The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title: The Effects of a Standardized Research E-Cigarette On The Human Lung: A Clinical Trial With Bronchoscopic Biomarkers

Principal Investigators: Peter Shields, MD; Mark Wewers, MD

Sponsor: National Institute on Drug Abuse and the James Cancer Hospital

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you, and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

The use of electronic cigarettes (e-cigs) or vaping is rapidly increasing in both smokers and non-smokers. It is unknown if there is a health risk when the ingredients are inhaled into the lungs as a vapor. This study is being done to understand the impact, such as inflammation in the lungs, when switching cigarette smokers to e-cigs. We are interested in studying lung inflammation because in smokers this has been linked to cancer, lung disease and other medical problems. This information will help us learn if there is any short-term harm to the lung when using e-cigs. This information will also allow the federal government and the state to decide if regulations are needed to reduce the harm, if any.

This study is a randomized clinical trial of 128 smokers. Participants may be assigned to continue smoking, use an e-cig device provided by the study, such as the standardized research e-cig (SREC), or quit smoking with nicotine replacement therapy (NRT) for 10 weeks. The SREC was produced under contract by the federal government with certain specifications for use by smokers in research studies. Participants will attend 9 visits including two bronchoscopy procedures and have 6 calls. You will also be asked to complete questionnaires, provide specimens and undergo assessments.

1. Why is this study being done?

The purpose of this study is to assess effects of e-cig use on the lungs, such as changes in inflammation, over the 10-week period.

2. How many people will take part in this study?

A total of 128 participants will complete the study.

3. What will happen if I take part in this study?

Orientation: We will explain this study in detail answer any questions you may have. If you are willing to participate, you will be asked to sign this document and confirm your eligibility. You will complete questionnaires that ask about your background, such as medical history, previous tobacco use, work history, social history and lifestyle, occupational and environmental exposure, alcohol use and drug use. You may be given a jug and asked to collect urine for a 24-hour period prior to your bronchoscopy procedure.

All females of child-bearing potential must agree not to become pregnant and to use an approved form of birth control (birth control pills, implants, IUD, Depo-Provera, or double barrier method (e.g., condoms and diaphragm) while participating in the study.

You may also be provided with a device to test the amount of carbon monoxide (CO) in your breath. This device will be used at home daily for the duration of the study and requires an App (iCO Quit) on your phone or electronic device to send results to the study team. By agreeing to be in the study and use the mobile App, you will be required to agree to the terms of service of the App, if applicable, and that you should review those terms of service before agreeing. Staff may also arrange for periodic remote visits by Zoom or another approved electronic platform to visually observe the testing and results.

You will be given the option to refer people to this study. We will provide coupons/flyers and a unique code that you can give to individuals who you think may be interested in. You can also share the information via text or social media. You will be compensated for each person you refer, up to a maximum of 6 people, who meets the basic criteria (current smoker, age 21 or older, willing to be screened).

Preparing for the bronchoscopy: This study will follow OSU standards for performing bronchoscopies, which may include requiring COVID-19 testing prior to the procedure. Testing procedures may be coordinated by staff, and you may be asked to follow standard testing protocols. If you test positive for COVID-19 before the first bronchoscopy, you may be placed on a wait list for at least three months and re-tested before undergoing the bronchoscopy; if you test positive before your follow-up bronchoscopy, your participation will be withdrawn by the principal investigators.

The night before the bronchoscopy, you should not eat or drink anything after midnight or at least 8 hours before the test. We will let you know if there are any of your regular medicines, herbs, supplements, or vitamins you should or should not take the morning of your bronchoscopy. The day of the bronchoscopy, you may be asked to provide urine, nasal, blood, and saliva samples.

You will need someone to drive you home after the procedure so please plan accordingly. If your procedure is performed at the Clinical Research Center (CRC) and you do not have a ride home from the procedure, prior to the procedure, study staff may try to arrange for you to stay at the research center for up to 24 hours at no cost to you. This option is not guaranteed.

Bronchoscopy 1: Your next visit will be for a bronchoscopy. A bronchoscopy is a commonly used procedure to view the airways and diagnose lung disease. During the bronchoscopy, the doctor will use a device (bronchoscope) to see the inside of the lungs by inserting a tube through your nose or mouth.

