**Principal Investigator: Dr. Ellen Burnham**
**COMIRB No: 14-1957**
**Version Date: 01/18/2019**
**Study Title: Inhaled Cannabis, Oxidative Stress and the Pulmonary Innate Immune Response**

## Cannabis and Control Consent

☐ **Cannabis Patient**

☐ **Control Patient**

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You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

### Why is this study being done?

This study plans to learn more about what heavy cannabis/marijuana smoking does to lung health.

People who smoke marijuana/cannabis for long periods of time might be at risk for developing symptoms of chronic bronchitis (including cough, phlegm production, wheezing and shortness of breath). It is also believed that exposure to marijuana smoke can alter the lung's ability to fight infections increasing the risk of diseases like pneumonia. Additionally, given the similarity between marijuana and tobacco smoke, there is a possibility that chronic marijuana smoking can increase one's risk of chronic obstructive pulmonary disease (COPD – including chronic bronchitis and emphysema).

Long term effects of smoking marijuana are not well understood. Previous studies have enrolled patients who smoke marijuana and tobacco, so effects from smoking only marijuana are not known.

### CANNABIS SMOKING subjects

You are being asked to participate in this study because you currently smoke marijuana (cannabis), you have been smoking marijuana (cannabis) for a long time and you do not smoke tobacco.

### CONTROL (NON-CANNABIS SMOKING) subjects

You are being asked to participate in this study because you have NEVER smoked cannabis/marijuana and you do not smoke tobacco.

**Other people in this study:**

Up to *120* people from your area will participate in the study.

**What happens if I join this study (CANNABIS and CONTROL)?**

If you join the study, you will be scheduled for a visit at the University of Colorado Hospital Clinical and Translational Research Center. This visit will include the following:

a. Examination: You will undergo a brief medical history, physical examination, vital signs including seated blood pressure measurements, weight, pulse rate, respiratory rate and temperature.
b. Questionnaire: You will be asked to complete a questionnaire regarding tobacco use, drug use, medical history and respiratory health. This questionnaire will take 60-90 minutes. You will also be asked to complete a questionnaire regarding urinary symptoms. This questionnaire will take 5 minutes.
c. Blood draw*:* Approximately 6 teaspoons of blood will be drawn to see if you qualify to have a bronchoscopy in this study. We will also look at the blood to see how well your body may be able to fight off lung disease and infections.
d. Exhaled breath condensate (EBC): Another type of sample we will collect is called exhaled breath condensate, or EBC. EBC is the water vapor that you exhale as a normal part of breathing, and can give researchers an idea of what might be going on inside of the lung. To collect EBC, we will have you breathe through a mouthpiece into a small tube that will collect the water vapor in your breath. We will collect this for 10 minutes.
e. Oral Rinse: You will be asked to rinse your mouth with 20 mL of salt water (saline solution) for 60 seconds and then spit it into a sterile collection cup.
f. Urine sampling: You will be asked to provide a urine sample to see if you qualify for to have a bronchoscopy in this study. This will include a urine "drug test" to evaluate for recent use of cannabis, tobacco, heroin and cocaine and amphetamines. If you are currently using heroin, cocaine or amphetamines you will not be eligible to participate in this study. We will also look to see how well your kidneys are working. We will examine several types of cells in the urine to see how the body may be able to fight infections.
g. Chest X-Ray: The chest x-ray will look for any abnormalities in the lungs by taking a radiographic (using xrays) picture of your chest. The chest xray is done as an extra safety precaution before the bronchoscopy procedure. If you are a woman, you will have a urine pregnancy test before the chest x-ray, and will not continue in the study if you are pregnant.

h. Pulmonary Function Testing: Pulmonary function test is a breathing test that measures how fast air moves in and out the lungs. This will show us that your lungs work normally. The breathing test is done as an extra safety precaution before the bronchoscopy procedure.

All of the above tests will take approximately 2 hours to complete and will be performed at the University of Colorado Hospital. If any of these tests are not normal, you will not be asked to continue in this study. If results are not normal we will make sure you have a referral to a doctor that can assess and treat the problem(s) as appropriate. If the above tests are normal, you will continue with the study (the same day, after the above studies have been completed and are found to be normal) which includes the following:

i. Bronchoscopy: The bronchoscopy test **must** be done at the University of Colorado Hospital Clinical and Translational Research Center (CTRC). A separate consent form (other than this one) will need to be signed by you for the bronchoscopy. Before starting, your heart rate, blood pressure, breathing rate, and level of oxygen in the blood will be measured. You should not have eaten or drank anything, including water, at least 6 hours prior to the procedure.

