The Role of Nicotine Dose and Route of Delivery in Affecting Adoption of E-cigarettes and Reducing Exposure to Toxic Combustion Products

Document Date: May 9, 2022

NCT03492463

DUHS IRB Application (Version 1.31)

General Information

***Please enter the full title of your protocol:**

The Role of Nicotine Dose and Route of Delivery in Affecting Adoption of E-cigarettes and Reducing Exposure to Toxic Combustion Products

***Please enter the Short Title you would like to use to reference the study:**

ENDS-Switch
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

Add Study Organization(s):

List Study Organizations associated with this protocol:

Primary Dept?	Department Name
◆	**DUHS** - Duke Default Department

Assign key study personnel (KSP) access to the protocol

*** Please add a Principal Investigator for the study:**

(Note: Before this study application can be submitted, the PI MUST have completed CITI training)

Rose, Jed

3.1 If applicable, please select the Key Study personnel: (Note: Before this study application can be submitted, all Key Personnel MUST have completed CITI training)
*** Denotes roles that are not recognized in OnCore. Please select an appropriate role that is recognized in all clinical research applications (iRIS, OnCore, eREG, etc.)**

A) Additional Investigators, Primary Study Coordinator (CRC), and the Primary Regulatory Coordinator (PRC):

Claerhout, Susan
Primary Regulatory Coordinator
Davis, James
Co-PI

B) All Other Key Personnel

Campbell, David
Other*

Claerhout, Susan
Research/Physician Assistant
Maultsby, Linda
Other*
Melcher, Betsy
Research/Physician Assistant
Mukhin, Alexey
Other*
Pallin, Kendra
Clinical Research Specialist/Study Assistant
Thomas, Leah
Other*

***Please add a Study Contact:**

Campbell, David
Claerhout, Susan
Rose, Jed

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g., The study contact(s) are typically the Principal Investigator, Study Coordinator, and Regulatory Coordinator.)

Oncore

Please select the Library for your Protocol:

This field is used in OnCore. Determines the Reference Lists, Forms, Protocol Annotations, Notifications, and Signoffs available for the protocol. Protocols that require reporting to the NCI (National Cancer Institute), must select the Oncology library.

- ○ Oncology
- ◉ Non-Oncology

Protocol Application Type

Select the type of protocol you are creating:

Please see additional criteria and information in the policy titled "Reliance on the IRB of Another Institution, Organization, or an Independent IRB" on the **IRB web site**.

- ◉ Regular Study Application - Most common. The IRB will determine if the study is eligible for expedited review or requires full board review upon submission.
- ○ Application for Exemption from IRB Review - Includes Exempt, Not Human Subject Research, & Not Research.
- ○ External IRB Application - Any study using an external IRB as the IRB-of-Record.
- ○ Trainee Research While Away from Duke - Research conducted by medical students overseen by the Office of Curriculum & other student/trainee research away from Duke.
- ○ Individual Patient Expanded Access, Including Emergency Use - Use of an investigational product under expanded access, including emergency use of an investigational drug or biologic or emergency use of an unapproved device.

Conflict of Interest

Do any of the participating study investigators or other key personnel (or their immediate family/significant other) have a financial or intellectual interest in, or are receiving compensation from, the sponsor or the drugs, devices or technologies used in this research?

(●) Yes ( ) No

Has this conflict been disclosed to the Duke COI Committee?

(●) Yes ( ) No

Are any key personnel an inventor of any of the drugs, devices or technologies used in this research?

(●) Yes ( ) No

Have you filed an Inventor Disclosure Form?

(●) Yes ( ) No

Do any key personnel have or anticipate (within the year) any financial relationships (e.g., consulting, speaking, advisory boards, patents, equity, options) that could be perceived to overlap or present a conflict of interest with the current research?

(●) Yes ( ) No

Describe the overlap:

Rose Research Center provides clinical trials services to JUUL Labs. Given his relationship with JUUL, Dr. Rose will not be permitted to serve as PI on Duke research that may result in direct commercial advancement of JUUL products. It is not legal to use Duke's non-profit resources to advance the commercial prospects of a for-profit entity unless the research is performed in such a manner that the Public Benefit is assured. While he can in general perform research in fields of science that may ultimately be useful to companies, he will not be permitted to act as PI for any research that results in a direct commercial advancement of JUUL products. The Research Integrity Office (RIO) has reviewed Dr. Rose's NIH grants, and he may continue to serve as the Duke PI on the NIH award which uses the JUUL e-cigarettes and formulated cartridges.

Do any key personnel have a conflict of interest management plan (issued by the Duke University School of Medicine Research Integrity Office) with this company?

(●) Yes ( ) No

If Yes, please give the name(s) of the relevant personnel.

Dr. Jed Rose

Oversight Organization Selection

CRU (Clinical Research Unit) or Oversight Organization Selection:

Please select the CRU.

Psychiatry

The Clinical Research Unit that takes responsibility for this study.

- More information on CRUs can be found on the Duke Office of Clinical Research (DOCR) website, **http://docr.som.duke.edu**
- Questions concerning CRU selection should be directed to docr.help@dm.duke.edu.
- For questions about the Campus Oversight Organization, please visit **Campus Oversight Organization**.

List all Key Personnel on the study who are outside Duke:

- **Note:** You will also need to attach the documentation of Human Subjects Certification for each individual, if they have completed the certification somewhere other than Duke.
- **If outside key personnel will have access to Duke PHI, a data transfer agreement AND external site IRB approval (or IRB authorization agreement) will be needed.** See HRPP policy **Use of Research Data by Former Duke Students or Former Duke Faculty and Employees**
- In the panel below, "PHI" is Protected Health Information.

Entry 1

Name	
Study Role	
Email Address	
Institution / Organization	
Will he/she have access to Duke P.H.I.?	○ Yes ◉ No
Is he/she an unpaid volunteer at Duke on the study?	○ Yes ◉ No

Indicate the Protocol source below:

The protocol source is the author of the protocol. If the protocol is a joint authorship between multiple sources, select the primary author.

An IRB fee may be assessed for all research that is supported by for-profit entities and requires full board review. For additional information, see the **IRB fees section of the IRB web site**

- ◉ PI initiated
- ○ Commercial / Industry (for-profit entity) initiated
- ○ Federal Government initiated
- ○ Cooperative Group Initiated
- ○ Foundation (non-profit group) initiated
- ○ Other

Sponsor and Funding Source

Add all funding sources for this study:

View Details	Sponsor Name	Sponsor Type	Contract Type:	Project Number	Award Number
⊟	National Institute on Drug Abuse	Federal Government	Grant		

Sponsor Name:	National Institute on Drug Abuse
Sponsor Type:	Federal Government
Sponsor Role:	Funding
Grant/Contract Number:	P50DA027840
Project Period:	From:08/15/2015 to:05/31/2020
Is Institution the Primary Grant	

Holder:	Yes
Contract Type:	Grant
Project Number:	
Award Number:	
Grant Title:	Center for Adaptive Treatment of Cigarette Addiction
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

⊟	Principal Investigator	Duke	Grant		

Sponsor Name:	Principal Investigator
Sponsor Type:	Duke
Sponsor Role:	Protocol Control Data Coordination Monitoring Coordinating Center;
Project Period:	From:08/15/2015 to:05/31/2020
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Grant
Project Number:	
Award Number:	
Grant Title:	
PI Name: (If PI is not the same as identified on the study.)	
Explain Any Significant Discrepancy:	

Is this a federally funded study?

◉ Yes ○ No

Does this study have any of the following?

- Industry sponsored protocol
- Industry funded Duke protocol
- Industry funded sub-contract from another institution
- Industry provided drug/device/biologic
- SBIR/STTR funded protocol

○ Yes ◉ No

As part of this study, will any samples or PHI be transferred to/from Duke to/from anyone other than the Sponsor, a Sponsor subcontractor, or a Funding Source?

○ Yes ◉ No

Is the Department of Defense (DOD) a funding source?

○ Yes ◉ No

For Federally funded studies:

Is your funding subject to, and does it comply with, the funding agency's policy for data sharing?

○ Yes ◉ No

Enter the Grant Number or Other Federal Agency Proposal or Application Number:

P50DA027840

Note: The Federal Funding Agency ID Number is the Sponsor's grant number assigned to your project and available on your Notice of Award (example: R01HL012345).

If known, enter the SPS (Sponsored Projects System) number if applicable:

230139

In the Initial Submission Packet, attach the following:
(1) The entire grant, or an explanation of why a grant is not needed.
(2) NIH institutional Certificate form related to data sharing (if applicable).

The entire grant is needed so that it may be reviewed against the protocol for concordance.

Have you successfully synced your protocol to OnCore by clicking the 'Sync Data Over API' button at the top of this page?

Please verify that the protocol has been created in OnCore before submitting this application for PI Signoff.

◉ Yes, I synced my protocol to OnCore and verified it was successfully sent by logging into OnCore.
○ I may have forgotten! I'll click it again right now, just to be sure, and verify it was successfully sent by logging into OnCore.

Mobile Devices and Software

Does this study involve the use of a software or a mobile application?