The following tests and information may be collected:

- Heart rate, blood pressure, height, and weight.
- Oxygen level in the blood through a skin test.
- Exhaled Carbon Monoxide (CO) level may be measured by blowing into a tube to assess your tobacco use.
- Pulmonary function tests (PFTs) may be performed to measure how much air flows in and out of your lungs. This is done by you exhaling into a tube.
- Fractional exhaled nitric oxide (FeNO) concentration in your exhaled air may be measured by you blowing into another tube. This is a measure of inflammation.
- Saliva will be collected.
- Nasal samples may be collected by pushing salt water into your nose with a syringe and pulling fluid back into the syringe. This is done up to 5 times and may be done on both sides of your nose. Nasal brushing may also be performed by inserting a small brush into your nasal passage and gently rotated (3-5 times) to brush inside of your nose.
- A urine sample may be collected. All females of child-bearing potential (i.e., not postmenopausal or surgically sterile) will provide a spot urine sample to be used for a urine pregnancy test. Pregnant participants will be removed from the study.
- Two blood tubes will be collected at the bronchoscopy. An additional two tubes of blood may also be collected at the 2nd bronchoscopy visit.
- The samples you provide may be used to screen for recent exposures to chemicals such as marijuana and tobacco. You will be asked to not use any other tobacco products or marijuana for the duration of the study. However, if you do use these products, it is very important to inform study staff so we can account for the exposures in our results.

The bronchoscopy procedure will be explained again, and you have an opportunity to ask any questions. Just prior to the bronchoscopy, we will numb your nose, throat, and the area around the vocal cords. Medication that will help you relax during the procedure will be given through an IV unless you ask for it not to be given. As with any medicine, there are possible side effects, and if needed, additional medicines may be given to lessen or stop any bad side-effects. During the bronchoscopy, we will monitor your heart activity (EKG, electrocardiogram), oxygen in your blood (pulse oximetry), and breathing. In some cases, you may receive a chest x-ray. In the case of an emergency, pulmonary and/or critical care board-certified physicians trained in advanced care for critically ill patients are immediately available and can perform life-saving care if needed, as would be typical for patients in the hospital.

A computer will be used to randomly select which lung will be tested. During the procedure, the doctor will look through a bronchoscope to make sure the placement in the lung is correct. Medication will be injected as needed to control the cough reflex. After the bronchoscope is in place, a small amount of sterile salt water (about 3 tablespoons) is placed into the lung and immediately suctioned back, washing off cells lining the area. This will be done approximately 5 to 7 times. A small brush also will be used to collect cells from your lung. This will be done approximately 4 to 5 times. After the test, your vital signs will be monitored and the IV removed. You will be asked not to eat or drink anything for 2 hours after because your throat muscles will still be numb.

Clinical Trial: The trial will last about 10 weeks. The 10 weeks starts at the first bronchoscopy (Day 1) when you are randomized to one of four groups. Study staff will review your group assignment. For all groups except the continued smoking group, you will receive smoking cessation counseling as you transition to stop smoking by using the e-cig or NRT. If you need additional counseling or support beyond that provided during visits and calls, you can contact study staff. The study groups are:

- Continue to smoke your usual brand of cigarettes and avoid using cannabis.

- Exclusive nicotine e-cig use group, such as nicotine SREC, where you will be asked to switch completely to the e-cig after 2 weeks and stop smoking cigarettes entirely and avoid using cannabis. During the first two weeks, you may continue to smoke your cigarettes while you transition to the e-cig and try smoking less each day. You will be given instructions on how to use the device, and we expect that it may take one week or more to get used to it. We will encourage you to use the device every 1-2 hours while awake, and as needed with cravings.

