Sample Collection Details

Sample Collection Details

1. * **Select all of the types of samples that will be collected as part of this study.**
   - [ ] Amniotic Fluid
   - [x] **Blood**
   - [ ] Buccal Smears
   - [ ] Saliva
   - [ ] Tissue
   - [x] **Urine**
   - [x] **Other**
   - [ ] None of the Above

2. * **If Other, please describe the type of sample being collected:**
Breath for carbon monoxide sample.

3. * **Select all of the methods of blood collection that will be utilized in this study:**

- [ ] Individual Needle Stick(s)
- [x] **Indwelling Catheter Placed Solely for This Study**
- [ ] Indwelling Catheter Placed for Other Reason(s)
- [ ] Blood Collected at the Same Time as Non-Research Blood Collection(s)
- [ ] Unused Blood Originally Drawn for Clinical Purposes
- [ ] Other

4. * **In order to collect urine, will an indwelling catheter be placed solely for the research study:**

- ○ Yes
- ● **No**

5. * **Describe how the samples will be collected and the collection schedule. For each type of sample, include information about**

- The procedures that will be followed to collect the sample
- The role(s) of the individuals who will collect the sample
- The volume/size range of the sample
- The timing and frequency of sample collection

Urine will be collected at screening to test for pregnancy (women only). Urine will not be stored for later use.

Upon arrival at the CBPL/CSTP for the research session, participants' breath CO will be measured to ensure compliance with the overnight abstinence criteria (i.e. CO < 10 ppm; see Breland et al., 2006). CO will also be measured before and after bouts to be analyzed as a study outcome measure (change in CO before and after bouts).

Blood will be collected via intravenous catheter 4 times at each session (7 ml each time), for a total of 12 samples per person in the entire study (84 ml in total). Blood will not be collected more than 2 times per week.

6. * **Will genetic testing or analyses be conducted on any of the samples:**

- ○ Yes
- ● **No**

ID: HM20012013 View: SF2 - Active Internet Data Collection

Active Internet Data Collection

1. * **Describe the platform/technology chosen for collecting the data and transmitting data securely over the internet. Give the rationale for selecting this technology.**
The in-person screening questionnaires and questionnaires administered during sessions may be administered via RedCap or via paper forms. All of the data will be stored in REDCap, and viewing will be restricted to those personnel associated with this protocol (listed under personnel).

2. * **Describe how data will be linked or unlinked to identifiers including email addresses, names, and/or IP address.**
Data will be linked (via a key stored in a separate location) to participant IDs and dates of birth.

3. * **Is there an alternative method for completion of the data collection other than the internet?**

- ● **Yes**
- ○ No

4. * **If yes, describe the alternative(s).**
Paper forms.

5. * **Describe how individuals will be able to skip or not answer particular questions. If any questions are mandatory, provide justification.**
Participants will be able to skip any question.

6. **If not including children, describe any procedures used to verify that research participants are adults.**
We ask participants for their age and date of birth several times (telephone or online screening, in-person screening) and verify that the answers are the same.

ID: HM20012013 View: SF2 - Secondary Data/Specimen Details

Secondary Data/Specimen Details

1. * **Describe the source and nature of the information/specimens being obtained.**

Provide information about:
1. where will the data/specimens come from (e.g., another researchers registry, pathology lab, commercial source, etc.
2. what type of data/specimens will be obtained
3. a list of all data elements that will be obtained (a data collection form or other documentation may be uploaded and referenced here)
Contact information and eligibility requirements are obtained from this registry. Eligibility questions include information about cigarette and electronic cigarette use, alcohol and drug use, health issues and medication use. This data is solely used for screening and eligibility purposes.

2. * **Describe how you will be granted access to the information/specimens**
The PI gives permission to study staff only to access the registry via RedCap.

3. * **Describe any identifiers or coded information that will be obtained that can be linked directly or indirectly to the identity of participants.**

Provide information about:
1. the associated identifiers, or how a code has been assigned
2. whether or not you will be granted access to the ability to re-identify participants
3. whether an agreement is in place between you and the provider indicating you will never have access to the ability to identify the participants
The registry contains identifying information such as names. If a participant enrolls in this study, they are given an alphanumeric code that is not directly connected to their registry information.

We can re-identify participants.

4. * **When the information/specimens were originally collected, did individuals provide consent for secondary research use of their data/specimens (i.e. consent to another research study or to a research registry)?**
- (●) **Yes**
- ( ) No

5. **If Yes, did the original research consent document allow for sharing of the data the information/specimens to be shared for the specific area of study that is proposed by this research?**
- (●) **Yes**
- ( ) No

6. * **Provide name(s) of the registry/repository being accessed, if applicable.**
CSTP Overall Screening and Registry

7. * **Site having responsibility for the management of this registry/repository:**
- (●) **VCU**
- ( ) Non-VCU

8. **Describe the Non-VCU organization and/or individual responsible for management and control of the registry / repository.**

9. **If the registry / repository is located at VCU, provide the IRB number for the registry / repository.**
HM20002567

10. * **Is the original consent form that participants signed upon entry into the registry /repository available?**
- (●) **Yes**
- ( ) No

11. **If NO above, describe in detail the allowed uses of the data information/specimens as outlined in the registry / repository consent. Be sure to describe any stipulations or limitations on the use.**

12. **If YES, the original consent is available, upload it for the IRB to reference**

Costs to Participants

1. * **Select all categories of costs that participants or their insurance companies will be responsible for:**
- [x] **Participants will have no costs associated with this study**
- [ ] Study related procedures that would be done under standard of care
- [ ] Study related procedures not associated with standard of care
- [ ] Administration of drugs / devices
- [ ] Study drugs or devices
- [ ] Other

2. * **Provide details of all financial costs to the participant, other than time and transportation. Additional details regarding standard of care costs will be requested on another screen, if applicable.**
There are no other financial costs to the participant, other than time and transportation.