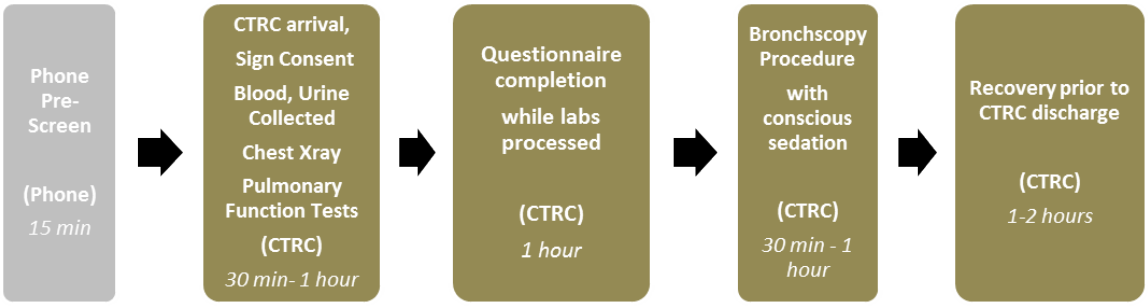
A small plastic catheter (IV) will be placed in a vein in your arm, and about 6 tsp of blood will be collected. The catheter will be taped into place. Your exhaled breath (you will exhale/blow into a refrigerated plastic tube) and oral rinse (you will swish 20 mL of salt water in your mouth and spit it into a sterile cup) will then be collected prior to the bronchoscopy.

A numbing medicine known as lidocaine will be sprayed in the back of your throat and inside of your nose. This is done to prevent coughing and discomfort. A small amount of relaxing medicine may be given through the IV catheter to help to comfort you as well. The sedating medicines we commonly use during this procedure are called Midazolam (Versed) and Fentanyl. Many patients find that they do not remember the procedure being performed after receiving these medicines. You may fall into a light sleep after the medicine has been given. You should wake up easily if your name is called. The medicine starts working in about 5 minutes and lasts in your body for about one hour. These medicines can lower your blood pressure and cause your breathing to slow. We will watch your blood pressure and level of blood oxygen through the whole procedure. This is to make sure you are safe.

A bronchoscope is a thin tube with a camera to see your lung. This tube will be passed through your nose and into a part of your lung where it will be held steady. First, we will use up to three soft, flexible brushes that we will insert one at a time through the bronchoscope to gently scrape off cells from inside your lung. Once we have brushed the inside of your lung, we will remove the brushes. Next we will inject 1½ ounces of sterile salt water (saline) through the

bronchoscope into the lung. This may be done up to six times. The salt water be immediately taken out through the bronchoscope and collected in a container.

The total amount of time it will take from start to finish for the bronchoscopy procedure is about two to three hours. Most of this time will be spent making sure you are ready and comfortable for the procedure. The actual procedure takes about 20 minutes. You will be watched for about one more hour after the procedure and then discharged when you are fully awake and stable. A timeline of study participation is provided below for clarification.




**Below, the above timeline is explained in words:**
ALL tests (consent, questionnaires, pulmonary function testing (PFTs), chest xray (CXR), urine sampling, blood sampling, exhaled breath, oral rince AND bronchoscopy) should take NO MORE than 5 hours.

1) Upon arrival to CTRC, after written consent is performed, you will have your blood and urine taken and sent for lab processing; CXR and PFTs are also completed. This first series of events will take between 30 minutes and 1 hour.
2) While processing occurs and results are pending, you will complete the questionnaire material. If laboratory results return with an abnormality that excludes you from bronchoscopy, the 5 hour duration will be truncated as no bronchoscopy, EBC or oral rinse is performed. UCH lab testing times vary with quick results returned in approximately 30 minutes, however, it could take up to 1 hour. If the abnormality is a positive urine tox screen, it could be a very short visit as no further study procedures occur and you will be discharged.
3) You will be transported to UCH radiology for CXR and UCH respiratory unit for PFTs. The process typically takes between 30 minutes and 1 hour. If the abnormality is an abnormal CXR or PFTs, the visit may be longer as these studies are evaluated for eligibility by study investigators.
4) However, you will ONLY undergo bronchoscopy (with a 1-2 hour post conscious sedation monitoring period) if all testing results meet enrollment criteria.