- Exclusive nicotine-free e-cig use group, such as nicotine-free SREC, where you will be asked to switch completely to the e-cig after 2 weeks and stop smoking cigarettes entirely and avoid using cannabis. One week after your first bronchoscopy, you may be offered a prescribed medication (Chantix, also known as varenicline) to help you quit smoking at no cost. If you choose to take the medication, you will take it daily throughout the study, and for up to 3 additional weeks. During the first two weeks of the study, you may continue to smoke your cigarettes while you transition to the e-cig, and we encourage you to try smoking less each day. You will be given instructions on how to use the device, and we expect that it may take

one week or more to get used to it. We will encourage you to use the device every 1-2 hours while awake, and as needed to address cravings. If you need Chantix beyond the recommended 12 weeks of therapy, you will need to contact your health care provider for a prescription.

- Quitting with nicotine replacement therapy (NRT) group where we will provide for you NRT patches (21mg) in combination with gum (4 mg) and/or lozenges (4 mg) and ask you to stop smoking and avoid using cannabis two weeks after the first bronchoscopy. You will start the NRT just before the end of the two weeks. You will be given instructions on how to use these products. If you experience side effects, dosages can be reduced and/or products changed. During the first two weeks, we will encourage you to reduce your smoking as much as possible to help you quit. You will remain smoke free for the next eight weeks.

You will be asked to report your daily tobacco and/or product use by phone or internet by completing an online survey. The survey link will be sent to you by text or email and your information is stored in a secure database. If you are assigned to one of the e-cig use groups, you will report the number of puffs per use and when the product was replaced. If you are assigned to the NRT use group, you will report the number of pieces or patches you use.

You will be contacted by phone or email within 72 hours of study product use, and there will be some contact with you on a weekly basis (phone or visit). You will receive counseling to help you follow use instructions.

All groups will return weekly or biweekly to assess product use and toxicity, monitor compliance, and receive additional products as needed. You will bring back your used and unused NRT or e-cig device and product at each visit. If assigned to the nicotine-free SREC group, you will be asked to return your unused Chantix medication at each visit.

At each visit, you will be asked to complete questionnaires. You will be offered the opportunity to complete the questionnaires online and measure your breath CO within 24 hours before your scheduled visit. You will have your weight, oxygen level in your blood, blood pressure and heart rate recorded. The samples we collect from you may be used to look at inflammation and cell function. We will study a broad group of topics such as metabolism, gene expression, methylation, and bacteria. Chemical exposure to smoke, marijuana or other products may also be assessed.

Bronchoscopy 2: During the tenth (10^{th}) week (day 71), participants in all groups will have a second bronchoscopy (same procedure as described above). The opposite lung will be tested at the second bronchoscopy. If assigned to any of the e-cig groups, you will be asked to use your device immediately prior to the visit. Before the bronchoscopy, you will also demonstrate using the e-cig device to assess inhalation. A web-cam may be used to communicate, but no images or audio will be captured or retained without your permission. If you are assigned to the nicotine e-cig group, two additional blood samples will be collected before and after you use the e-cig. You will also return study devices and unused product.

Staff will discuss the importance of remaining e-cig and tobacco-free with all participants. You will also be advised to not vape with THC or other similar e-liquids, add any substances to e-liquids, use black market devices or modify commercial devices.

Follow-up: You will be called 3 months after your second bronchoscopy to assess your tobacco use, including e-cig use.

Location of visits: Bronchoscopies may be performed at the OSU Hospital located at 410 West 10th Ave., Columbus, OH 43210, or at the Clinical Research Center (CRC) located on the 2nd Floor of Dodd/Davis Hall at 480 Medical Center Dr., Columbus, OH, 43210. Other visits may be held at the CRC or at the Center for Tobacco Research, an off-campus OSU research clinic located at 3650 Olentangy River Road, Suite 110 or 420, Columbus, OH, 43214**.**

Study completion: Participants who do not follow study instructions may be removed from the study.