Compensation

1. * **Describe any compensation that will be provided including:**
1. total monetary amount
2. type (e.g., gift card, cash, check, merchandise, drawing, extra class credit)
3. how it will be disbursed
Participants will receive $75 after completing the first session, $100 after completing the second session, and $125 after completing the third session (not counting the first lab visit for the in-person screening). Thus, the total amount participants could earn for the entire study is $300. If a participant chooses to leave the study early, he or she will keep the amount earned up to that point. In addition, if a session must be discontinued for reasons beyond the control of the participant, the participant will be paid for the time spent complying with study conditions before the session began ($15) and also the time spent in the laboratory ($15/hour). All payments will be in the form of cash.

This amount was chosen because of the number of hours that participants are asked to be in the laboratory (12.5 hours for sessions), which does not include the 12 hours that we ask them to abstain from tobacco products before they come to the lab for each session. In addition, we will insert an in-dwelling catheter for each session. With the time involved in the laboratory, time abstaining before coming to the laboratory (which can be very unpleasant) and possible

discomfort from the catheter, we feel that the compensation is appropriate, and not coercive–in order to receive payment, participants have to do quite a bit.

2. If compensation will be pro-rated, explain the payment schedule.

3. * Will Social Security Numbers be collected for compensation purposes only?

- (●) Yes
- ( ) No

ID: HM20012013 View: SF2 - Research Plan Complete

Research Complete

Protocol Progress:
- ● **INITIAL SETUP**
- ● **BACKGROUND, RATIONALE & GOALS**
- ● **RESEARCH PLAN**
- ④ CONSENT PLAN
- ⑤ RISKS, PRIVACY & CONFIDENTIALITY
- ⑥ POPULATIONS WITH SPECIAL CONSIDERATIONS
- ⑦ INSTITUTIONAL REQUIREMENTS
- ⑧ DOCUMENTS

Click Continue below to go to the next section

ID: HM20012013 View: SF2 - Consent Process

Consent Process

1. * List all consent groups:

	Group	Types	Waivers	Roles	Roles - Other	Consent	Coercion	Decision	Re-Consent
View	All participants	Written/Signed Consent by Participant	No Waivers Requested	Research Nurse Research Assistant Trainee/Student (i.e. not Student-Investigator)		Consent for this study will be obtained in the CBPL, at the in-person screening visit. Consent will be ongoing and assumed when a participant makes and completes follow up appointments. Lab staff will call the participants the day before their scheduled appointment and remind participants about upcoming appointments, go over study procedures, and check to make they are still interested in participating. This will occur before each appointment in which consent is assumed when participants show up for a session.	The research study will be described fully to participants, and they will be allowed to ask as many questions as they would like. At any point participants can choose to not continue with the various levels of screening for this study (the online/telephone consent/screening and in-person consent/screening).	Participants will be given as much time as needed to consider the research study and consent form before deciding whether or not to participate.	

2. Upload any consent / assent documents:

ID: HM20012013 View: SF2 - Consent Plan Complete

Consent Plan Complete

Protocol Progress:
● **INITIAL SETUP**
● **BACKGROUND, RATIONALE & GOALS**
● **RESEARCH PLAN**
● **CONSENT PLAN**
⑤ RISKS, PRIVACY & CONFIDENTIALITY
⑥ POPULATIONS WITH SPECIAL CONSIDERATIONS
⑦ INSTITUTIONAL REQUIREMENTS
⑧ DOCUMENTS

Click Continue below to go to the next section

ID: HM20012013 View: SF2 - Risks, Discomforts, Potential Harms and Monitoring

Risks, Discomforts, Potential Harms and Monitoring

1. * **Describe the risks of each research procedure to participants or others. For each identified risk, provide an assessment of the anticipated seriousness and likelihood of the risk. Some examples of possible risks include but are not limited to:**
   - **Physical risks (e.g. bodily harms or discomforts, side effects, etc.)**
   - **Psychological risks (e.g. emotional, mental, or spiritual harms or discomforts, changes to thoughts, beliefs, or behaviors, etc.)**
   - **Research data risks (e.g. loss of confidentiality and privacy)**
   - **Social or legal risks (e.g. impacts on relationships or reputation, legal or criminal justice actions for self or others, etc.)**
   - **Financial risks (e.g. impacts on income, employability, or insurability, loss of services, etc.)**
   - **Other risks (e.g. unforeseeable risks of experimental procedures, risks related to particular study designs (randomization, washout, placebo, withholding care/services, deception), etc.)**

   See the help text for additional guidance.