○ Yes ◉ No

List all software, including third party (non-Duke) and mobile apps, that will be utilized for ascertainment, recruitment, or conduct of the research/project: (eg, MaestroCare, DEDUCE):

Microsoft Access is used for logging subject information (Enrollment Log, Visit Log, etc.); this database is designed and maintained by the CRC (Al Salley, al.salley@duke.edu), and data are entered by key personnel. Main phone number: (919) 668-5055.

The Study Team will design CRFs in REDCap. Study participants will complete some study questionnaires on REDCap. Questionnaires will be completed within REDCap on a desktop computer in the office. The technician will log on to the REDCap site and will open the questionnaires for the subjects. Subjects will only have access to their questionnaires. Access to any other websites will be blocked by Psychiatry Information Technology. Remote participants will complete all surveys/questionnaires online via REDCap.

Other questionnaires will be completed on paper forms which were designed in Microsoft Word and Excel 2010.

We intentionally do not record calls and we do not allow for generic user input or long 'voicemail' style inputs. We require callers spell and pronounce their names and key in a telephone number to prevent excess unnecessary information from being collected.

Zoom will be used to verify the identity and date of birth of participants. It will also be used to verify CO readings. Zoom calls will not be recorded.

Multi-site Research

Is this a multi-site study?

○ Yes ◉ No

Complete for each site if Duke is the Primary grant awardee or coordinating center:

Entry 1

Site Name:	
City:	
State/Province:	
Country:	
	Site Contact Information
Primary Contact Name:	
Primary Contact Phone:	
Primary Contact Email:	
	Site Details
Does the site have an IRB?	○ Yes ○ No
Site IRB approval expiration date:	
If date not provided, explanation of why:	
Has the site granted permission for the research to be conducted?	○ Yes ○ No
Does the site plan to rely on the DUHS IRB for review?	○ Yes ○ No
What is the status of the study at this site?	○ Open ○ Closed
Site approval letters or site	

personnel lists:	Attach site approval letters, site closure letterS (if applicable), or site personnel lists in the Initial Submission Packet.

Research Abstract

Please type your Research Abstract here:

The Research Abstract should summarize the main points of your study in one paragraph. The following guidelines may help you:

1. Purpose and objective (1-2 sentences)
2. Study activities and population group (2-4 sentences)
3. Data analysis and risk/safety issues (1-2 sentences)

We propose to assess the relative role of nicotine dose and route of delivery in affecting successful switching from combustible cigarettes to e-cigarettes, as well as concomitant reductions in ad libitum cigarette smoking and exposure to harmful and potentially harmful constituents of combustion. The strategy will be to assess adoption of e-cigarette use and concomitant reduction in ad libitum smoking of subjects' usual brands of cigarettes over an 8-week period, during which they will receive nicotine or non-nicotine e-cigarettes, and nicotine skin patches. The nicotine patches will not be used as a therapeutic treatment in this study, but rather as a way to manipulate the nicotine dose, while varying the rate and route of nicotine delivery. Behavioral or "habit" aspects of e-cigarette use will be controlled for by the groups receiving non-nicotine e-cigarettes. One hundred thirty daily cigarette smokers will be randomly assigned to receive 8 weeks of exposure to the following conditions (65/group):

1. Nicotine containing e-cigarettes + 21 mg nicotine skin patches
2. Zero-nicotine e-cigarettes + 21 mg nicotine skin patches

The time commitment for subjects is 8 weeks once their participation begins, plus one follow-up session at four weeks. Subjects will return every two weeks to obtain e-cigarette and patch supplies, and for outcome measures of e-cigarette and combustible cigarette use to be collected; alternatively, remote partipants will be sent supplies in two shipments and will complete study questionnaires online. Ad libitum smoking will be assessed weekly using daily diary recordings of cigarettes smoked per day as well as the objective index of expired air carbon monoxide (CO) levels measured at the study visits.

The primary outcome measures will be the amount of combustible cigarette use and e-cigarette use in the last week of the 8-week exposure period. The main index of combustible cigarette use will be expired air CO. Self-reported cigarettes/day recorded on diaries will be a secondary index of cigarette consumption. The main index of e-cigarette use will be the number of cartridges consumed, based on self-report and counts of the number of unused e-cigarette tanks returned.

Continuing to smoke carries significant health risks. Subjects enrolling in this study are not being asked to quit smoking over the course of the study, but will be exposed to no additional risk from their usual smoking behavior. Their exposure to harmfully and potentially harmful constituents in combustible cigarettes may decrease to the extent they use e-cigarettes as an alternative to combustible cigarettes.

Research Summary

State your primary study objectives

We propose to assess the relative role of nicotine dose and route of delivery in affecting successful switching from combustible cigarettes to e-cigarettes, as well as concomitant reductions in *ad libitum* cigarette smoking and exposure to harmful and potentially harmful constituents of combustion.

The strategy will be to assess adoption of e-cigarette use and concomitant reduction in *ad libitum* smoking of subjects' usual brands of cigarettes over an 8-week period, during which they will receive nicotine or non-nicotine e-cigarettes, and nicotine skin patches. The nicotine patches will not be used as a therapeutic treatment in this study, but rather as a way to manipulate the nicotine dose, while varying the rate and route of nicotine delivery. Behavioral or "habit" aspects of e-cigarette use will be controlled for by the groups receiving non-nicotine e-cigarettes.

State your secondary study objectives

Please select your research summary form:

Standard Research Summary Template

This is the regular (generic) research summary template which is required for all regular applications (unless your protocol fits under the other research summary templates in this category). Use of these instructions is helpful for ensuring that the research summary contains all necessary elements.

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

We propose to assess the relative role of nicotine dose and route of delivery in affecting successful switching from combustible cigarettes to e-cigarettes, as well as concomitant reductions in *ad libitum* cigarette smoking and exposure to harmful and potentially harmful constituents of combustion.

The strategy will be to assess adoption of e-cigarette use and concomitant reduction in *ad libitum* smoking of subjects' usual brands of cigarettes over an 8-week period, during which they will receive nicotine or non-nicotine e-cigarettes, and nicotine or non-nicotine skin patches. The nicotine patches will not be used as a therapeutic treatment in this study, but rather as a way to manipulate the nicotine dose, while varying the rate and route of nicotine delivery. Behavioral or "habit" aspects of e-cigarette use will be controlled for by the groups receiving non-nicotine e-cigarettes.

We hypothesize that e-cigarette use will be higher, and concomitantly, combustible cigarette use will be lower, in the nicotine e-cigarette condition compared to the zero-nicotine e-cigarette condition (i.e., comparing Group 1 vs. Group 2).

Background & Significance

- Should support the scientific aims of the research

Cigarette smoking remains the leading cause of preventable disease and death in developed countries, due principally to its contributions to heart disease, chronic obstructive pulmonary disease (COPD), and cancer (Lando & Wilson, 2010). The annual death toll in the U.S. from diseases caused by smoking has been increasing steadily and is estimated to be the highest ever, 540,000/year (Carter et al., 2015).

The U.S. Surgeon General's Report of 2010 (USDHHS, 2010) concluded that the combustion products of smoke, rather than nicotine, were responsible for most smoking related diseases. E-cigarettes, which deliver nicotine in the absence of combustion, have been advanced as a tobacco harm reduction strategy. Thus far, however, only a minority of smokers have adopted e-cigarettes to satisfy their nicotine dependency without concurrent use of combustible cigarettes. A number of factors may serve as barriers to the adoption of e-cigarettes, including insufficient dose of nicotine and lack of familiar sensory/habit components (e.g., aroma, "throat hit") associated with smokers' usual brands of cigarettes. The present study will examine the relative roles of nicotine dose and route of administration in affecting the ability of smokers to transfer their dependency from combustible cigarettes (CC) to e-cigarettes.

There are several reasons why administration of a given dose of nicotine by inhalation (via e-cigarettes), vs. transdermal administration (via nicotine patches) would be more reinforcing and lead to greater switching from combustible cigarettes to e-cigarettes. First, inhaled nicotine reaches the bloodstream and brain much faster than transdermal administration (Rose et al., 2010), producing immediate reinforcing

effects. Also, inhaled nicotine produces familiar respiratory tract cues that smokers find rewarding (Rose, 2006). Indeed studies have reported a greater suppression of combustible cigarette use when smokers used e-cigarettes as an alternative compared with nicotine patch (McRobbie et al., 2014).

Although subjects receiving nicotine from e-cigarettes will no doubt receive a range of nicotine doses, depending on the extent of use, data from previous studies (Shahab et al., 2017) suggests that the mean dose is expected on average to be similar to that provided by a 21 mg/day patch (and actual mg/day, as estimated from the number of e-liquid cartridges consumed, will be a covariate in the statistical analyses.).