4. How long will I be in the study?

This study is estimated to require less than 20 hours of your time. Your participation for this study will include:

Visit		**Visit Duration**
Orientation	Visit	2-3 hours
Day 1 (W0) Bronchoscopy 1	Visit / procedure	Up to 4 hours*
Day 4	Call	20 minutes
Day 8 (W1)	Visit	1 hour
Day 15 (W2)	Visit	1 hour
Day 22 (W3)	Visit	1 hour
Day 29 (W4)	Visit	1 hour
Day 36 (W5)	Call	20 minutes
Day 43 (W6)	Visit	1 hour
Day 50 (W7)	Call	20 minutes
Day 57 (W8)	Visit	1 hour
Day 64 (W9)	Call	20 minutes
Day 71 (W10) Bronchoscopy 2	Visit / procedure	Up to 4 hours*
3 month follow-up	Call	20 minutes

*The bronchoscopy procedure typically takes 15 minutes and the remainder of the time is used to collect samples, physiologic measures, surveys, and observation after the procedure. Several factors may impact the duration of the procedure and visit.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

While completing the questionnaires, it is possible that you may become uncomfortable. If this occurs, you can refuse to answer any question(s).

As COVID-19 or other viral illnesses persist, study participation may increase your risk of viral exposure. According to the Centers for Disease Control and Prevention (CDC), signs and symptoms associated with COVID-19 are: fever or chills; cough; shortness of breath or difficulty breathing; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; and diarrhea. Severe conditions that may occur if infected with COVID-19 include: trouble breathing; persistent pain or pressure in the chest; new confusion; inability to wake or stay awake; and bluish lips or face.

Study procedures adhere to institutional standards and best practices. As the situation continues to evolve, study procedures may also adapt to address subject and personnel safety as well as study and institutional resources. Staff will implement precautions to limit viral exposure. Such precautions may include limiting physical interactions, when possible (e.g., remote/telephone visits or physical in-person distance), assessing signs and symptoms of viral illness (e.g., temperature and exposure assessments), and providing appropriate personal protective equipment (PPE) to participants and staff (e.g., masks, gloves, goggles, face shields, etc.). You may be asked to undergo COVID-19 testing prior to the bronchoscopy procedures. Bronchoscopy procedures as well as the PFT and measurement of exhaled CO and FeNO may be conducted in a room designed to control airflow. If warranted, the study may be temporarily suspended if there is significant community spread and resources (e.g., bronchoscopy staff or space) are limited. Specimens will be collected by trained staff using Universal Precautions for Prevention of Transmitting Bloodborne Pathogens.

As with any medical procedure, there are some risks or complications. For most patients who are having a bronchoscopy, serious risks and complications associated are **rare.** On the day of the procedure, the following risks will be discussed: cough, sore nose/nosebleed, sore throat/hoarseness, adverse reaction to lidocaine and other medications that you might be given, fever, airway injury, dental/vocal cord injury, pain, pneumothorax (collapsed lung), low blood pressure/fainting, bleeding, infection, pneumonia, heart complications, blood clots, and death. You must have a friend or family member accompany you home and you must not drive, as you may feel slightly dizzy from the medications described above. PFT, exhaled CO and FeNO measurements are safe for most people. You may experience dizziness, shortness of breath, or coughing. You may experience some bruising or minor discomfort with the placement of the IV and/or blood collection. Risks for nasal brushing and lavages are minor and may include discomfort associated with rubbing the brush against the inside of your nose, local burning feeling with eye tearing, and minimal local bleeding. These symptoms are temporary and should go away within a few minutes. Bleeding is rare.

Risks related to e-cigs use may include: throat irritation, dry cough, mouth irritation, nausea, headache, and dizziness, vertigo or light-headedness that are generally short-lived. Sore throat, dry mouth, shortness of breath and mouth ulcers have also occurred, but they are much less common. If you are assigned to use an e-cig, please stop using the e-cig and contact study staff if you experience pallor (pale appearance), cold sweat, nausea, salivation, vomiting, abdominal pain, diarrhea, dizziness, disturbed hearing or vision, tremor, mental confusion, or weakness, as these may be

symptoms of a nicotine overdose. If you are unable to contact the study staff, please stop using the e-cig until your contact. If you experience severe symptoms, please seek prompt medical attention. Cartridges for the e-cig are sealed; however, if cartridges were to leak, nicotine-containing liquid could pose a risk for poisoning, especially to children and pets. If stored improperly, overheating, fire, and/or explosion of the device may occur, leading to burns and possibly death. Risks related to long-term use of e-cigs are unknown.