   This protocol uses established methods and procedures and involves only minimal risk to participants. Twelve hours of tobacco abstinence may cause mild discomfort and nicotine abstinence symptoms. Nicotine abstinence symptoms that are not medically dangerous but participants may experience include; irritability, anxiety and restlessness, excessive hunger, difficulty concentrating, and sleep disturbance. The risks of using ECIG/tobacco products/nicotine are routine for the target population. Risks of nicotine use include sweating, lightheadedness, dizziness, nausea, vomiting, and nervousness. These effects are unlikely in individuals who use tobacco products regularly. In addition, some people who use e-cigarettes have experienced seizures (https://www.fda.gov/tobacco-products/ctp-newsroom/some-e-cigarette-users-are-having-seizures-most-reports-involving-youth-and-young-adults). These have been reported among individuals with a history of seizures as well as among individuals using other substances such as marijuana and amphetamines, as well as among others. Blood sampling involves the minor risk of infection and bruising at the catheter site.

   It is unlikely that the questionnaires will pose any potential risk or discomfort (no sensitive questions are being asked). Sessions are relatively short, and we find that participants tolerate 4-hour sessions well (i.e., they do not become fatigued).

   With any research, there is always a risk of loss of confidentiality. However, given the safeguards put in place by our research team and track record, we anticipate this risk will be minimal.

2. * **Describe how each of the risks/harms/discomforts identified above will be minimized:**
   Participant safety and rights will be protected by highly trained staff that are well-versed in the importance of maintaining confidentiality. Participants will be informed of the potential symptoms of nicotine abstinence/withdrawal, and will be told that they are free to leave the study at any time. Risk of infection from blood sampling is minimized by trained nursing staff, disposable equipment, and aseptic nursing procedures. In the 15 plus years of operation. the CBPL/CSTP has completed numerous IRB-approved studies without participant injury or a breach of confidentiality.

   In addition, non-invasive computerized monitoring equipment allows for minute-by-minute, real time monitoring of participants' heart rate and blood pressure (BP). Research personnel are trained to alert the research nurse if heart rate exceeds 120 beats per minute, if systolic BP exceeds 150 mm Hg, or if diastolic BP exceeds 100 mm Hg. Individuals whose heart rate and/or BP levels remain elevated will be monitored continually by the nurse, and if necessary emergency responders will be notified. Emergency medical coverage is available via the emergency room that is a half block away from the CBPL. The ER is approximately 1.5 miles away from the new laboratory location of the CSTP.

   In the case of nicotine abstinence symptoms, the project products will possibly alleviate these risks. Participants will be provided with water at all times.

   The risk of seizures is minimized by excluding participants with any history of seizures, and by having a full-time RN available, as well as monitoring of vital signs. In addition, some of the reported seizures occurred in users who were using other substances such as marijuana or amphetamines--the risk of seizures in this study is reduced as we are administering nicotine and no other substances.

   Participants will be able to view all questionnaires used in sessions before attending sessions, and will be informed of the length of each session. If participants do not want to answer the questionnaires, or feel that the length of the sessions will be too long, they can choose to not participate.

   Risk of loss of confidentiality will be minimized by only connecting participant data to participants by alpha numeric identifiers. These data can only be linked with identifiable information by using a key that is stored in locked cabinets. Research staff will also not release any participant study information to others without signed written approval from a participant.

3. * **Describe any potential risks or harms to a community or a specific population based on study findings (e.g. information that could be stigmatizing or derogatory):**
   None.

4. **Where appropriate, discuss provisions for ensuring necessary medical, professional, or psychological intervention in the event of adverse events to the subjects:**
   Individuals whose heart rate and/or BP levels remain elevated will be monitored continually by the nurse and if, necessary, emergency responders will be notified. Emergency medical coverage will be available via the emergency

room that is a half block away from the CBPL. The ER is approximately 1.5 miles away from the new laboratory location of the CSTP.

5. * **Describe criteria for when the investigator would withdraw an individual participant from the study; such as safety or toxicity concerns, emotional distress, inability to comply with the protocol, etc.:**
Participants may be withdrawn from the study if the PI or study nurse has any safety concerns (such as continuous high blood pressure or heart rate) during sessions, or if an intravenous catheter cannot be successfully inserted.

6. * **Summarize any pre-specified criteria that would trigger the investigator/sponsor/monitoring committee to stop or change the study protocol due to safety concerns:**
At this time we do not have a pre-specified criteria for stopping or changing the study protocol due to safety concerns.

Data and Safety Monitoring
Data and safety monitoring is a system for checking the study's data at regular intervals over the study period to identify and address issues that could affect the safety of research participants. This requirement is in accordance with 45 CFR 46.111.

The purpose of data and safety monitoring plan is to set forth study team procedures for monitoring/addressing:
- Participant safety (physical, psychological, etc.)
- Data validity
- Early stopping (termination) based upon changes in risks and benefits.

7. * **Indicate if this study will have a Data Safety Monitoring Board (DSMB) or a Data Safety Monitoring Plan (DSMP): [Required for all greater than minimal risk studies]**

- [ ] DSMB
- [ ] DSMP
- [x] **No DSMB/DSMP [Note: This response is not applicable for greater than minimal risk studies]**

Privacy

Privacy refers to an individual's right to control how others view, record, or obtain information about them. When privacy is violated it can involve such things as

- Being asked personal questions in a public setting;
- Being publicly identified as having a particular characteristic or diagnosis;
- Being seen entering a place that might be stigmatizing;
- Being photographed, videotaped or observed without consent;
- Disclosure of personal information to unauthorized people

Privacy is not the same as confidentiality because privacy protections apply to people, and confidentiality protections apply to data. Confidentiality protections should be described on the Data Confidentiality page of this form, not here.