Design & Procedures

- Describe the study, providing detail regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

Design Overview

The study will comprise a randomized, double-blind parallel-arm study to ascertain the role of nicotine dose and route of administration in reducing use of combustible cigarettes and in facilitating adoption of e-cigarettes. One hundred thirty daily cigarette smokers will be randomly assigned to receive 8 weeks of exposure to the following conditions (65/group):

1. Nicotine containing e-cigarettes + 21 mg nicotine skin patches
2. Zero-nicotine e-cigarettes + 21 mg nicotine skin patches

Nicotine and non-nicotine e-cigarettes will be purchased from JUUL Labs. The JUUL is a rectangular closed-system e-cigarette. This e-cigarette was commercially available as of August 8, 2016 and does not contain any alterations to the chemistry or physical characteristics. Each JUUL Pod pack contains 4 pods. Each JUUL Pod contains 0.7mL with 5% nicotine by weight, approximately equivalent to one pack of cigarettes or 200 puffs. Multiple flavors will be used in this study in order to more accurately mimic real world conditions. Subjects will receive packs containing tobacco-flavored and mint-flavored or menthol-flavored pods. Subjects will be provided with enough additional packs of pods to use during the smoking period. JUUL Pods are sealed system cartridges for use in the JUUL e-cigarette. Each pod is contained in tamper resistant blister packs. The nicotine patches will be purchased from Duke Outpatient Pharmacy.

Ad libitum smoking will be assessed weekly using daily diary recordings of cigarettes smoked per day as well as the objective index of expired air carbon monoxide (CO) levels measured at the study visits.

Screening and Session Procedures

Interested potential subjects will respond to advertisements by contacting our Center to be phone screened. Potential subjects also will have the option to complete a REDCap screening survey on the Duke Center for Smoking Cessation website. Potential subjects will be given a brief description of the study and will be asked questions to assess eligibility and interest. Eligible subjects interested in participating will be scheduled for the screening visit.

After granting their informed consent, potential subjects will complete a smoking history form and will have their expired air CO measured. Subjects will provide a urine sample for testing of illicit drug use (all participants) and for pregnancy (women of child bearing potential only). Potential subjects will fill out the Medical History Form and Review of Systems Form on REDCap, as well as asked about any other medical issues they are aware of, on the revised Preliminary Contact Form. A Physician Assistant will review this information with the potential participant either during the screening visit or during a brief (approx. 15 minute) phone call. The screening visit will last approximately 1.5 hours.

The time commitment for subjects is 12 weeks once their participation begins. Subjects will return every two weeks (for eight weeks -- i.e., 5 visits) to obtain e-cigarette and patch supplies, and for outcome measures of e-cigarette and combustible cigarette use to be collected. Four weeks after Study Visit 5, subjects will return for one follow-up session.

Sessions

The first study visit (V1) will take place approximately one week after the screening visit. Subjects will complete baseline questionnaires and will be randomized to one of the two groups. Subjects will be tested for exhaled air carbon monoxide, and saliva samples will be collected for analysis of smoking related chemicals (e.g., cotinine). Subjects will also complete questionnaires assessing their dependence on cigarettes (Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al., 1991)), and rewarding effects of cigarettes (modified Cigarette Evaluation Questionnaire (Cappelleri et al., 2007)).

Subsequent study visits will occur approximately two weeks apart (with a five-day window on either side of the scheduled visit). If a participant does not attend a visit and it cannot be rescheduled within the allowable window, the visit will be considered a missed visit; if participants miss two consecutive visits they will be withdrawn from the study. Participants will be tested for exhaled air carbon monoxide, and will also complete questionnaires assessing their dependence on cigarettes (Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al., 1991)), and rewarding effects of cigarettes (modified Cigarette Evaluation Questionnaire (Cappelleri et al., 2007)).

Questionnaires will be completed within REDCap on a desktop computer in the Center office. The technician will log on to the REDCap site and will open the questionnaires for the subjects. Subjects will only have access to their questionnaires. Access to any other websites will be blocked by Duke Psychiatry Information Technology.

At the first (V1) and final (V5) sessions, participants will provide saliva and urine samples. The saliva sample will be used for analysis of smoking related chemicals (e.g., cotinine). The urine sample will be used to assess total urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), a metabolite of the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). The half-life of NNAL is 10 days (Goniewicz et al., 2009), yielding a valuable index of sustained reductions in cigarette smoking. The half-life of expired air CO, in contrast, is 4.5 h (Sandberg et al., 2011). Total urinary nicotine equivalents (a measure of total nicotine intake) will also be assessed.

Subjects will also be given diaries to record the number of cigarettes smoked each day and e-cigarette cartridges used, and will be instructed to return the diaries at the next visit. At Sessions V1-V4, participants will be dispensed a sufficient supply of skin patches and e-cigarette refill tanks (pods) to last until the next session. Participants will be given pods with both flavors (Virginia tobacco and cool mint or menthol) of e-liquid. They will be asked to return all used and unused pods and used patches at their subsequent visit for proper disposal and compliance monitoring.

Four-week Follow-up

Study participants will return to the laboratory for a brief follow-up session four weeks after Session V5. This session will include an expired air CO reading, collection of saliva and urine samples, and completion of several questionnaires on REDCap.

Remote Study Participation

Potential subjects who live in North Carolina but do not live close enough to travel to our Center will be able to participate in the study remotely. Interested individuals will complete the online REDCap initial screening survey and provide contact information. The responses of potential participants who agree to be in the study will be reviewed by study staff who will then contact eligible respondents by phone to answer any questions and explain how to electronically sign and date the e-consent form. A PDF copy of the signed consent form will be emailed to participants. Participants will then report to a LabCorp facility close to them to provide a urine sample to test for illegal drugs and pregnancy (for females of child bearing potential). If the urine tests are negative, participants will be sent a CO monitor for measuring carbon monoxide (CO), and study e-cigarettes and nicotine patches. Participants will record daily diary entries about their cigarette and e-cigarette use on paper diaries. Participants will complete surveys (asking about potential side effects, mood, and experiences with the e-cigarettes, patches and their usual brand cigarettes) at five time points, once every 2 weeks, and at follow-up 4 weeks after stopping the use of study e-cigarettes and patches. CO readings will be obtained at screening and evisit 5.

Electronic Screening Survey: Interested individuals will respond to various advertisement strategies (television, social media advertisement, etc.) by completing a public online REDCap screening survey. After reading a brief description of the study in the survey, interested potential participants will complete questions regarding smoking and medical history in order to assess safety and eligibility for participation in the study. Potential participants will be deemed ineligible if they decline to complete the initial online screening survey, fail to leave their contact information, or do not meet eligibility criteria based on survey responses. Eligible individuals interested in participating will be contacted via phone by study personnel to discuss the process of remote e-consent.

eConsent: Because of the nature of this study and the number of questionnaires that participants are expected to complete, we will not recruit potential participants who do not read, are blind or who do not read/understand English. We are not equipped to validate alternate versions of our questionnaires, most of which are not published. Questionnaires cannot be administered orally by a translator or by Technicians to illiterate or blind individuals because the data obtained would not be comparable to self-administered questionnaires.

Over the phone, potential participants who passed the initial screening survey will be given instructions on how to view the electronic REDCap Informed Consent Form (ICF). If eligibility could not be determined based on survey responses, study staff will follow-up concerning any additional information needed to determine eligibility, such as information about medical conditions. Potential participants who are eligible will then be sent a link to the eConsent form via email and will be given an adequate amount of time to thoroughly read the consent form and have any questions answered by study staff. The final section of the consent form will ask participants to make a selection between three choices: 1) I have read the consent document and I wish to participate in the study, 2) I have read the consent document and have questions that I would like answered before I decide whether to participate in the study, or 3) I have read the consent document and I DO NOT wish to participate in the study. If participants have questions about the information contained in the consent form, they will be prompted to contact study staff and NOT sign the consent form. If participants have no questions and select "I have read the consent document and I wish to participant in the study," an additional form will open and participants will provide First Name, Last Name, an electronic signature (with their finger on a touchscreen device or a stylus/mouse on a computer), the date of the signature, and an email address. Participants will also be provided a PDF copy of the electronically signed consent form for their records.

Identity Confirmation: Participants will be contacted via Zoom in order to verify their identity and age by viewing their picture ID. The Zoom session will not be recorded. Identity and age of the participant will be cross-verified with the contact information provided at LabCorp for the initial drug screen/pregnancy test as recorded on results sent by LabCorp to the Duke Center for Smoking Cessation (CSC).

LabCorp Drug/Pregnancy Test: Potential participants who pass the initial screening survey will be asked to go to a local LabCorp facility (information on locations provided to them by research staff) to provide a urine sample for testing of illicit drug use (all participants) and for pregnancy (women of child bearing potential only). Participants will complete this test at no cost to them. Participants will be asked to provide a copy of their driver's licenses/photo ID upon check-in. Results of the test(s) will be sent directly to the study medical providers via the LabCorp Beacon online system. Drug screens and pregnancy tests must be negative in order for participants to continue in the study.

CO Monitor: Participants who are still eligible after drug and pregnancy screens will be sent a carbon monoxide (CO) monitor (Covita micro basic Smokerlyzer, valued at $620). Study staff will also provide troubleshooting recommendations for possible problems that may arise. Participants will be asked to use the CO monitor to obtain a CO reading during a Zoom meeting with research staff. The research staff will write the CO reading displayed on the monitor on a study visit form. The Zoom meeting will not be recorded. The initial CO measurement, evaluated by study staff, will be used to determine whether participants meet the minimum CO inclusion requirement. Participants will also complete preliminary questionnaires on REDCap, including smoking history and demographic information.