As of 10/28/19, the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and several states and federal health departments are investigating a multi-state outbreak of severe lung disease associated with using e-cigarette/vaping products. The investigation is ongoing and has not identified a cause, but all cases have reported use of vaping devices/products. The majority of patients have reported vaping cannabis oil, such as THC, obtained on the black market or other sources.

The FDA has advised consumers to protect themselves by not using vaping products of any kind obtained off the street or black market and to refrain from using THC oil or modifying/adding any substance to vaping products purchased at stores. We recommend that you use only the products that we provide in the study and do not add any substances to the e-fluids or alter the device in anyway.

To date, the investigation has not identified any single substance or e-cigarette product that has been consistently associated with illness. If you continue to use vaping device/e-cigarette products, you should watch for unexpected symptoms (e.g., cough, shortness of breath, chest pain, nausea, vomiting, diarrhea, abdominal pain, fatigue, fever, weight loss) and promptly seek medical attention for any health concerns. You can also call your local poison control center at 1-800-222-1222.

We will be asking about your health at every study visit and please call us if you experience any of the health issues described.

The most common adverse reactions associated with Chantix (varenicline) include: nausea, abnormal (e.g., vivid, unusual, or strange) dreams, constipation, flatulence, and vomiting. Other side effects reported after using Chantix include: changes in mood, psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic, as well as suicidal ideation, suicide attempt, and completed suicide; seizures; interaction with alcohol; cardiovascular events; sleepwalking; angioedema and hypersensitivity reactions; serious skin reactions; and accidental injury. If you are assigned to the nicotine-free SREC group, choose to take Chantix, and experience any of these symptoms, please stop taking the medication, contact study staff, and immediately seek medical care. Dr. Tsai or another doctor associated with the study will review the reported symptoms and provide additional instructions (e.g., dose reductions) as needed.

NRT products are safer than cigarettes. The negative health effects of cigarettes are proven. Of the 4,000 chemicals found in tobacco smoke, over 60 are known to cause cancer. By using NRT to quit smoking you reduce your exposure to many chemicals found in tobacco smoke. Risks related to the use of NRT, which is an over-the-counter sold medication, are minor. It should be noted that the dosage delivered from NRT or combination NRT is generally less than levels delivered from smoking.

The most common side effects related to Lozenge use may include hiccups, mouth or throat irritation, heartburn, or other stomach problems such as nausea.

The most common side effects related to Gum use may include hiccups, mouth or throat irritation, heartburn, or other stomach problems such as nausea. Please stop using the gum and contact study staff if you experience symptoms of an allergic reaction (such as difficulty breathing or rash).

The most common side effects related to Patches use may include headache, nausea, upset stomach, and dizziness. Please stop using the patches and contact study staff if you experience skin redness caused by the patch that does not go away after four days, or if your skin swells, or you get a rash. If you experience vivid dreams or other sleep disturbances, you may remove the patch at bedtime and apply a new one in the morning.

Please stop using any of the assigned NRT product if you experience mouth, teeth or jaw problems, persistent indigestion, severe sore throat, irregular heartbeat or palpitations, nausea, vomiting, dizziness, diarrhea, weakness, or rapid heartbeat, as these may be symptoms of a nicotine overdose.

7. What benefits can I expect from being in the study?

This trial, with the use of counseling, may encourage you to quit smoking long-term. Otherwise, there are no anticipated direct benefits to you, but information you provide will help understand how e-cigs impact the lung. This information may help the FDA regulate e-cigs.

8. What other choices do I have if I do not take part in the study?

We encourage those participants who use tobacco to quit. If needed, you can contact cessation services, such as the national quit line (1-800-QUIT-NOW) or talk with your doctor.

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

Referring individuals to the study is optional. Your participation in the study will not be affected if you do not invite others or if those you invite do not meet the criteria outlined above.

9. What are the costs of taking part in this study?

There are no costs for taking part in this study. The bronchoscopy procedures, study devices, COVID-19 precautions, or other assessments conducted as part of this study will be paid for by the study. Study products (e.g., SREC, Chantix, and NRT) will be provided at no cost. Participants assigned to continue smoking their usual brand cigarettes will not be provided cigarettes.