1. * **Describe how the research team will protect participants' privacy throughout the course of the study. Address privacy in the context of the following research activities as applicable:**

- Identification of potential participants or secondary data/specimens of interest
- Recruitment and screening activities
- The informed consent process
- Conduct of the study procedures
- Data dissemination

See the help text for additional guidance.
Participants' privacy and comfort will be addressed throughout the course of the study. During the intake process and session, participants will be seated in a private room. All study procedures will take place behind closed doors. Participants will be informed that they may withdraw from the research study should they find any research procedures unacceptable. All participants and data will be treated with professional standards of confidentiality. Data are identified by alphanumeric code only and stored under double lock or in REDCap. Participants' names are not directly linked to data. Briefly, an alphanumeric code is assigned to each participant when they provide informed consent, and the numeric part of the code relates to the order in which the individual consented. This alphanumeric code appears on all data (under double lock). Access to the key and the consent documents is restricted to study investigators and staff: these individuals perform the informed consent and conduct the study with he participants so they already know who the participants are and observe the participants as data are collected. When results for the study are reported, data will only be presented in aggregate, rather than by individual participants to maintain privacy. Participant identifiable information will never be presented with any study data. Participants' research related information will be withheld, consistent with the law, unless permission is given to release such information. Effectiveness is indexed by previous experience: we have used these procedures for over 15 years and have not had a single incident in which a participants's confidential information has been compromised.

Data Confidentiality and Storage

Confidentiality refers to the way private, identifiable information about a participant or defined community is maintained and shared.

1. * **Specify where this study's paper and electronic research data and/or physical specimens will be stored and how they will be secured from improper use and disclosure.**

See the help text for additional guidance.

Paper based records will be kept in study three ring binders that are stored in large upright locked cabinets in a locked room and only accessed by authorized study personnel. All computers and storage devices will be kept in locked

cabinets and/or within locked laboratory rooms. Electronic records will be made available only to those personnel in the study through the use of access controls and encryption. Identifiers will be removed from study-related data, and data will be coded with a key stored in a separate, secure location. Electronic data (with study IDs only) is stored in RedCap and/or in Excel spreadsheets that are saved either on hard drives and/or a VCU server. Data from the online registry, as well as the in-person screen and from sessions will be stored in and can only be accessed through the password-secured system RedCap. Only approved CBPL staff and faculty will have keys to access this information.

We have a data security management plan on file with HAStech.

2. * **Who will have access to study data?**
Only CBPL/CSTP staff and faculty will have access to study data. The sponsor will not have access to the data. Other staff or faculty who are not listed on the protocol will not have access to participant data.

3. * **If research data that contains any of the 18 HIPAA identifiers will be released to person(s) or group(s) outside of the VCU study team, identify the data recipient(s) along with their institutional or organizational affiliation(s).**
No data with HIPAA identifiers will be released outside of the VCU study team.

4. * **Select all identifiers that will be collected as part of this study (including for recruitment, data gathering, data analysis, etc.), even if the data will eventually be anonymized:**
   - [x] **Names**
   - [x] **Geographic Locators Below State Level**
   - [x] **Social Security Numbers**
   - [x] **Dates (year alone is not an identifier)**
   - [ ] Ages >89
   - [x] **Phone Numbers**
   - [ ] Facsimile Numbers
   - [x] **E-mail Addresses**
   - [ ] Medical Record Numbers
   - [ ] Device Identifiers
   - [ ] Biometric Identifiers
   - [ ] Web URLs
   - [ ] IP Addresses
   - [ ] Account Numbers
   - [ ] Health Plan Numbers
   - [ ] Full Face Photos or Comparable Images
   - [ ] License/Certification Numbers
   - [ ] Vehicle ID Numbers
   - [ ] Other Unique Identifier
   - [ ] No Identifiers
   - [ ] Employee V#

5. * **If the study will code (i.e. de-identify) the research data by replacing subjects' names with assigned subject IDs, explain the following aspects of the coding process:**

   - The process for how subject IDs will be generated/assigned (e.g. random, sequential)
   - Whether there will be a key that links the subject ID with direct identifiers.

   If a key will be created, describe
   - The place where the key will be stored
   - The role(s) of all individuals who will have access to the key
   - When the key will be destroyed

   See the help text for additional guidance.

Data are identified by alphanumeric code only and stored under double lock. Participants' names are not directly linked to data. Briefly, an alphanumeric code is assigned to each participant when they provide informed consent, and the numeric part of the code relates to the order in which the individual consented. This alphanumeric code appears on all subsequent documents/data forms. A key is maintained in the study binder so the we can demonstrate that a particular data set is associated with a particular consent document. The key and consent documents are stored separately from each other and separately from all data (under double lock or in RedCap). Access to the key and the consent documents is restricted to study investigators and staff: these individuals perform the informed consent and conduct the study with the participants so they already know who the participants are and observe the participants as data are collected. Data keys will be destroyed 5 years after the completion of the study.