**A responsible person must be available to drive you home or accompany you home via taxi or public transportation. You will not be allowed to operate a car or heavy machinery after the procedure until the following day.**

Study participation will occur at the University of Colorado Clinical and Translational Research Center (CTRC) and will last up to 4-5 hours (for xray, pulmonary function tests, lab draws, bronchoscopy). If evaluation demonstrates you are ineligible for bronchoscopy (abnormal pulmonary function tests, abnormal chest xray, etc), your visit will last 2 hours

**What are the possible discomforts or risks?**

Discomforts you may experience while in this study include:

**Risks from Bronchoscopy:** Overall, the risks for the bronchoscopy procedure are very low. Some patients do find the procedure uncomfortable. During the procedure, you may experience some coughing and a sensation of difficulty breathing. In the 24 hours following the procedure, fever is possible 8% of the time. Additionally, sore throat is not uncommon after the procedure and typically resolves within 24 hours.

The following have been reported less than 1% of the time: bleeding in the lungs, collapse of the lung (pneumothorax), severe difficulty breathing or bronchospasm, and death. From the sedating medication alone, you may experience: momentary fall in blood pressure (5%), slowing of the breathing rate (10%), nausea and vomiting, headache, or hiccoughs (each less than 5% of the time). The numbers given in parentheses are the chance that that complication could happen to you. No long lasting effects on memory have been reported from this medication.

**Risks of lidocaine:** There is a rare risk of an allergic reaction to the medication. If you have a known allergy to lidocaine, we will not use any lidocaine.

**Risks from pulmonary function testing:** You may experience a feeling of lightheadedness from breathing through the spirometry tubing. Also, there is a rare but serious risk of a collapsed lung (less than 1%).

**Risks from completing survey:** There are no known health risks to filling out this survey, however, you may feel uncomfortable answering sensitive questions.

**Risks of having blood taken:** In this study we will need to get about 6 teaspoons of blood from you. We will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.
**Risks of having an IV inserted into your vein:** In this study we will insert a needle, connected to a plastic tube, into a vein in your arm. We will use the tube to take blood samples or give you fluids. You will feel some pain when we first

insert the tube into your vein. You may have some redness, swelling, or bruising where the tube goes under your skin.

In some cases, this type of tube can cause an infection where it goes under the skin.

In rare cases, it can cause a blood clot in the vein. You will have this tube inserted for less than 24 hours.

**Risks from exhaled breath condensate (EBC) collection:** You may experience a feeling of lightheadedness after breathing through the EBC collection tube for a few minutes. There are no other known risks of this procedure.

**Risks from a chest x-ray:** As part of this study we will perform an X-ray of your chest. X-rays are a type of radiation. Your natural environment has some radiation in it. This series of X-rays will give you about the same amount of radiation that you would get from your environment in 2 days.

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

*If you decide to take part in this research study, you will be required to give us information about your alcohol and other drug use.* A Certificate of Confidentiality has been obtained from the Federal Government for this study to help insure your privacy. This Certificate means that the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative or other proceedings. But, if you request disclosure, we can release the information.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA)

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances.

- If it is determined that you intend to harm yourself or others

The study may include risks that are unknown at this time which may relate to marijuana's illegal status at the federal level.

**What are the possible benefits of the study?**

This study is designed for the researcher to learn more about the effects of marijuana smoking on the lung. This study is not designed to treat any illness or to improve your health. The procedures may help you in earlier detection of a disease.

If you decide to take part in this study, there is no promise that your health will improve. Also, there are risks as mentioned in the Discomforts and Risks section above.

**Who is paying for this study?**

This research is being sponsored by the University of Colorado Clinical and Translational Sciences Institute.

**Will I be paid for being in the study?**

You will be paid up to $250 in the form of a Visa gift card for your participation in the study. If you do not qualify for the bronchoscopy test but complete other screening tests at the University of Colorado Hospital CTRC, you will be compensated for your time with a $25 Visa gift card.

It is important to know that payments for participation in a study is taxable income.

**Will I have to pay for anything?**

It will not cost you anything to be in the study.

**Is my participation voluntary?**

Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

**Can I be removed from this study?**

The study doctor may decide to stop your participation without your permission. This would be done if he or she thinks that being in the study may cause your harm, or for any other reason. Also, the sponsor may stop the study at any time.

It is your choice to decide to take part in this study and you can discontinue your participation at any time.

