UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and
AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position:_____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the title of this research study (this "Research Study")?

Randomized, Controlled Cross-over Comparison of Oral Cannabidiol to Oral Opioid for Postoperative Photorefractive Keratectomy Pain Control

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator: Walter A. Steigleman, M.D. - (352) 265-2020
Research Coordinator:
Coinvestigator: Sonal S. Tuli, M.D.- (352) 265-2020
Coinvestigator: Yujia Zhou, M.D. (352) 265-2020

4. Who is paying for this Research Study?

The sponsor of this study is the Consortium for Medical Marijuana Clinical Outcomes Research.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

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

a) In general, what is the purpose of the research? How long will you be involved?

We will compare the safety and efficacy of oral cannabidiol (CBD) to oral codeine-acetaminophen for controlling pain after photorefractive keratectomy (PRK). PRK is a commonly performed corneal refractive surgery used to correct refractive errors, similar to laser-in-situ keratomileusis (LASIK). If you participate in this study, you will first be evaluated in the clinic to find out if the PRK procedure might work for you. If you are eligible, you will undergo PRK in one eye, then the other eye two weeks later. You will also take surveys and return for postoperative clinic visits most likely for about 3 months after your surgery. This study therefore usually involves participation for about 4 months. Some patients with thicker glasses before surgery may take longer to stabilize and may need to be followed for up to 6 months after surgery.

b) What is involved with your participation, and what are the procedures to be followed in the research?

Participation involves several clinic visits, PRK surgery in each eye, 1 at a time separated by 2 weeks, taking the prescribed narcotic pain medication or CBD, and completing surveys on your symptoms for up to four months. The first visit is a routine refractive surgery consultation, not part of the research study, where your eligibility and measurements for PRK will be evaluated. After this, you will schedule two PRK surgeries, one for each eye, separated by two weeks. After each surgery, you will receive standard postoperative treatment for PRK including bandage contact lens, artificial tears, medicated eyedrops (steroid, non-steroidal anti-inflammatory drug, and antibiotic), oral Ibuprofen, and either codeine-acetaminophen or CBD.

Since we are trying to find out which pain-relieving medicine might be better, you will receive a different pain medicine after each eye surgery. The order of pain medications will be randomized, much like the flip of a coin. Some subjects will receive CBD after the first eye surgery and then the codeine/acetaminophen after the second eye and other patients the order of medications will be reversed. All subjects will receive either of the 2 pain medications after each eye surgery. There is no placebo group for this study. For each eye, you will then return to the clinic for postoperative evaluation for up to 6 months after the second eye's surgery and complete surveys about your vision, experience, and pain level. You will be expected to take the prescribed medications as instructed to the best of your ability and report any missed medications to the principal investigator.

c) What are the likely risks or discomforts to you?

PRK is a refractive surgery, which includes several known risks and discomforts related to the surgery itself. For PRK not part of a study, some patients report experiencing pain, anxiety, and discomfort during the surgery, although most patients tolerate the surgery well. In the week after surgery, eye irritation, dry eye, eye pain, blurry vision, glare, visual halos, and light sensitivity are common. Complications such as bruising, corneal scarring, infection, bleeding, loss of vision, double vision, and severe dry eye are rare but possible. You may also experience constipation, stomach upset, nausea,

dizziness, allergic reaction, and loss of appetite because of some of the routine medications used after PRK.

Specific to this study, there is no expected increased risks of surgical complications as mentioned above. One significant difference of this study is that routine PRK now usually involves treating both eyes at the same time on the same day whereas during this study, one eye will be treated on one day and the other eye treated 2 weeks later. Some of the discomforts of PRK surgery may be experienced twice by patients participating in this study. For some patients with strong glasses prescriptions before surgery, they may experience difficulties with vision and depth perception as the eyes may not work well together in the 2 weeks between surgeries. By enrolling in this study, you will experience more clinic visits, recovery time, and surveys than if you had undergone PRK outside of this study.

One of the medications used for postoperative pain in this study is CBD. CBD is not federally approved to treat this condition. Some side effects patients report when using CBD are sleepiness, decreased appetite, diarrhea, liver enzyme elevations, fatigue, malaise, rash, insomnia, sleep problems and infections. CBD may cause sleepiness impairing the ability to safely drive or operate machinery. Patients should not drive or operate machinery until they understand the effect CBD has on their function.

Use of CBD may result in a positive drug test for marijuana or THC for about a month after taking it. So, you need to wait at least 30 days after the last dose of CBD before taking a drug test for a job or other reasons.