ID: HM20012013 View: SF2 - Data Retention

Data Retention

1. * **Select all of the ways information obtained during pre-screening and/or screening will be handled for individuals who DO NOT qualify for the study:**
   - [ ] Immediately destroy the information
   - [ ] Store until the end of study & then destroy
   - [x] **Use as "screening failure" data by members of the study team**
   - [ ] Provide to others outside of the research team (with the participant's permission)

- [ ] Request permission from participant to maintain the information
- [ ] Other
- [ ] N/A - study does not require screening procedures

2. * **Will participants be able to withdraw their data (paper, electronic, or specimens) from the study (e.g. ask that it be destroyed or returned) if they no longer wish to participate? (FDA-regulated studies should select No - see help text)**
   - (●) **Yes**
   - ( ) No

3. **If Yes , describe the process (oral, written, email, letter, etc.) that participants should use to request withdrawal of their data/specimens. Identify if there is a timepoint when withdrawal will no longer be an option and/or if the amount of data that can be withdrawn is reduced at different points in the study.**
   If any participant wants to withdraw his or her data, he/she can contact the PI, who will work with staff to remove all of the participant's data. Participants will be able to do this at their convenience via phone, email, or in-person.

4. * **What will happen to the research materials (e.g. data, specimens, documents, etc.) when the research has been completed?**
   - (●) **Stored indefinitely with identifiers removed**
   - ( ) Stored indefinitely with identifiers attached
   - ( ) Destroyed at the end of study once the minimum time required for data retention has been met per VCU Data Retention Policy and/or sponsor retention requirements
   - ( ) Destroyed when notified by sponsor but not less than the minimum time required for data retention per VCU Data Retention Policy
   - ( ) Other

Sharing Plan

This page addresses times when investigators may be required to share information about participants or may desire to share their research information/specimens with the aim of advancing science. This page creates a plan for when and how information/specimens could be shared.

Try to anticipate all reasonably foreseeable sharing so that the consent document can also reflect that information. However, it is acceptable to amend this page later and explain either how re-consent of previously and currently enrolled participants will occur or why re-consent should not be required.

The IRB reviews this page against the consent document (if one exists) to demonstrate the ethical principle of Respect for Persons by confirming that plans for sharing do not go against what participants would understand about the use of their data/specimens.

The IRB also ensures there are adequate protections for the privacy of participants and the confidentiality of participants' data/specimens when data is shared with others.

1. * **Is it likely investigators could discover information about child/elder abuse or neglect that would require mandatory reporting by the investigators or staff?**

   The Code of Virginia requires that most medical personnel and all employees of institutions of higher education report suspected child/elder abuse or neglect.
   - ( ) Yes
   - (●) **No**

2. * **Will the sponsor or investigator obtain a Certificate of Confidentiality for this study?**

   Certificates of Confidentiality (CoC) are issued by the National Institutes of Health (NIH), the FDA and CDC to protect identifiable research information from forced disclosure. All human subject research studies regardless of funding can qualify to receive a CoC. A CoC is automatically issued for research that was ongoing on December 13, 2016. or initiated after that date. For more information, see
   https://humansubjects.nih.gov/coc/
   - ( ) No - Will not obtain CoC for this study
   - (●) **Yes - CoC has been obtained or issued automatically**
   - ( ) Yes - CoC request is pending
   - ( ) Yes - Plan to submit request for CoC and will amend study/ICF once status of request is known

3. * **Select the way(s) that <u>individual-level</u> information or biospecimens (including DNA) may be used <u>by the VCU PI or VCU study team for other future research projects</u> (i.e. analyses beyond/apart from the aims of this study)?**
   See help text for definitions.

   - [ ] Will use directly identifiable information or specimens.
     ('Directly identifiable' means that identifiers like name, medical record number, social security number, etc. are included in/attached to the dataset/specimens. Maintaining identifiable data for future research is treated as a registry by the VCU IRB. The IRB must approve the new research use in an amendment to this study or as part of a new study before the project is initiated. You will be asked more questions about this on a later page)

- [ ] Will use de-identified or indirectly identifiable information or specimens.
('De-identified' means that a linkage/key code exists that links identifiers to data/specimens. When the researcher holds both the data and the key, the VCU IRB considers the subjects to be readily identifiable. Maintaining identifiable data for future research uses is treated by the IRB as a registry. The IRB must approve the new research use in an amendment to this study or as part of a new study before the project is initiated. You will be asked more questions about this on a later page)

- [ ] Will use anonymized information or specimens.
('Anonymized' means that 1) no linkage/key codes exist that link identifiers to data/specimens; and 2) subjects cannot be readily identified, i.e. no direct or indirect identifiers or identifiable combinations of variables. The VCU IRB considers uses of anonymized data/specimens to not be human subject research.)

- [ ] Will use aggregate results (summary-level results), not individual-level information or specimens.
(The VCU IRB considers uses of aggregate data to not be human subject research because there are no individual subjects.)

- [ ] Will contribute to an existing registry or repository
(You will be asked more questions about this on a later page.)

- [ ] Will not use information/specimens for purposes beyond this study.
- [ ] Not sure and will submit an amendment when known
- [ ] Other use(s) of individual-level information in a way not listed above

4. * Select the way(s) the VCU PI/study team may share individual-level information or biospecimens (including DNA) with other researchers who are not on this study team (i.e. for analyses beyond/apart from the aims of this study).
See help text for definitions.