Randomization and E-cigarette Distribution: After the 1-week training/baseline period is complete and any concerns or questions about the CO monitoring have been addressed, the participants will be assigned a participant number that will determine their randomly assigned study condition, and will be sent by study staff the first shipment of study patches and e-cigarette devices and cartridges containing e-liquid corresponding to their group assignment (nicotine containing e-cigarettes vs. zero-nicotine e-cigarettes). Packages containing nicotine patches and e-cigarettes and liquids require signature by someone who is 21 years of age or older for delivery; the packages will not be delivered if no one appropriate is available to sign for them. This supply will be designed to last through the first 4 weeks of the study; if participants remain in the study, they will be sent a second shipment to use for the final 4 weeks.

Study Milestones: Remote participants will complete study milestones ("e-visits") that correspond to the study visits attended by local participants: baseline, week 2, week 4, week 6 and week 8, plus 4-week follow-up; they will take approximately one hour each to complete and include the same questionnaires that are completed at the in-person study visits, as well as a CO measurement at e-visit 5. The first (baseline) study milestone (V1) will take place after the participants receive their first shipment of e-cigarettes but before they start using them. At this time, participants will be called by study staff and given instructions on how to use the e-cigarettes. They will be asked to switch from cigarette use to use of e-cigarettes during the study. They will then be instructed on the use of daily self-report diaries to be completed on paper. In these diary entries, participants will record the number of conventional cigarettes smoked each day and the number of occasions of e-cigarette use (an occasion defined as taking at least one puff). Participants will be emailed a survey link to complete the questionnaires online via REDCap. Participants will have 72 hours to complete the survey until it expires and it is considered a "missed milestone"; if participants miss two consecutive milestones they will be withdrawn from the study. The

diary entries will be reported to the research staff by phone after e-visit online surveys have been completed.

Each subsequent study milestone (V2-V5) will occur 2 weeks after the previous one, with the follow-up milestone occurring 4 weeks after milestone 5. Participants will be sent a link by email on each study milestone date with instructions to complete the REDCap questionnaires. After the second milestone is completed, participants will be sent a second shipment of e-cigarette cartridges to use until the end of study. At the time of the baseline and final milestones (V1 and V5) and follow-up, participants will be asked to collect a urine sample for NNAL analysis and a saliva sample for analysis of smoking related chemicals (e.g., cotinine), and send these samples to the Duke CSC via UPS.

Participants will be called within 3 days after the first day of study intervention to make sure the study products are being used as directed as well as to ask about any study related side effects. Any reports of side effects, in addition to responses to the Side Effects Form completed online at the study milestones, will be reviewed by the study medical provider. The provider will call the participant if any of the side effects require follow up.

Return and Re-use of the CO monitor: Participants will be asked to return the CO monitor after the CO reading has been obtained during the screening process. If they are accepted into the study and complete e-visits 1-4, then a CO monitor will be sent to them to obtain the CO reading at e-visit 5. The participant will be asked to return the CO monitor after e-visit 5. Upon return of the CO monitor, research staff will disinfect the monitor before sending it to another participant.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

We propose to enroll up to 1600 smokers in order to identify 130 participants who meet all criteria to be accepted into the study and to be randomized into one of four experimental conditions.

Inclusion Criteria

• Are 21-65 years old;
• Smoke an average of at least 10 cigarettes per day;
• Have smoked for the past year;
• Have an expired air CO reading of at least 10ppm;
• Have a self-reported body weight of < 350 lbs.;
• Are able to read and understand English.

Potential subjects of child bearing potential must agree to use two forms of contraception during their participation in this study. Women are considered past the age of child-bearing potential if:

• They are greater than 55 years of age;
• They are at least 50 years of age AND have not menstruated for at least 12 months, OR have a documented Follicle Stimulating Hormone (FSH) level of greater than 40 mIU/mL;
• They are at least 45 years of age AND have not menstruated for at least 18 months, OR have a documented Follicle Stimulating Hormone (FSH) level of greater than 40 mIU/mL.

Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use.

Potential subjects must agree to avoid the following during their participation in this study:

• Participation in any other nicotine-related treatment study protocol outside of this protocol;
• Use of tobacco products other than cigarettes, including pipe tobacco, cigars, e-cigarettes (other than those provided during the study), snuff, and chewing tobacco;
• Use of experimental (investigational) drugs or devices;
• Use of illegal drugs;
• Use of exclusionary medications.

Exclusion Criteria

• Actively seeking treatment for nicotine dependence;
• Uncontrolled high blood pressure (self-report);
• Coronary heart disease with symptoms (e.g., chest pain);
• Heart attack in the past year;
• Cardiac rhythm disorder (irregular heart rhythm with symptoms);
• Chest pain in the last month (unless history indicates a non-cardiac source);
• Symptomatic heart disorder such as heart failure;
• Advanced liver or kidney disease that requires medication or dialysis, paracentesis;
• Bleeding stomach ulcers in the past 30 days;
• Lung disease that requires oxygen;
• Major brain disorder (including stroke with residual deficit, brain tumor, and seizure disorder);
• Migraine headaches that occur more frequently than once per week;
• Recent, unexplained fainting spells;
• Diabetes with insulin use;
• Current cancer or treatment for cancer in the past six months (except basal or squamous cell skin cancer);
• Other major medical condition (as determined by study medical provider);
• Diagnosis of thought disorder; such as bipolar disorder or schizophrenia;
• Psychiatric hospitalization within the past 12 months;
• Pregnant or nursing mothers;
• Use (within the past 7 days) of illegal drugs (or if the urine drug screen is positive for THC, Cocaine, Amphetamine, Opiates, Methamphetamines, PCP, Benzodiazepines, or Barbiturates), unless recent use of prescription opiates or benzodiazepines were taken for management of acute symptoms (e.g., tooth extraction, recent surgery, or sleep);
• Use of experimental (investigational) drugs within the past 7 days;
• Use of psychiatric medications including antidepressants and anti-psychotics may be permitted if the condition is stable (study medical provider discretion).
• Use of opiates, benzodiazepines, and muscle relaxants (unless taken for sleep or acute symptoms such as tooth extraction or recent surgery) within the past 7 days (study medical provider discretion);
• Use of Wellbutrin, bupropion, Zyban, Chantix, varenicline, nicotine patch, nicotine replacement therapy, clonidine or any other smoking cessation aid within the past 30 days;
• Use of cigars, cigarillos, pipes, Hookah, dissolvable nicotine, snuff, chewing tobacco, or e-cigarettes within the past 7 days;
• Diagnosis of alcohol abuse or dependence or self-report of consuming more than 6 drinks on one occasion more than one day per week;
• Significant adverse reaction to nicotine patch in the past;
• Current or recent participation (in the past 30 days) in another smoking treatment study at our Center or another research facility;

Assessment of Eligibility

Potential subjects who do not have a self-reported diagnosis of the above listed conditions may be excluded if the study physician or physician assistant determines that the history reveals information that may jeopardize the subjects' safe study participation. For medical conditions that do not appear above, the study physician will be consulted, and if the medical condition does not jeopardize safe study participation, then the subject may be enrolled.

Subject Recruitment and Compensation

- Describe recruitment procedures, including who will introduce the study to potential subjects. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about approximately how many DUHS subjects will be recruited. If subjects are to be compensated, provide specific prorated amounts to be provided for expenses such as travel and/or lost wages, and/or for inducement to participate.

Subject Recruitment

Smokers with no major health problems will be recruited from communities in and around Durham, North Carolina, and, for remote participation, across the state of North Carolina. Recruitment will occur through television, newspaper and internet advertisements, flyers, Facebook, Duke List, and by word-of-mouth. We will also recruit via the Duke Primary Care Research Consortium. This consortium oversees all

research within Duke Primary Care, a network of over 30 clinics primarily around the Research Triangle Area. The consortium is primarily interested in whether studies offered to patients would provide safe and effective means for supporting or improving health outcomes. Duke Primary Care clinics serve a broad cross section of the community. Patients from the Duke Primary Care Research Consortium will be recruited from 1 of the 30 clinics. A study team member will conduct a query into the electronic health record through DEDUCE (Duke Enterprise Data Unified Content Explorer) to identify potentially eligible patients. DEDUCE is an electronic technology system designed to enable access to specific patient data fields across the Duke Health System for approved research purposes. After identifying individuals who fall within our recruitment categories, we will directly contact these patients by MyChart message and/or telephone to offer them additional information about the research study (Duke's Cold Call Policy). Any potential subjects who have opted out of contact for research studies will not be contacted for this study.

Potential subjects will be pre-screened on the phone by a member of the Duke CSC. If potential subjects meet the pre-screening study requirements and are still interested in participation, they will attend a physical screening session at the Duke CSC, located at 2424 Erwin Road, Suite 201, Durham, NC 27705, or complete screening procedures online and by visiting a local LabCorp facility. If after the screening process it is determined that they qualify for participation, participants will attend subsequent study visits at the Duke Center for Smoking Cessation located at 2424 Erwin Road, Suite 201, Durham, NC 27705, or online via REDCap and phone contact.