If you encounter transportation issues, please contact study staff to determine if alternative transportation can be arranged and paid for by the study (e.g., Lyft). Transportation services are not guaranteed and will not be available for bronchoscopy visits.

In the event you do not have a ride home after the bronchoscopy visit, the study staff may arrange for you to stay at the research center at no cost to you. This cost would be paid for by the study. This option is not guaranteed and would need to be arranged in advance of the procedure.

10. Will I be paid for taking part in this study?

You will be paid for your participation as outlined below.

Visit		**Compensation**
Orientation	Visit	$60
Day 1 (W0) Bronchoscopy 1	Visit / procedure	$250
Day 4	Call	$5
Day 8 (W1)	Visit	$40
Day 15 (W2)	Visit	$40
Day 22 (W3)	Visit	$40
Day 29 (W4)	Visit	$40
Day 36 (W5)	Call	$5
Day 43 (W6)	Visit	$40
Day 50 (W7)	Call	$5
Day 57 (W8)	Visit	$40
Day 64 (W9)	Call	$5
Day 71 (W10) Bronchoscopy 2	Visit / procedure	$300
3 month follow-up	Call	$10
Recruitment Referrals		Up to $60
Bonus (Daily CO, Random Visit)		Up to $200
Total		**Up to $1140**

Travel: Compensation for travel is included in the amounts listed above. If the study arranges and pays for transportation services (e.g., Lyft), up to $10 may be deducted from the visit payment.

Recruitment Referrals: You can earn $10 for each smoker you refer who is at least 21 years old and completes a telephone screening - up to $60 total.

Bonus: You will measure and report your CO daily. If your reading is 6 or less at least 5 days per week, you will receive an additional $20 per week (up to $160 total). If you are assigned to continue smoking your usual brand cigarettes, you will be compensated if you send CO results at least 5 days per week.

The samples you provide will be used to help confirm you followed the instructions for using the product, medication, or device assigned. If your samples show you followed study instructions **and** if all aspects of a randomly selected visit were completed (e.g., surveys, returned product and/or packaging, etc.), you will receive a $40 bonus. If you do not provide a sample (e.g., a 24-hour urine) or laboratory analysis indicates you did not follow study instructions, the bonus will not be provided. If the randomly selected visit is missed or instructions were not followed, it will be considered as "not following instructions" and you will not receive the bonus. If you are assigned to continue smoking

your usual brand cigarettes, you will receive the bonus as long as you provide samples, attend the visit that is selected, and follow the study instructions for that visit.

The bonus will be given after the 3 month follow-up call.

If you are found to be ineligible at time of the bronchoscopy procedure, you will be given $25 for your time, plus $7 for transportation or parking.

By law, payments to subjects are considered taxable income.

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects' research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

13. Will my de-identified information and bio-specimens be used or shared for future research?

Yes, your information and bio-specimens (samples) may be used without additional permission for future research.

Using a separate consent form, we will ask permission to use your information and bio-specimens in future research for a companion study "The Effects of a Standardized Research E-Cigarette on the Human Lung: A Clinical Trial with Bronchoscopic Biomarkers – REPOSITORY" (2018C0188).

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

We will work to make sure that no one sees your data without approval. However, because we are using the Internet, there is a chance that someone could access your online responses without permission. In some cases, this information could be used to identify you. Your data will be protected with a code to reduce the risk that other people can view the responses.

If the doctor performing the procedure feels you should be informed, he or she will discuss the findings at the time of the procedure, contact you by phone after the procedure or have a staff member contact you after the procedure. This information may include a recommendation to follow-up with your health care provider.

Participants referring individuals to studies is a commonly used recruitment tool. Despite best efforts to ensure privacy and confidentiality, such as using a unique referral code and refusing to discuss anyone's identity or study status, it is possible that there may be a loss of privacy and/or confidentiality.

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

Certificate of Confidentiality: This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as

allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIDA which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law (such as to report child abuse and neglect, or harm to self or others).

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document, such as including research data in the medical records.