- [ ] Will share directly identifiable information or specimens with other researchers.
('Directly identifiable' means that identifiers like name, medical record number, social security number, etc. are included in/attached to the dataset/specimens. Maintaining identifiable data for future research uses is treated by the VCU IRB as a registry. The data recipient's use of identifiable data would require them to obtain IRB review. You will be asked more questions about this on a later page.)

- [ ] Will share de-identified or indirectly identifiable information or specimens with other researchers.
('De-identified' means that a linkage/key code exists that links identifiers to data/specimens. The VCU researcher maintains the key but does not share it with any other researchers. The recipient's use of de-identified data/specimens may not be human subject research if there is documentation that the key will never be shared with the recipient, but they should check with their own IRB about review requirements. You will be asked more questions about this on a later page.)

- [x] Will share anonymized information or specimens with other researchers.
('Anonymized' means that 1) no linkage/key codes exist that link identifiers to data/specimens; and 2) subjects cannot be readily identified (i.e. no direct or indirect identifiers or identifiable combinations of variables). The VCU IRB considers uses of anonymized data/specimens by other researchers to not be human subject research, but the recipient should check with their own IRB about review requirements.)

- [ ] Will only share aggregate results (summary-level results), not individual-level information or specimens.
(The VCU IRB considers uses of aggregate data to not be human subject research because there are no individual subjects. The data recipient should check with their own IRB about review requirements.)

- [ ] Will contribute to an existing registry or repository (You will be asked more questions about this on a later page.)
- [ ] Will submit data to an NIH genomic data repository (You will be asked more questions about this on a later page.)
- [ ] Will not share information/specimens with other researchers.
- [ ] Not sure and will submit an amendment when known
- [ ] Other sharing of individual-level information with other researchers

5. * Since you responded in a question above that you may use or share anonymous, individual level data, indicate why the proposed use or sharing of anonymous data/specimens is not inconsistent with what participants would have reasonably understood from the consent document about the uses of their information. (Select all that apply.)

There are no items to display

6. * The Principal Investigator certifies that prior to releasing an anonymized dataset or anonymized specimens the following conditions will all be met:

- all 18 HIPAA identifiers (including all dates) will be removed;
- all indirectly identifiable data elements (unusual, rare, uncommon data) will be removed, grouped, suppressed, or otherwise transformed to no longer be readily identifiable;
- a different subject ID will be assigned than the one used for the main study and a linkage key will not be kept; and
- the PI will review the dataset/specimens to confirm that the remaining information could not be used alone or in combination with any other information to re-identify the participants represented in the data.

See help text for more information.
Yes

7. * The Principal Investigator certifies that after the study has been closed with the VCU IRB, the following conditions will be met whenever individual level research information and/or specimens are used or shared:

- The identities of participants who are represented in the dataset/specimens will not be readily ascertainable or otherwise re-identifiable by the recipient;
- if a linkage/code key is created, it will be maintained at VCU and not shared with the recipient under any circumstances;
- The PI will have no knowledge that the remaining information could be used alone or in combination with any other information to identify the individuals represented in the data; and
- The PI agrees to abide by this sharing plan even after the study has been closed with the VCU IRB.

Yes

8. If the Certificate of Confidentiality has been obtained by the PI, upload it here:

ID: HM20012013 View: SF2 - Pertinent and Incidental Findings

Pertinent and Incidental Findings

1. * Is it likely investigators could discover a participant's previously unknown condition (e.g. disease, suicidal thoughts, wrong paternity, pregnancy, genetic results, or other findings that may be of importance to health or well-being) or if a participant is engaging in illegal or reportable activities:
   - (●) Yes
   - ( ) No
2. * Describe any possible pertinent or incidental findings stemming from research-only procedures that may be of importance to a subject's health or well-being or which may relate to illegal or reportable activities.
   During screening, we assess blood pressure. If a participant's blood pressure is high, our study nurse advises the participant to talk to their own doctor and to get treatment.
3. * Explain what actions or procedures should research personnel take to handle such a discovery :
   Participants will have to report marijuana usage as part of the screening process. Although this is an illegal activity, the research staff will not take any actions. We have a CoC as this is NIH-funded (and thus the CoC is automatic).
4. * Will findings be disclosed to participants and/or any other person/group outside of the study team?
   - ( ) Yes
   - (●) No
5. If pertinent and/or incidental findings will not be disclosed, explain why not:

ID: HM20012013 View: SF2 - Risk Benefit Complete

Risk Benefit Complete

Protocol Progress:
- ● INITIAL SETUP
- ● BACKGROUND, RATIONALE & GOALS
- ● RESEARCH PLAN
- ● CONSENT PLAN
- ● RISKS, PRIVACY & CONFIDENTIALITY
- ⑥ POPULATIONS WITH SPECIAL CONSIDERATIONS
- ⑦ INSTITUTIONAL REQUIREMENTS
- ⑧ DOCUMENTS

Click Continue below to go to the next section

ID: HM20012013 View: SF2 - Populations with Special Considerations

Populations with Special Considerations

1. * Check all participant groups that will be either
   a) Specifically included in this study or
   b) Discernable in the research data/specimens.