Subject Compensation

Local (in-person) participants will be paid $25 for completing the Screening procedures. Subjects will be reimbursed $25 per visit for completing the five study visits, plus $60 for completing the follow-up visit. In addition, subjects will receive a payment of $10 for each of the 5 visits attended in which they return their completed take-home diaries with questions in which they record smoking behavior and patch and e-cigarette use, as well as their used and unused e-cigarettes and patches. Subjects who do not complete each visit will still receive payment for the ones completed. Thus, subjects who complete the screening and five visits and hand in their completed take-home diaries and study investigational product (IP) each time and also attend the follow-up visit will receive a total payment of $335.

Remote participants will be paid $35 for completing the Screening procedures ($10 for completing online surveys and CO readings, and $25 for visiting a LabCorp facility and providing a urine sample). Subjects will be reimbursed $25 per milestone for completing the five study e-visits, with an additional $15 for e-visit 1 and an additional $5 for e-visit 5. Those milestones involve collecting and sending urine and saliva samples. In addition, participants will receive $30 for completing the follow-up e-visit. In addition, subjects will receive a payment of $5 at the time of milestones 1-5 for completing 75% of the daily diary entries. Subjects who do not complete each e-visit will still receive payment for the ones completed. Subjects will also receive $50 for returning the CO monitor after screening and an additional $50 for returning the CO monitor at the end of the study. Thus, subjects who complete the screening and five e-visits and complete 75% of the daily diaries and also complete the follow-up e-visit will receive a total payment of $335.

Consent Process

- Complete the consent section in the iRIS Submission Form.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

We will not include subjects who do not have the capacity to give legally effective consent.

Study Interventions

- If not already presented in #4 above, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i.e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant women, prisoners or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

Conventional (combustible) cigarettes: Continuing to smoke carries significant health risks. Subjects enrolling in this study are not being asked to quit smoking over the course of the study, but will be exposed to no additional risk from their usual smoking behavior. Their exposure to harmfully and potentially harmful constituents in combustible cigarettes may decrease to the extent they use e-cigarettes as an alternative to combustible cigarettes.

Potential side effects of Nicotine patch: The nicotine patch poses very little risk and is approved for over-the-counter sales as a smoking cessation treatment. It is not being used as a treatment for nicotine dependence in this protocol but the risks will be minimal. Insomnia and abnormal dreams are common and expected side effects associated with 24-hour nicotine patches. If a subject complains of disturbed sleep, he or she will be instructed to remove the patch at bedtime and apply a new one the next day at the usual time. Skin irritation may occur, although this will be minimized by changing the site of patch application daily. If a subject develops itching or a rash at the patch site, he or she will be advised to use 1% hydrocortisone cream on the affected area. Symptoms associated with nicotine toxicity include lightheadedness, dizziness, nausea, fainting and vomiting. A less likely side effect of nicotine patches is somnambulism. If a subject reports significant side effects, the dose of the nicotine patch may be reduced if necessary.

Electronic Nicotine Delivery Systems (ENDS): ENDS, or "e-cigarettes," have been marketed in the U.S. since 2007 and have been used worldwide by millions of smokers. While the potential risks of long-term use of e-cigarettes are unknown, most experts agree that the constituents of e-cigarettes are less harmful than those of combustible cigarettes (Grana et al., 2014). Although it is conceivable that participants could receive an overdose of nicotine, this is extremely unlikely inasmuch as smokers can control the dose according to how they puff and inhale from the devices, as they do with conventional cigarettes. The main side effect that is anticipated with the relatively short 8-week duration of exposure to ENDS in the proposed project is mild irritation of the respiratory tract from inhalation of the propylene glycol and nicotine contained in the product. Should any clinically significant changes occur, the study physician will recommend discontinuation of ENDS use if it is indicated.

The Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), state and local health departments are investigating a respiratory syndrome associated with the use of e-cigarettes. People with this syndrome have reported a wide variety of symptoms including cough, shortness of breath, chest pain, nausea, vomiting, diarrhea, fatigue, fever, and abdominal pain.

In a New England Journal of Medicine article entitled "Vaping-Induced Lung Injury" (September 6, 2019), Dr. Christiani stated that "[a]bout 80% of the persons who vaped and became ill reported having used both nicotine products and tetrahydrocannabinol (THC) or cannabidiol (CBD) products". Thus far, investigators have not found a single product linked to all reports of this respiratory syndrome. Most cases have been linked to "street" products or substances added to e-cigarettes -- changes not intended by e-cigarette manufacturers. The e-cigarettes used in this study will be obtained directly from JUUL, a manufacturer registered with the FDA, and will not be altered in any way. Overall, the respiratory syndrome associated with e-cigarette use has been reported in less than 1 in 1,000 people who use e-cigarettes.

Subjects will be monitored throughout the duration of the study for side effects and severe adverse effects (SAEs). They will be instructed to report any side effects to the study technicians, who will communicate these reports immediately to the medical staff. The most appropriate course of action will be determined,

which may include options for dose reduction or termination of study intervention. Participants will be reminded that they have the option to withdraw from the study at any time. Subjects will also be given the 24-hour emergency contact numbers in the event that side effects or adverse events occur between sessions. SAEs will be reported to the IRB and will be monitored until resolution or stabilization.

The sponsor for this study will ensure the investigational tobacco product is distributed only to qualified members of key personnel in accordance with this protocol.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

There are no costs to participants for taking part in this study. All the study costs, including any study supplies and procedures related directly to the study, will be paid for by the research grant awarded to Duke University.

Data Analysis & Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

The primary outcome measures will be the amount of combustible cigarette use and e-cigarette use in the last week of the 8-week exposure period. The main index of combustible cigarette use will be expired air CO, a highly sensitive and specific measure of smoke inhalation. As a secondary measure (at the first (V1) and final (V5) sessions), we will assess total urinary 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), a metabolite of the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). The half-life of NNAL is 10 days (Goniewicz et al., 2009), yielding a valuable index of sustained reductions in cigarette smoking. The half-life of expired air CO, in contrast, is 4.5 h (Sandberg et al., 2011).

Self-reported cigarettes/day recorded on diaries will also be a secondary index of cigarette consumption. The main index of e-cigarette use will be the number of cartridges consumed, based on self-report and counts of the number of unused e-cigarette tanks returned. We hypothesize that e-cigarette use will be higher, and concomitantly, combustible cigarette use will be lower, in the nicotine e-cigarette condition compared to the zero-nicotine e-cigarette condition (i.e., comparing Group 1 vs. Group 2). This hypotheses will be evaluated using General Linear Modeling (GLM) techniques to assess the significance of the nicotine factor, using a 1-tailed alpha=0.05. A one-tailed comparison is justified given that a higher dose of nicotine in the e-cigarette would only be expected to decrease use of conventional cigarettes. Moreover, there would be no interest in pursuing the nicotine e-cigarette plus nicotine patch combination if it led to greater smoking than the placebo e-cigarette plus nicotine patch. Thus, the 5% Type I error rate can reasonably be assigned to the 1-tailed comparison. Covariates in the analysis of combustible cigarette use will include the amount of e-cigarette use, since that will affect the overall dose of nicotine received by subjects, as well as baseline combustible cigarette use, and baseline demographic and smoking history variables (the latter will also serve as covariates in the analysis of e-cigarette use as a dependent measure). We predict at least a moderate effect size (0.5) for each of the main effects, nicotine and route of administration, so that a sample size of 50 per group will yield at least 80% power to detect the hypothesized effects.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

Data Safety Monitoring Plan (DSMP)

To address potential safety issues in addition to collection of the primary study outcomes, severe side effects and adverse events potentially associated with the study will be examined, recorded and then reported to the IRB in a manner consistent with Duke HRPP policies. The principal investigator will be responsible for monitoring data collection and safety of this study.

Data collection for this study will be carried out at the Durham clinical site of the Duke Center for Smoking Cessation (CSC) or remotely via REDCap and phone contact. All members of the study team will complete research integrity ("code of conduct") and CITI (Collaborative Institutional Training Initiative) Human Research Curriculum and clinical laboratory safety training as required by Duke University Medical Center. All study staff who are involved in data collection, management, and processing will be thoroughly trained following standards of procedures prior to working on this project.

Study staff responsible for data collection will use a checklist for completion for each study visit of each participant. Missing Data Forms, along with explanations should missing data occur, will be completed by the study staff for each study visit/e-visit.

Microsoft Access will be used for logging subject information (Enrollment Log, Visit Log, etc.). Data will be entered by the study staff. The key study personnel will further examine the computerized data entries and original records for accuracy and completion.