Another medication used in this study is ibuprofen which is in the family of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs such as ibuprofen, cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events. NSAIDs such as ibuprofen, cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in the treatment and may increase with duration of use.

The codeine/acetaminophen pain medication, also known as Tyelnol #3, contains an opioid medication with a risk of misuse, abuse, and addiction. The period of use in the study is only for up to 5 days, and therefore, the risk of it becoming habit-forming is likely lower than that of opioids used for a longer duration. Patients with a personal history of misuse, abuse, and addiction to opioids or prefer to not take any opioids should not participate in this study.

d) What are the likely benefits to you or to others from the research?

There may be no direct benefit to you. By participating in this study, you will receive PRK surgery at no cost to you, which costs an estimated $4000 for both eyes. The results from this study will also help other ophthalmologists determine whether CBD is an effective treatment for pain and discomfort after PRK. Current evidence demonstrates that opioid use is associated with some unpleasant side-effects and that legitimate opioid prescriptions may result in future use. This study may demonstrate that CBD is a safe, effective alternative to opioid medication.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

PRK services are available outside of this study if you decide not to enroll. Non-surgical alternatives include refractive prescriptions for glasses or contact lenses. LASIK or other forms of refractive surgery are also options not included within this study. Some patients may be eligible for cataract surgery instead of refractive surgery.

Additional and more detailed information is provided within the remainder of this Informed Consent form. Please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

If you are seeking refractive surgery, you will be evaluated and informed of all surgical and nonsurgical options (see section 5e above) regardless of your participation in this study. Your doctor will do several tests on your eyes to determine your visual acuity, eye pressure, and eye health during your initial visit and evaluate your eligibility for each of these surgical and nonsurgical options. If you are eligible for PRK and elect to undergo the surgery, you will be counseled on the risks and benefits before scheduling surgery.

PRK takes a few minutes for each eye, and you will be given local or topical anesthetic eyedrops. During surgery, an eyelid holder will be placed on the eye to prevent blinking. Your surgeon will remove the surface tissue of your cornea using a brush, laser, alcohol solution, or specialized blade. A laser programmed with your eye measurements will reshape your cornea, and you may smell and hear this process. Your vision will be blurry, and you will not be able to see the surgery. Afterwards, you will receive a protective contact lens, medicated eyedrops, and pain medication to take after surgery. Your doctor will see you again in the days, weeks, and months after surgery to ensure that you are healing well and adjust your treatment to best improve your vision.

7. What will be done only because you are in this Research Study?

If you participate in this study, you will have two separate surgeries separated by 2 weeks, instead of both eyes at once, and you will also take surveys in addition to your normal care. Once you decide to participate in the study, the first eye surgery will be scheduled. This will require a 1 week follow up visit. Then, 2 weeks after the first eye surgery, the second eye will have surgery. The second eye surgery will also have a 1 week follow up visit. Each surgery will also have a 1 month follow up visit. So, after enrolling in the study, each eye will have a surgery day and a 1 week and 1 month follow up. This is 6 total visits in less than 2 months. There will likely be increased time spent during each visit of at least 30 minutes for additional testing and completing surveys because of your participation in the study.

If you had PRK not as part of this study, you would have both eyes treated on the same day and only have a single 1 week and 1 month visit and would not necessarily complete additional testing or surveys.

The PRK procedure and routine postoperative medications (eye drops) are the standard for patients having PRK not part of this study. The main differences from routine PRK for this study is that each eye will be treated separately 2 weeks apart and that for 1 of the eye surgeries, the medication used for pain control will be CBD, which is not currently FDA approved for treating pain.

Your surgery costs will also be waived if you participate in this study.

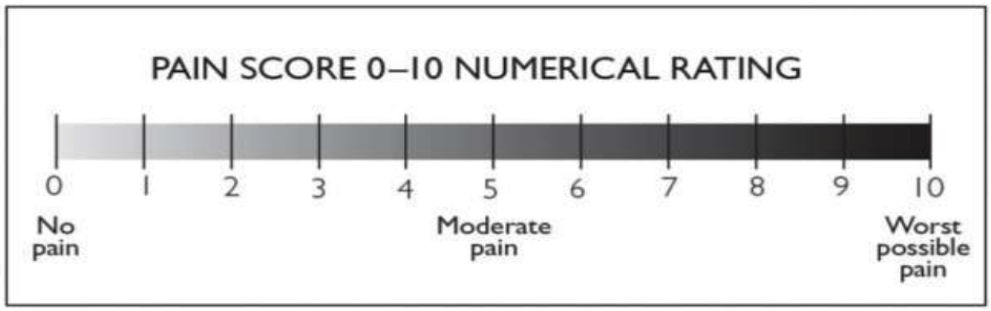
An example of the surveys is below:

PRK Study Pain Diary

Surgery Date:

Name: Last 4 Phone #: Surgery Eye (R/L):

Thank you for participating in the PRK study. This is the paper of your pain diary, but you can also fill in the electronic version instead. If you need to speak to an investigator, please call (352) 265-2020.