   If the research is aimed at involving a broader subject population and may incidentally includes a listed population, only check the box if the participant group will be discernable in the research data/specimens. (Selections will branch)
   - [ ] Children
   - [ ] Emancipated minors
   - [ ] Wards of the State
   - [ ] Pregnant women or fetuses
   - [ ] Neonates or Post-delivery Materials
   - [ ] Prisoners
   - [ ] Decisionally Impaired Adults
   - [ ] VCU / VCUHS students or trainees
   - [ ] VCU / VCU Health System employees
   - [ ] Individuals with limited English proficiency
   - [ ] Active military personnel
   - [ ] Student populations in K-12 educational settings or other learning environments
   - [ ] Members of a federally recognized American Indian and Alaska Native tribe
   - [x] None of the Above

Populations with Special Considerations Section Complete

Protocol Progress:
● **INITIAL SETUP**
● **BACKGROUND, RATIONALE & GOALS**
● **RESEARCH PLAN**
● **CONSENT PLAN**
● **RISKS, PRIVACY & CONFIDENTIALITY**
● **POPULATIONS WITH SPECIAL CONSIDERATIONS**
⑦ INSTITUTIONAL REQUIREMENTS
⑧ DOCUMENTS

Click Continue below to go to the next section

Study Funding

1. * **Have you applied for funding:**
   - (●) **Yes**
   - ( ) No

2. **Is this study already funded:**
   - (●) **Yes**
   - ( ) No

3. * **Select all funding sources for this study (pending or awarded):**
   - [ ] Industry
   - [x] **Direct Federal**
   - [ ] Indirect Federal
   - [ ] State/Local Government
   - [ ] Non-Profit - Sponsored Project
   - [ ] Non-Profit - Gift
   - [ ] Internal Grant
   - [ ] Investigator/Departmental Funds
   - [ ] None
   - [ ] Other

4. **Select all related proposals:**

RAMS-SPOT ID# (FP/PT/PD#)	Sponsor	PI	Title	Status	Start	End
PT108771	National Institute on Drug Abuse/NIH/DHHS	Thomas Eissenberg	Center for the Study of Tobacco Products	Awarded	9/1/2013	8/31/2018

5. **If the following conditions are ALL met, provide the index code where ORSP will charge Single IRB (sIRB) fees associated with this review:**
   1. **The study is externally funded (fees do not apply if the study is not funded), AND**
   2. **Multiple sites are executing the same research protocol (i.e. multicenter research), AND**
   3. **VCU IRB will provide IRB review on behalf of one or more non-VCU sites**

6. * **Does the funder require the IRB to review this proposal for grant congruence?**
   - (●) **Yes**
   - ( ) No

7. **If grant congruence review is requested, upload the entire grant proposal (exclusive of budget and appendices).**

   If Industry was selected above, upload the OSP Subject Injury Language Memo or other documentation from OSP approving the consent form's subject injury language.

Types of Sites

VCU Site Information

1. * **Select all VCU sites that will be utilized in this study:**
   - [ ] Children's Hospital of Richmond at VCU
   - [ ] Clinical Research Services Unit (CRSU)

- [ ] Massey Cancer Center
- [ ] VCU Health Community Memorial Hospital
- [ ] VCU Medical Center
- [ ] VCU Monroe Park Campus
- [ ] VCU Qatar
- [x] **Other VCU Site**

2. * **Provide details regarding each VCU Site including:**
   - what clinics / facilities will be used
   - resources that are available for the conduct of this study
   Resources include personnel time, equipment, space, hospital beds, etc

All laboratory work (participant screening, product administration, and data collection) will be conducted at VCU's Clinical Behavioral Pharmacology Laboratory (CBPL) or at the Center for the Study of Tobacco Products laboratory. VCU's CBPL and CSTP were designed for smoking research, and includes a ventilation system that expels smoke to the outside and observation windows so that staff members are not exposed to second-hand smoke unduly. The CBPL/CSTP has been the site for many studies of tobacco users and electronic cigarette (ECIG) users (e.g. Eissenberg et al., 1999, Breland et al., 2002, 2006; Cobb et al., 2010; Vansickel & Eissenberg, 2012). The CBPL/CSTP staff are experienced in subject recruitment, conducting research sessions, and maintaining a schedule that will ensure timely sessions at the convenience of participants. The PI and one of the Co-PIs are regularly available on site, the medical monitor will be on-call, the research nurse is available full-time, and the CBPL is located directly across from the emergency department of MCV Hospital. The ER is located approximately 1.5 miles away from the new CSTP lab.

Biological samples will be stored in a -80C freezer in a locked laboratory area. Data will be stored in the laboratory.