Emergency Unblinding

This is a blinded protocol such that all participants and all study personnel except for the Clinical Research Coordinator and the Research Program Leader are blinded to group allocation. During specific circumstances it will be necessary to unblind other study personnel, such as study team medical personnel. Emergency unblinding will occur under the discretion of the study physician (or one of the study physician assistants) in any situation in which unblinding is deemed necessary to ensure or promote the safety of a study participant. The decision to unblind for safety reasons may occur for a number of reasons and it is not possible to enumerate all potential circumstances. Examples of reasons for unblinding to ensure participant safety include situations in which it is necessary to know which study drugs the subject was taking in order to manage the side effect(s), advise the subject on the risk of future negative drug reactions, uncover potential safety information about the drug, and/or determine whether the adverse event is study related. In those situations, the Clinical Research Coordinator or Research Program Leader will inform the study physician (or physician assistant handling the event) of that subject's study condition. If unblinding occurs, that subject's data will be censored and will not be included in final data analyses.

Privacy, Data Storage & Confidentiality

- Complete the Privacy and Confidentiality section of the iRIS submission form.

Describe Role of External Personnel:

External key personnel will assist in data collection, data entry, data analysis, and recruitment under the supervision of our staff. They will also shadow all aspects of the research process, including consent, but will not be conducting consent independently. They will not be accessing Maestro or OnCore but will have access to our paper and electronic PHI in REDCap (name, address, phone, DOB, medical history, SSN for payment). Onsite training on research practices, confidentiality/privacy, and HIPAA will be conducted during their first week.

Study Scope

Does the subject population contain >50% malignant hematology or oncology patients, or their caregivers?

○ Yes ◉ No

Are you using a drug, biologic, food, or dietary supplement in this study?

◉ Yes ○ No

Are you using a medical device, an algorithm (whether computer based or not), an in vitro diagnostic test, or using samples to look for biomarkers in this study?

◉ Yes ○ No

Does this study involve a Humanitarian Use Device (HUD)?

○ Yes ◉ No

Does this study employ magnetic resonance, including imaging (MRI), spectroscopy (MRS), angiography (MRA) or elastography (MRE) beyond the standard of care?

○ Yes ◉ No

Does this study specify or require the performance of diagnostic procedures using ionizing radiation (x-rays, DEXA, CT scans, nuclear medicine scans, etc.) that are beyond the standard of care?

○ Yes ◉ No

Does this study specify or require the performance of therapeutic procedures using ionizing radiation (accelerator, brachytherapy or systemic radionuclide therapy) that are beyond the standard of care?

○ Yes ◉ No

Will the participant be subjected to increased or decreased ambient pressure?

○ Yes ◉ No

Do you plan to recruit subjects from Duke Regional Hospital (DRH)?

○ Yes ◉ No

Do you plan to recruit subjects from Duke Raleigh Hospital (DRAH)?

○ Yes ◉ No

Does this study utilize the Duke Early Phase Clinical Research Unit (DEPCRU)?

○ Yes ◉ No

Are you using the Duke logo in any advertisements?

(•) Yes ( ) No

Is this study retrospective, prospective, or both?

"Retrospective" means that data or samples already in existence (collected prior to the study submission) will be used.
"Prospective" means there will be data or samples collected in this study for research purposes.

( ) Retrospective
(•) Prospective
( ) Retrospective and Prospective

If the study is both retrospective and prospective: Is this a review soley of information collected for non-research purposes (i.e. a review of medical records)?

( ) Yes ( ) No

Does this protocol include any research using botulinum toxin, including the FDA-approved clinical product (Botox)?

( ) Yes (•) No

Does this protocol involve the administration of any of the following materials to humans?

- Any viral vector or plasmid
- Any cells that have been modified by a viral vector
- Any other genetically-modified cells
- Any genetically-modified virus, bacterium, or other agent
- Any other recombinant or synthetic nucleic acid

( ) Yes (•) No

Subject Population Groups and Enrollment

Population Groups (Select targeted population groups only):

Note:

- If Minors are included, the study will be routed to the Department of Pediatrics for Pediatric Risk Assessment.
- Students and Employees over whom Key Personnel have a supervisory role may not be enrolled in this study

[x] Adults
[ ] Minors who are Wards of State
[ ] Minors
[ ] Duke Patients
[ ] Pregnant Women
[ ] Fetuses
[ ] Prisoners
[ ] Adults incapable of giving consent
[ ] Adults with diminished capacity
[ ] Handicapped subjects
[x] Students
[x] Employees
[ ] Healthy Controls
[ ] Deceased subjects

☐ Blanket Protocol

Students and Employees over whom Key Personnel have a supervisory role may not be enrolled in this study.

Please select any population groups excluded from participation in this study:

☑ Pregnant women

Will you administer a pregnancy test to eligible female subjects prior to the start of study activities?

◉ Yes ○ No

Maximum number of subjects to be consented at Duke:

Enter a single number. If you anticipate consenting a range of subjects, enter the **upper** limit of the range. The number should represent the maximum number of subjects for the life of the study.

1600

Maximum number of subjects to be consented at all sites:

Enter a single number. If you anticipate consenting a range of subjects, enter the **upper** limit of the range. The number should represent the maximum number of subjects for the life of the study.

1600

Subject Procedures and Costs

Biobank - Does this study involve the collection, use, tracking, banking (storage) or distribution of human biological specimens?

Human biological specimens include blood or its components, healthy or diseased tissue, bodily fluids, DNA /RNA or human stem cells.

◉ Yes ○ No

Procedures

Check all the apply:

☐ Genetic Testing
☐ Gene Transfer
☐ DNA Banking
☐ Testing for Reportable Infectious Diseases
☐ Human Cell Banking
☐ *Use of Human Embryonic Stem Cells
☐ *Use of Human-induced Pluripotent Stem Cells
☐ *Use of Other Cells Derived from Human Embryos
☐ *Use of Human/Animal Chimeric Cells
☐ *Specialized Cell Populations for Cell Therapy
☐ Use of Human Tissue
☑ Use of Bodily Fluids
☐ Use of Blood (or its components)
☐ Not Applicable

Will blood be drawn in this study for research purposes?

○ Yes ◉ No

Will the Operating Room be used in this study?

Include only research time, not clinical care time.

○ Yes ◉ No

Will there be extra costs to subjects or insurance as a result of the research (e.g. tests, hospitalization)?

○ Yes ◉ No

Will there be Subject Compensation?

◉ Yes ○ No

Compensation for Travel / Lost Income (in USD):

335

Other Subject Compensation:

None

Subject Recruitment Materials

For each document to be reviewed, use the table below to provide the following information:

Attach a copy of each advertisement that you will be using with this study in the Initial Submission Packet. If any Ad will have multiple wording variations, attach a copy of each version of the Ad.
All materials that will be used to advertise the study in order to recruit subjects must be approved by the IRB.

Types of subject recruitment materials include, but are not limited to, the following:

Direct Advertising
Posters
Billboards
Flyers
Brochures

Media Advertising
Newspaper Ads
Magazine Ads
Radio Ads
TV commericals / Video
Internet website
Social Media

Other Types of Advertising
Newsletter
Email
Postcards / Letters

(Note: Doctor-to-Doctor letters do not require IRB approval)

Document name	Material category	Location material displayed	Has this material previously been approved by the IRB?
Final_DukeCSC_ECig_Study_062018	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ◉ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Spectrum cable channels	○ Yes ◉ No
Final_DukeCSC_ECig_Study_062018	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Facebook	○ Yes ○ No
ENDS-Switch Facebook Ad	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Facebook	○ Yes ◉ No
	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet	Please be specific. For example, "Duke" would not be an	

ENDS Switch BannerAd	website / Email Letter / Postcard Phonescript Radio Television / Video Newsletter / Newspaper / Magazine Other	appropriate location. "Duke Hospital Television" would be an appropriate response. To be placed on various websites by Spectrum/Time Warner	Yes No
ENDS Switch Craigslist Ad	Billboard / Flyer / Poster Brochure Internet website / Email Letter / Postcard Phonescript Radio Television / Video Newsletter / Newspaper / Magazine Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Craigslist	Yes No
ENDS Switch Poster	Billboard / Flyer / Poster Brochure Internet website / Email Letter / Postcard Phonescript Radio Television / Video Newsletter / Newspaper / Magazine Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. These posters will be displayed in the Triangle area.	Yes No
		Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Durham	

ENDS Switch Print Ad	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ◉ Newsletter / Newspaper / Magazine ○ Other	/Raleigh: News & Observer (http://www.newsobserver.com/), and Herald Sun (www.heraldsun.com) & The Independent Weekly (www.indyweek.com). a. Local papers: Southside Shopper, Carolina Weekly, Raleigh Coffee News and the Triangle JobFinder. b. College newspapers: UNC Daily Tarheel, Duke Chronicle, NCSU Technician & NCCU Campus Echo. www.dukesmoking.com www.clinicalconnection.com www.centerwatch.com www.dukehealth.org http://psychiatry.duke.edu Google Adwords Facebook Craigslist	○ Yes ○ No
ENDS Switch Print Web Ad	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. www.dukesmoking.com www.clinicalconnectio	◉ Yes ○ No