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

I. What information may be used and given to others?

- Past and present medical records: The bronchoscopy procedure and potential need for COVID-19 precautions may require accessing your electronic medical record. IHIS may be used to access your medical record and may include the results from your procedure and COVID-19 test. Only authorized study personnel will have access to the data;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  HIV / AIDS;
  Hepatitis infection;
  Legal and illegal drug use;
  Physical exams;
  Laboratory, x-ray, and other test results;
  Diaries and questionnaires;
  The diagnosis and treatment of a mental health condition;
- Records about any study drug you received;
- Records about the study product you received (if applicable);
- Records about the study device you received (if applicable); and
- Specimens.

II. Who may use and give out information about you?

- Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
    - working for or with the sponsor; or
    - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic or physician's office record;
- Others:
    - Research collaborators, such as investigators assisting with data analyses;
    - Health care facilities, research site(s), researchers, health care providers, or study monitors involved in this study;
    - Private laboratories and other persons and organizations that analyze your health information in connection with this study;
    - Contract Research Organization(s);
    - Independent data and safety monitoring boards and others who monitor the conduct of the study; and
    - Centers for Disease Control and Prevention

IV. Your information <u>may</u> be given to:

- Your health information may also be shared with federal and state agencies that have oversight of the study or to whom access is required under the law. These may include the following:
    - The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
    - National Institutes of Health;
    - Ohio Department of Job and Family Services;
    - Governmental agencies in other countries;
    - Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
    - The Ohio State University units involved in managing and approving the research study including:
        - The Office of Research and the Office of Responsible Research Practices;
        - Members and staff of The Ohio State University's Institutional Review Boards, including the Western Institutional Review Board;

- University data safety monitoring committees; and
- Centers for Disease Control and Prevention

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For medical concerns contact the physician who performed the bronchoscopy or Dr. Tsai at (240) 426-3324.

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact Peter Shields, the Principal Investigator, at (614) 293-6786 or study staff at (614) 366-4542.

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact the OSU HIPAA Privacy Officer at (614) 293-4477.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Peter Shields, the Principal Investigator, at (614) 293-6786.

Signing the consent form

Future contact

We would like your permission for study staff to contact you if we need to discuss or clarify your questionnaire responses or to participate in future studies. Only individuals authorized by the principal investigator will contact you.

Please sign and date below if you agree to be contacted in the future.

Signature: _____ Date: _____

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of subject	**Signature of subject**
	AM/PM
	Date and time
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)**
	AM/PM

Relationship to the subject | **Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent | **Signature of person obtaining consent**

AM/PM

Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness | **Signature of witness**

AM/PM

Date and time

Printed name of witness | **Signature of witness**

AM/PM

Date and time

The Effects of a Standardized Research E-Cigarette On The Human Lung: A Clinical Trial With Bronchoscopic Biomarkers

Phone: **[phone number]**
Email: ecig-study@osumc.edu

* General in-person visit tasks include completing surveys, physical measures and CO
* You will complete a short daily survey for the duration of the trial

Day of Visit	Visit Type*/Location	Duration of Visit
Orientation	In Person (CTR)	2-3 hours
Day 1 (W0) / Bronchoscopy 1	Procedure (CRC)	Up to 4 hours ~2 hour: Surveys, physical measures, and sample collection ~15 minutes: Bronchoscopy ~1-2 hours: Observation
Day 4	Call	20 minutes
Day 8 (W1)	In Person (CTR)	1 hour
Day 15 (W2)	In Person (CTR)	1 hour
Day 22 (W3)	In Person (CTR)	1 hour
Day 29 (W4)	In Person (CTR)	1 hour
Day 36 (W5)	Call	20 minutes
Day 43 (W6)	In Person (CTR)	1 hour
Day 50 (W7)	Call	20 minutes
Day 57 (W8)	In Person (CTR)	1 hour
Day 64 (W9)	Call	20 minutes
Day 71 (W10) / Bronchoscopy 2	Procedure (CRC)	Up to 4 hours ~2 hour: Surveys, physical measures, and sample collection ~15 minutes: Bronchoscopy ~1-2 hours: Observation
3 Month Follow Up	Call	20 minutes