**What happens if I am injured or hurt during the study?**

If you have an injury while you are in this study, you should call Dr. Ellen Burnham immediately. Their phone number is (303) 724-6079.

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

## Who do I call if I have questions?

The researcher carrying out this study is Dr. Ellen Burnham. You may ask any questions you have now. If you have questions later, you may call Dr. Burnham at (303) 724-6079. A Research Subject Advocate is also available on the Clinical Translational Research Center at 720-848-6662 to answer questions relating to participation in this study. You will be given a copy of this form to keep.

If you have questions regarding your rights as a research subject, please call the Colorado Multiple Institutional Review Board (COMIRB) office at (303) 724-1055 or, CTRC Advocate at (720) 848-6662.

**Optional Consent and Authorization for Specimen and Data Banking for Future Research**

Dr. Ellen Burnham would like to keep some of the blood, urine, exhaled breath, oral rinse, bronchoscopy samples and data that is taken during the study but is not used for other tests. If you agree, the samples and data will be kept and may be used in future research to learn more about lung diseases. The research that is done with your samples and data is not designed to specifically help you. It might help people who have lung diseases and other diseases in the future. Reports about research done with your samples and data will not be given to you or your doctor. These reports will not be put in your health records. The research using your sample and data will not affect your care.

The choice to let Dr. Burnham keep the sample and data for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want Dr. Burnham to use your samples and data any longer, and they will no longer be used for research. Otherwise, they may be kept until they are used up, or until Dr. Burnham decides to destroy them.

If a subject wants his or her sample discarded, this will be done with the subject's written request (see address below). The subject will be given a phone number

(see number below) to call should he or she want discuss having his/her specimens destroyed (which will be done via written consent).

CC: Dr. Ellen Burnham
12700 E 19th Ave
Research 2, Box C272, 9th floor
Aurora, CO 80045

(303) 724-6079

When your samples or data are given to other researchers in the future, Dr. Burnham will not give them your name, address, phone number or any other information that will let the researchers know who you are.

Sometimes sample or data are used for genetic research (about diseases that are passed on in families). Even if your sample or data are used for this kind of research, the results will not be told to you and will not be put in your health records. Your sample and will only be used for research and will not be sold. The research done with your sample and data may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your sample and include learning more about what causes lung disease and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. Dr. Burnham will protect your records so that your name, address and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any sample collection and storage by Dr. Burnham.

Please read each sentence below and think about your choice. After reading each sentence, check “yes” or “no.” If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give my permission for my data, blood and tissue to be stored in a central tissue bank at the University of Colorado Denver, for future use by the study investigators:

1. I give my permissions for my blood, urine and bronchoscopy samples to be kept by Dr. Burnham for use in future research to learn more about how to prevent, detect, or treat lung diseases.

☐ Yes ☐ No _____Initials

2. I give my permissions for my blood, urine and bronchoscopy samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

☐ Yes ☐ No _____Initials

3. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

☐ Yes ☐ No _____Initials

**Who will see my research information?**

The University of Colorado Denver and the hospital(s) it works with have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.
The institutions involved in this study include:

- University of Colorado Denver
- University of Colorado Hospital

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University of Colorado Denver and its affiliate hospitals may not be covered by this promise.

We will do everything we can to keep your records a secret. It cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Primary Investigator, at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Dr. Ellen Burnham
12700 E. 19th Ave.; C272
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information.

- Federal offices such as the Food and Drug Administration (FDA) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- Officials at the institution where the research is being conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

**Information about you that will be seen, collected, used and disclosed in this study:**

- Name and Demographic Information (name, age, sex, ethnicity, address, phone number, email address). Your name, phone number and email address will be kept separate from research specimens and data.
- Portions of my previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Alcoholism, Alcohol or Drug abuse

**What happens to the Data, Blood and Specimens that are collected in this study?**

Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, blood, or other specimens are given by you to the investigators for this research and so no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, blood, or other specimens collected from you.

- If data, blood, or other specimens are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or IRB approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

**HIPAA Authorization for Optional Additional Study Procedures** –

In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

Some of these optional procedures may involve genetic testing or the use of your genetic information. Your genetic information will not be released to others.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:

_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

**Agreement to be in this study and use my data**

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____ Date:_____

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name: _____

Investigator: _____ Date: _____
Investigator must sign within 30 days

Witness Signature:_____ Date_____

Witness Print Name:_____

Witness of Signature ☐

Witness of consent process ☐