	○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	n.com www.centerwatch.com www.dukehealth.org http://psychiatry.duke.edu Google Adwords Facebook Craigslist Duke List Electronic Job Finder Other websites	
ENDS Switch Web Ad	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. www.dukesmoking.com www.clinicalconnection.com www.centerwatch.com www.dukehealth.org http://psychiatry.duke.edu Google Adwords Facebook Craigslist Duke List Electronic Job Finder Other websites	◉ Yes ○ No
ENDS-Switch Facebook Ad-2	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Facebook	○ Yes ◉ No

ENDS-Switch Facebook Ad-3	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Facebook	○ Yes ◉ No
ENDS-Switch Reminder Letter	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ◉ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. NA	○ Yes ◉ No
ENDS-Switch Reminder Email	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ◉ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. NA	○ Yes ◉ No
	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital	

Generic Flyer	○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Television" would be an appropriate response. These flyers will be posted in the Triangle and surrounding areas including college campuses.	○ Yes ◉ No
Generic Bus Ad	◉ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. This ad will be posted on buses in the Triangle and surrounding area.	○ Yes ◉ No
TV Ad	○ Billboard / Flyer / Poster ○ Brochure ○ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ◉ Television / Video ○ Newsletter / Newspaper / Magazine ○ Other	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response. Spectrum On Demand markets in NC	○ Yes ◉ No
ENDS-Switch Facebook Ad-Remote	○ Billboard / Flyer / Poster ○ Brochure ◉ Internet website / Email ○ Letter / Postcard ○ Phonescript ○ Radio ○ Television / Video	Please be specific. For example, "Duke" would not be an appropriate location. "Duke Hospital Television" would be an appropriate response.	○ Yes ◉ No

	○ Newsletter / Newspaper / Magazine ○ Other	Facebook	

Consent Process

Attach draft consent forms in the Initial Review Submission Packet.

Consent forms must be MS Word documents and follow the specific format outlined by the IRB. **Click here** to download a copy of the consent form template.

Note: Please do not edit the section of the footer that contains the Protocol ID, Continuing Review and Reference Date fields. Those fields will be used to stamp the final consent form when it is approved by the IRB. If you want to add an internal version date, please put it in the header.

Who will conduct the consent process with prospective participants?

Give the person's role in this study (PI, Study Coordinator, etc.):

The consent process will be conducted by Clinical Research Coordinators, Clinical Research Specialists (Clinical Trials Assistants), Physician and Physician Assistants. Dr. Rose will not be involved in the consenting process.

Who will provide consent or permission?

(Select all that apply):

- ☑ Participant
- ☐ Parent(s) or Legal Guardian(s)
- ☐ Legally Authorized Representative (LAR)

How much time will the prospective participant (or legally authorized representative) have between being approached about participating in the study and needing to decide whether or not to participate?

If you are not giving the person overnight to consider whether or not to participate, please justify.

Potential subjects are given as much time as they need to make an informed decision.

Where will the consent process occur?

The consenting process will occur at the Duke Center for Smoking Cessation in a private office/room. For remote participants, the consenting process will occur via REDCap e-consent and phone conversations with study staff.

What steps will be taken in that location to protect the privacy of the prospective participant?

Only the potential subject and the person obtaining consent will be present. For remote participants, phone conversations will take place in private staff areas.

How much time will be allocated for conducting the initial consent discussion, including presenting the information in the consent document and answering questions, with each prospective participant?

There is no set amount of time devoted to conducting the initial consent discussion. Each potential subject is allowed as much time as necessary to ask questions.

What arrangements will be in place for answering participant questions before and after the consent is signed?

The consenter will go through the consent form page-by-page with the potential subject before the consent form is signed. They will discuss the study procedures, length of time involved in the study, risks, benefits, alternatives to study participation, confidentiality, costs and compensation, research related injuries, their right to decline participation at anytime and the contact information for both the principal investigator and the IRB. The potential subject will be given the opportunity and encouraged to ask questions then and throughout their study participation.

For remote participants, the REDCap e-consent survey will offer the alternative "I have read the consent document and have questions that I would like answered before I decide whether to participate in the study". Potential participants will be encouraged in the introduction to the consent form to ask any questions prior to signing: "If you have any questions or if there is information that you do not clearly understand, please call the study staff at 919-668-1327 or 919-668-5055 to clarify **before** signing this consent form." Study staff will also talk with participants on the phone and make sure they understand the study before beginning study procedures.

Describe the steps taken to minimize the possibility of coercion or undue influence.

It is made clear to the subjects both in the ICF and by the person obtaining consent that they may withdraw from the study at any time. We are also careful that our compensation is sufficient to reimburse for time and travel expenses but is not coercive.

What provisions will be in place to obtain consent from participants who do not read, are blind or who do not read/understand English?

Because of the nature of this study and the amount of questionnaires that subjects are expected to complete we do not recruit potential subject who do not read, are blind or who do not read/understand English. We are not equipped to validate alternate versions of our questionnaires, most of which are not published. Questionnaires cannot be administered orally by a translator or by key personnel to illiterate or blind subjects because the data obtained would not be comparable to self-administered questionnaires.

Do you plan to obtain written consent for the conduct of research?

(●) Yes ( ) No

Protected Health Information (PHI)

Indicate how you intend to use potential subjects' Protected Health Information (PHI):

( ) I will review, but not record, PHI prior to consent.
(●) I will record PHI prior to consent.
( ) I do not intend to use PHI prior to consent.
( ) I will record PHI without consent. (decedent research, database repository, chart review)

Request for Waiver or Alteration of Consent and/or HIPAA Authorization

Will the population include deceased individuals?

( ) Yes (●) No

This waiver request applies to the following research activity or activities:

- [x] Scheduling of research activities in MaestroCare and/or the recording of PHI via telephone for screening purposes prior to obtaining written consent for the research. Scheduling of research activities in MaestroCare and/or the recording of PHI via telephone for screening purposes prior to obtaining written consent for the research. (If you check this box, please complete all sections below.)
- [x] Ascertainment (identification, selection) and/or recruitment of potential subjects while recording identifiable private information, such as protected health information (PHI), prior to obtaining the subject's consent. (If you check this box, please complete sections B and C below.)
- [ ] Conduct of the research project without obtaining verbal or written consent and authorization. (If you check this box, please complete sections B and C below.)

Note: Answer the questions below as they pertain solely to PHI collected prior to consent.

Provide the following information:

List the elements of informed consent and/or HIPAA authorization for which waiver or alteration is requested:

- Provide the rationale for each.

All elements of consent and HIPAA authorization are being requested for waiver. It is not possible to ascertain whether someone is a suitable study candidate without asking about protected health information.

List the specific protected health information (PHI) to be collected and its source(s):

- (Note: PHI = health information + identifiers)

Name, phone number, e-mail address and a history of medical conditions and smoking behavior and tobacco use will be collected verbally and electronically from the potential subjects.

Criteria for Waiver: The DUHS IRB may waive the requirement for informed consent and authorization if all of the following criteria are met:

- Please respond to each item in the space below using protocol-specific language to provide justification:

a) The research or clinical investigation involves no more than minimal risk to subjects:

The PHI collected during the initial screening will be used solely for recruitment review. The PHI is necessary for the purposes of this review only. The pre-enrollment PHI will not leave this office

b) The waiver or alteration will not adversely affect the rights and welfare of the subjects. Include a description of any measures to be taken to ensure that the rights and welfare of subjects will be protected:

There is no adverse effect on the rights and welfare of potential subjects because all PHI that is to be collected prior to informed consent will be de-identified if the subject does not qualify for the study. After obtaining informed consent, the information will be protected according to the usual standards of confidentiality applicable to research studies. The identifiers will be kept in the Data Manager's office and the office will be locked when unoccupied. Only those individuals listed as key personnel will have access to this information. For subjects who choose not to enroll in this study and do not provide consent, their pre-enrollment PHI will be de-identified.

c) Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

Potential subjects will be given a description of study procedures and requirements prior to any questions being asked about their health status.

d) If this research activity relates to research involving deception, explain how subjects will be provided with additional pertinent information after study participation and what information will be provided. Otherwise indicate "not applicable":

This research will not involve deception.

e) The use or disclosure of protected health information involves no more than minimal risk to the privacy of individuals, based on, at least, the presence of the following elements (e1. and e2.)

Demonstrate that the use or disclosure of PHI involves no more than minimal risk to the privacy of subjects by describing the plans requested below:

e1) An adequate plan to protect the identifiers from improper use and disclosure.
Describe the plan (how protection will be accomplished) and indicate where the PHI will be stored and who will have access:

The identifiers will be stored in a secure database on a server hosted by Duke Health Technology Services or on a paper form which will be kept in a locked office within our locked Center, and only those individuals listed as key personnel will have access to this information. Identifiers will only be kept for individuals who complete the survey and are eligible for study participation. If an individual answers "yes" to the question about illegal drug use the survey will end and no identifiers will be collected (including IP address).

e2) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

Describe the plan (how and when identifiers will be destroyed and by whom). If there is a health or research justification for retaining the identifiers or such retention is otherwise required by law, provide the reason to retain identifiers:

For potential subjects who choose not to enroll in this study and do not provide consent, their pre-enrollment PHI will be de-identified.

e3) Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule. By electronically signing this submission, the PI provides this written assurance:

The protected health information will not be reused or disclosed to any other person or entity except (i) as required by law, (ii) for authorized oversight of the research study, or (iii) for other research for which the use or disclosure of PHI would be permitted by the HIPAA Privacy Rule.

f) The research could not practicably be conducted or carried out without the waiver or alteration:

- Explain why informed consent/authorization can not be obtained from subjects.