Non-VCU Site Information

Non-VCU sites should be selected whenever any of the following situations apply::
a) Non-VCU sites that will be collaborating on a VCU-led study
b) Non-VCU sites that will be deferring to the VCU IRB for IRB review
c) Non-VCU sites where VCU investigators will be overseeing study interventions or interactions
d) Non-VCU sites/locations where VCU investigators will conduct study activities

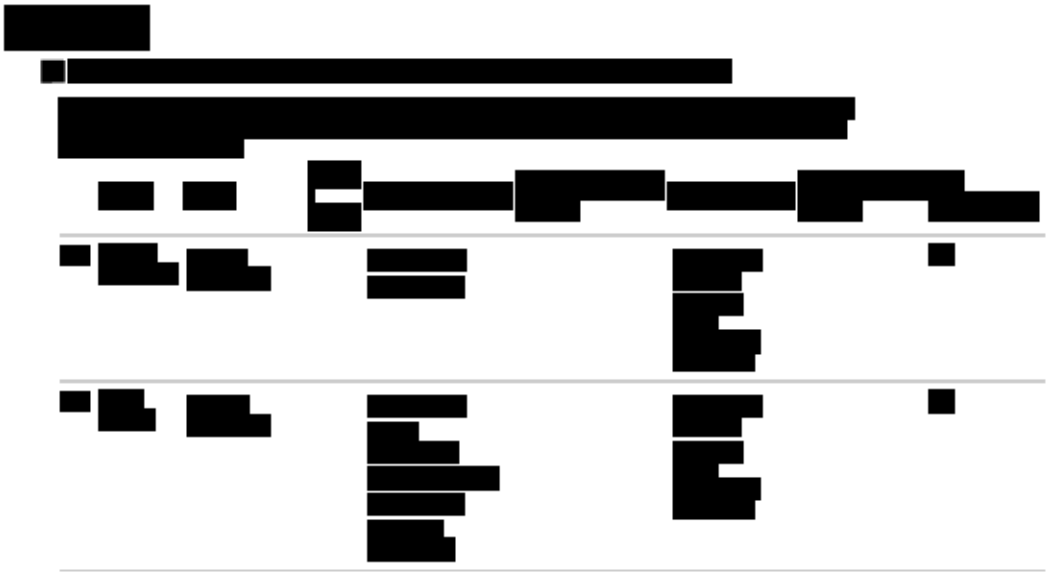
3. * **Select any of the following non-VCU sites utilized in this study:**
- [ ] McGuire VAMC
- [ ] Foreign Sites
- [ ] Other Non-VCU Sites
- [x] **No Non-VCU Sites**

•
For Non-VCU Sites: For each site or institution listed as "Site Engaged -- Requests to Rely on VCU IRB Review," upload:

- Completed Local Context Form for Relying on VCU's IRB
- Site specific informed consent form(s) and HIPAA authorization(s), if applicable

For Foreign Sites: For each Cultural Consultant upload a CV/Biosketch that includes a clear description of cultural expertise:

ID: HM20012013 View: SF2 - Personnel



[redacted]

3. * **Describe the process that will be used to ensure that all persons at all involved sites assisting with the research are adequately informed about the protocol and their research related duties and functions:**
This study will be conducted in Dr. Eissenberg's Clinical Behavioral Pharmacology Laboratory (CBPL) or in a new laboratory called the CSTP laboratory. In over 15 years, the CBPL/CSTP has conducted numerous IRB-approved studies involving cigarette smokers. All laboratory personnel are experienced, well-trained, and aware of their protocol-related responsibilities. Additionally, all lab personnel including the study PI and one of the Co-PIs work on the same floor of the same building and communicate daily in person regarding all study related issues. Lab meetings are held bi-monthly in order to communicate the status of specific studies and any issues related to ongoing studies. Thus, communication may occur as often as every day, either in person or via email.

4. **CV/Biosketch: (required for PI, Medically/Psychologically Responsible Investigators and Student/Trainee Investigators)**

Conflict of Interest

The PI should ask the questions on this page of all research personnel who are engaged in the research, including subrecipient investigators and personnel.

1. * **To the best of your knowledge, do you (as PI) or any other engaged individual have a financial interest related to this study?**

   Financial interests include utilizing your licensed intellectual property in the study; serving as a paid consultant, or advisory board member, or officer/director with a related entity; and equity or business ownership in a company that is related to this project.

   - (●) **Yes**
   - ( ) No

2. * **If Yes, provide:**
   - Name(s) of the engaged individual(s) with a related financial interest
   - Brief description of the financial interest Any individual named here should be designated as a 'COI investigator' on the Personnel page,
   even if they were not initially designated as a 'COI investigator',
   and complete a Financial Interest Report (FIR) in the Activity and Interest Reporting System (AIRS).

   Tom Eissenberg is a paid research in litigation against the tobacco industry.

3. * **To the best of your knowledge, do you (as PI) or any other engaged individual have a non-financial interest related to this study?**

   Non-financial interests could include such things as:
   - utilizing your unlicensed intellectual property in the study,
   - serving as an unpaid advisory board member or officer/director with a related entity, and
   - equity or business ownership in a company that has yet to make a profit and is related to this project
   - conflicts of time/effort,
   -personal and professional relationships/affiliations,
   - intellectual passions or personal beliefs
   - other factors that could create bias in the study

   - (●) **Yes**
   - ( ) No

4. * **If Yes, provide:**
   - Name(s) of the engaged individual(s) with a related non-financial interest
   - Brief description of the non-financial interest Any individual named here should also complete a Financial Interest Report (FIR) in the Activity and Interest Reporting System (AIRS), even if they were not initially designated as a 'COI investigator.'

   Tom Eissenberg is named on a patent application for a device that measures the puffing behavior of electronic cigarette users.

5. **Describe any institutional conflict of interest that you or any member of the research team are aware of that pertains to this research:**

   An institutional conflict of interest is a situation in which financial interests of the University or University leadership may affect research activities at VCU.

   None.

[redacted]