Place a check in the box that corresponds to your pain at each of the following times and document the number of pain pills taken at each time point.

	0	1	2	3	4	5	6	7	8	9	10	# of Pills
Pre-surgery												
Post-surgery												
Post-surgery PM												
Post-op day 1 AM												
Post-op day 1 PM												
Post-op day 2 AM												
Post-op day 2 PM												
Post-op day 3 AM												
Post-op day 3 PM												
Post-op day 4 AM												
Post-op day 4 PM												
Post-op day 5 AM												
Post-op day 5 PM												

It is possible that your research information with all personally identifiable information removed, could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If any identifiable information was collected as part of this research, it is possible that your research information, with all personally identifiable information removed, could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect demographic information, results of physical exams, medical history, eye measurements, surgical details, and surveys for the purpose of evaluating your eligibility for this study and for statistical analysis.

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- The Consortium for Medical Marijuana Clinical Outcomes Research (study sponsor)
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections
- Government agencies which are responsible for overseeing public health concerns, such as the Centers for Disease Control and federal, state and local health departments
- The IRB that reviewed this Research Study and ensures your rights as a study subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

You will be part of this research study for up to 6 months. This includes the time from your initial surgery to your last postoperative visit and usually for 3 months after your second surgery. Some patients with thicker glasses before surgery may need additional time for vision to stabilize. Such patients will be examined in clinic visits for up to 6 months to monitor this process.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

Thirty-five people are expected to take part in this research study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

During PRK surgery which is part or is not part of this research study patients may experience pain, anxiety, and discomfort during the surgery. In the week after surgery, eye irritation, dry eye, eye pain, blurry vision, glare, visual halos, and light sensitivity are common. Complications such as bruising, corneal scarring, infection, bleeding, loss of vision, double vision, and severe dry eye are rare and possible after PRK surgery with or without participation in the research study. You may also experience constipation, stomach upset, nausea, dizziness, allergic reaction, and loss of appetite because of some of the routine or study medications. Some patients may still require glasses or retreatment after surgery. Each of these risks is true for PRK surgery with or without participation in the research study.

The CBD oral solution used in this research study is not federally approved to treat this condition, although this substance is generally recognized as safe for certain individuals. It is possible that it's use may result in a positive drug screen for marijuana. If you have a work or other social situation where a positive drug screen may cause a problem, you should not participate in the study. If you are pregnant or considering pregnancy, you should not participate in the study.

By enrolling in this study, you will undergo PRK for each eye on separate days about 2 weeks apart and experience more clinic visits and surveys than if you had undergone PRK outside of this study.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

You may or may not benefit from participating in this study. The potential benefit is that the CBD will provide effective pain relief in place of opioids, which can possibly result in their future use.

13b. How could others possibly benefit from this Research Study?

The findings from this study will also help other ophthalmologists determine whether CBD is an effective treatment for pain and discomfort after PRK. Current evidence demonstrates that opioid use is associated with unfavorable side-effects and that legitimate opioid prescriptions fuel the opioid addiction crisis. This study may demonstrate that CBD is safe, effective alternative to opioid medication for other patients.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

14. What other choices do you have if you do not want to be in this study?

If you do not want to be in this study, you have the option to pursue surgical and nonsurgical treatments for refractive errors. These options include refractive prescription for glasses, other refractive surgeries such as LASIK, or cataract surgery. You also have the option of pursuing PRK surgery without enrolling in this study for a commercial fee estimated around $4000.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for

any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

You are unable to complete any/all portions of the study protocol including medication use, follow up visits and patient reported outcomes tools.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

No. There will be no extra cost to you for participating in this Research Study.

17. Will you be paid for taking part in this Research Study?

You will not be paid for taking part in this research study. Only the cost of surgery and study-related medications will be waived.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact the Principal Investigator listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing Date