This waiver is necessary to allow us to collect and record contact information from potential subjects who are interested in participating in this study on the phone prior to seeing the potential subject in person (in order to decide whether they should be seen in person) and therefore prior to an opportunity to obtain written consent.

g) The research could not practicably be conducted or carried out without access to and use of the protected health information:

It is not possible to ascertain whether someone is a suitable study candidate without asking about protected health information.

h) For research using biospecimens or identifiable information, the research could not practicably be carried out without access to and use of the protected health information:

Biospecimens will not be collected until written consent is obtained. It is not possible to ascertain whether someone is a suitable study candidate without asking about protected health information, and it must be identifiable so that we'll know which information goes with which potential subject. For potential subjects who choose not to enroll in this study and do not provide consent, the pre-enrollment PHI will be de-identified.

Waiver of Documentation of Consent and HIPAA Authorization for Scheduling in MaestroCare and/or the recording of PHI via telephone for screening purposes:

These research activities prior to obtaining written consent for the study presents no more than minimal risk of harm to subjects:

(•) True
( ) False

These are procedures for which written consent is normally not required outside of the research context:

(•) True
( ) False

An IRB-approved phone script will be used to obtain verbal consent from subjects for scheduling and/or screening prior to obtaining written consent for the study:

(•) True
( ) False

Drugs, Biologics, and Other Substances

Select Protocol Phase (for studies with FDA regulated drugs or biologics only). Choose only one:

( ) Phase 0
( ) Phase I
( ) Phase I/II
(•) Phase II
( ) Phase II/III
( ) Phase III
( ) Phase IV
( ) N/A
( ) Pilot

Drugs, biologics, or other substances being evaluated as a part of this research study:

Add all drugs, biologics, or other substances being evaluated as a part of this research study for which an IND is provided for the indication used in this study.
Also add any other drugs, biologics or other substances here that are being used as a part of this research study, for which an IND is not provided.

List every other drug, biologic or other substance for which side effects are described in the consent form.

View Details	Drug Name	FDA Approved	A new drug or a new use of approved drug:	IND Number
⊟	**Drug/Biologic/Substance Generic Name:** Nicotine patches **Generic Drug Name:** **Investigational Drug Name:**	No	No	

Drug/Biologic/Substance Generic Name:	Nicotine patches
Generic Drug Name:	
Investigational Drug Name:	
Drug/Biologic/Substance Source:	
Is the drug/substance being provided to the subject free-of-charge?	No
Is the Drug FDA Approved?:	No

Is this drug/biologic or other chemical, metabolite, nutritional substance or other substance to be used in this research subject to the provisions of the Controlled Substances Act?	No
Does this Drug have an IND Number?	No
IND Number	
IND Holder:	
IND details:	
If FDA Approved and an IND is not required, Please provide a rationale for exemption:	
Will drug/substance be shipped from Duke to external locations	
Dose Range:	
Frequency:	
Will this drug, biologic, chemical, metabolite, nutritional substance or other substance be manufactured or compounded at Duke?	
Drug Storage Restrictions (including temperature, etc.):	
As indicated in the Investigator's Brochure or other available documentation, what is the highest FDA Use-in-Pregnancy Rating for drug used for research purposes in this study?:	

Are you using an investigational pharmacy at Duke?

Please be aware that inpatient administration of an investigational drug requires the use of the Duke IDS or Oncology ICS, as per Department of Pharmacy policy.

○ Yes ◉ No

Who will be responsible for the storage, inventory and control of the drug/biologic or other chemical, metabolite, nutritional substance or other substance to be evaluated in this research?

The IDS is available to assist any investigator (upon request) with storage and control of investigational drugs in the outpatient setting

The Medical Director of the Duke Center for Smoking Cessation (CSC) will be responsible for the ordering of the study drugs and will ensure storage of these drugs in the CSC laboratory. Dispensing logs will be maintained to monitor and track the inventory.

Where will the drug/biologic or other chemical, metabolite, nutritional substance, or other substance to be evaluated in this research be stored?

Once the drugs are received they will be stored in a temperature maintained locked room. Only authorized key personnel have access to this room.

From where will the drug/biologic or other chemical, metabolite, nutritional substance or other substance to

be evaluated in this research be dispensed?

Dispensing of the drugs will occur at the Duke CSC office located in Durham, NC.

At the completion of this research study, what will be done with the unused or returned investigational drug /biologic or other chemical, metabolite, nutritional substance or other substance?

The unused e-cigarettes will be kept in inventory until all subjects have completed the final study visit. Subjects will be permitted to keep the e-cigarettes that have been given to them. E-cigarettes that are returned will be disposed of in biohazard containers.

Devices

Include all devices being evaluated in this study:

Include all devices being evaluated in this study to determine their safety or effectiveness, and include information about a humanitarian use device where requested.Also dd devices without an IDE here, including any Humanitarian Use Device that does not require an IDE because it is to be used according to its FDA approved product labeling and its safety or effectiveness is not being evaluated.

Complete an IDE Billing Notice as applicable. This can be attached with the Brochure in the Initial Submission Packet.

View Details	Device Name	Is the Device FDA Approved	Will the device to be evaluated or the Humanitarian Use Device be manufactured at Duke?	IDE /Compassionate Use Request Number
⊟	JUUL electronic cigarette	Yes	No	

Device Source	Juul labs
CMS Category	☐ A ☐ B
Is the device provided to subject free of charge?	Yes
Is this a HUD (HDE)?	No
HDE Number	
Is the Device FDA Approved	Yes
Will the device to be evaluated or the Humanitarian Use Device be manufactured at Duke?	No
Do you have an IDE number for this device?	No
IDE/Compassionate Use Request Number	
IDE Holder	N/A
IDE Details	
In the opinion of the sponsor, select the level of risk associated with this device	No Significant Risk

⊟	Micro + Basic Smokerlyzer	Yes	No	

Device Source	Covita

CMS Category	☐ A ☐ B
Is the device provided to subject free of charge?	Yes
Is this a HUD (HDE)?	No
HDE Number	
Is the Device FDA Approved	Yes
Will the device to be evaluated or the Humanitarian Use Device be manufactured at Duke?	No
Do you have an IDE number for this device?	No
IDE/Compassionate Use Request Number	
IDE Holder	N/A
IDE Details	
In the opinion of the sponsor, select the level of risk associated with this device	No Significant Risk

Who will be responsible for the storage, inventory and control of the device to be evaluated or the Humanitarian Use Device?

The Medical Director of the Duke Center for Smoking Cessation (CSC) will be responsible for the ordering of the e-cigarettes and will ensure storage of these e-cigarettes in the CSC laboratory. Dispensing logs will be maintained to monitor and track the inventory.

Where will the device to be evaluated or the Humanitarian Use Device be stored?

Once the e-cigarettes are received they will be stored in a temperature maintained locked room. Only authorized key personnel have access to this room.

Who will be responsible for giving or administering the device to be evaluated or the Humanitarian Use Device to the research subject?

The Duke CSC research staff will be responsible for giving the device to be evaluated.

From where will the device to be evaluated or the Humanitarian Use Device be dispensed?

The device will be dispensed from the Duke Center for Smoking Cessation

At the completion of this research study, what will be done with the unused or returned device or the Humanitarian Use Device?

The unused e-cigarettes will be kept in inventory until all subjects have completed the final study visit. Subjects will be permitted to keep the e-cigarettes that have been given to them. E-cigarettes that are returned will be disposed of in biohazard containers.

Privacy and Confidentiality

Explain how you will ensure that the subject's privacy will be protected:

Consider privacy interests regarding time and place where subjects provide information, the nature of the information they provide, and the type of experience they will be asked to participate in during the research.

Subjects who participate in person will be consented and complete all study questionnaires in a private location. Subjects will be given a unique identifier to protect their confidentiality.

Describe how research data will be stored and secured to ensure confidentiality:

How will the research records and data be protected against inappropriate use or disclosure, or malicious or accidental loss or destruction? Records and data include, for example, informed consent documents, case report forms or study flow sheets, survey instruments, database or spreadsheets, screening logs or telephone eligibility sheets, web based information gathering tools, audio/video/photo recordings of subjects, labeled specimens, data about subjects, and subject identifiers such as social security number.

All data collected on paper will be stored in locked cabinets within the Center for Smoking Cessation. Except when required by law, subjects will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Duke University Health System (DUHS). For records disclosed outside of DUHS, a unique code number will be assigned. The key to the code will be kept in a locked file in the PI's office.

Application Questions Complete

Please click Save & Continue to proceed to the Initial Submission Packet.

The Initial Submission Packet is a short form filled out after the protocol application has been completed. This is an area to attach protocol-related documents, consent forms, and review the application.