Title: A Randomized Controlled Trial of Topical Cannabidiol for the Treatment of Thumb Basal Joint Arthritis

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Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

Medical Record # _____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study. Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a copy of this form.

Who is funding this study?

This study is being funded by the Southeastern Society of Plastic and Reconstructive Surgeons Annual Research Award.

Key Information About This Research Study

Principal Investigator:	Brent DeGeorge MD, PhD Department of Plastic Surgery University of Virginia 415 Ray C. Hunt Dr. Charlottesville VA 22903 434-760-3297 bd6u@virginia.edu

You are being asked to take part in a research study. You do not have to take part in this study. You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers or others before you make a decision.

What problem is this study trying to solve?

This study is trying to find out if a novel cream containing Cannabidiol (CBD) helps improve symptoms of arthritis in your thumb. We will be looking at how well you tolerate the CBD Cream and how well it works by comparing it to a cream that does not contain any CBD. By participating in this study you will receive both creams, but you will not know which one you will be applying. You will receive either the CBD cream for the first two weeks followed by the cream without CBD, OR the cream without CBD for the first two weeks followed by the CBD cream for two weeks. The CBD Cream has not been approved by the FDA and is investigational. You are being asked to take part in this study because you have arthritis of the thumb joint.

Why would you want to take part in this study?
You might like to take part in this study because a potential benefit of this treatment is the potential pain relief and gain of hand function if the CBD is effective at improving symptoms.

Why would you NOT want to take part in this study?
You might not want to take part in this study because you will have to have blood drawn two times in this study. Once will be to determine if you are eligible and once will be to determine if CBD Cream is safe.

If you are a female, you may not want to take part in the study if you are unwilling to use birth control during the study and for 30 days after the last day of CBD Cream use.

If you are a male, you may not want to take part in the study if you do not wish to use birth control during the study and for 90 days after the last day of CBD Cream use. You are also asked not to donate sperm during this timeframe. Acceptable methods of birth control are covered later in this form.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form.
If you take part in this study you will:

- Have blood drawn for labs (complete blood count, basic metabolic panel, liver function tests, and pregnancy testing performed (if applicable)) to determine if you are eligible for the study.
- Have a urine pregnancy test performed (if applicable).
- Have your medical history taken to see if you qualify for the study.

- Visit the UVA Hand Clinic once a week for 5 weeks after you have qualified for the study. Each visit will last about 1 hour.
- Apply both CBD cream and cream without CBD to your thumb joint twice daily for four weeks.
- Keep a daily diary of any differences you see on the area where you put the cream as well as any surrounding areas.
- Have vital signs (heart rate and blood pressure) measured at every study visit.
- Be asked questions about thoughts of suicide at every study visit.
- Be asked questions if the CBD Cream makes you sleepy or groggy.
- The physician will ask if you are taking any medications at every visit.
- Have the physician examine your hand at the CBD Cream application site.
- Have blood drawn at the final study visit.

What is the difference between being in this study and getting usual care?
If you take part in this study, the following things will be done differently than if you do not take part in this study.

- You would not receive CBD cream on your hand outside of this study and be asked to keep a daily diary.
- You would not be asked questions about thoughts of suicide and if CBD Cream makes you sleepy or groggy.
- You would not be asked to use birth control for up to 90 days.

This is a research study about a novel CBD cream that has not been proven to be safe or helpful. This drug is not approved by the U.S. Food and Drug Administration (FDA). CBD is available over the counter for general use, however this novel cream has only been tested in a small study of healthy volunteers.

What other treatments may I receive if I decide to not take part in this study?
The following alternative treatments are available to you if you decide not take part in this study:

- Standard of care for thumb joint arthritis

You are being asked to be in this study, because you have arthritis of the thumb joint.

Up to 40 people will be in this study at UVA.

How long will this study take?

Your participation in this study will require 7 study visits over 6 weeks period of time. Each visit will last about one hour.

What will happen if you are in the study?

During the research, if we learn you are having thoughts about suicide or hurting yourself or others, the research staff will ask you more questions about your thoughts. Based on your response, the staff may provide you with help to get treatment. This may include: working with you to contact your doctor or therapist, referral to a therapist to discuss your thoughts, contact a trusted family member, significant other or clergy or work with you on a plan that may include getting you to a hospital for safety and treatment.

SCREENING/ BASELINE (visit will last about 1 hour)

Visit 1

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:

- Review of your medical history, including history of mental illness and drug abuse
- Physical exam and vital signs (heart rate and blood pressure)
- Standard blood tests (approximately 2 Tablespoons of blood) to check your blood count, and certain salts and sugars, and your liver and kidney function.
- Blood pregnancy test (if applicable) (about 1 Teaspoon of blood)
- Urine pregnancy test (if applicable)
- Review of medications you are currently taking
- Complete a questionnaire (C-SSRS), which asks questions about whether you have thoughts about suicide or have thoughts about actions of self-harm.

If these tests show you are eligible, you will return to the clinic (within 7 days) to begin study intervention.

Visits 2 and 4

During these clinic visits the study doctors will take your vital signs (heart rate and blood pressure) and ask you the same questions about suicide that you were asked in the previous visit. You will be asked questions about your current pain level and questions about your activity level. If applicable, you will be given a urine pregnancy test. You will be asked about any new medications you are taking.

You will have standard blood tests (about 2 Tablespoons of blood) to check your blood count, and certain salts and sugars, and your liver and kidney function.

RANDOMIZATION and STUDY TREATMENT

You will be randomly assigned to 1 of 2 study treatment groups. You have an equal chance of being assigned to any one of the groups. In both groups you will receive the CBD cream, as well as a cream with no CBD, which acts as a placebo. A placebo is a harmless substance that looks like the study drug, but which should have no effect. You will not be able to find out which one you got (the real drug or the placebo) until the study is done. If your doctor needs to know, the people doing this study can find out. Neither you nor your doctor can choose which treatment you are assigned. Neither you nor your doctor will know which study treatment you will get until the study is done. But if your doctor needs to know, the people doing this study can find out.

The difference in the two groups is the timing of when you will be asked to use the CBD Cream or placebo, as shown in the table below.

GROUP 1: CBD Cream for two weeks followed by placebo for two weeks.
GROUP 2: Placebo for two weeks followed by CBD Cream for two weeks.

During these visits, the study doctor will examine the area where you will be instructed to put the cream. Your doctor will show you the correct way to apply the cream and all supplies will be given to you at this time.

The cream will be applied to the base of your thumb twice a day, for fourteen (14) days. It is important that you not get the application site wet for at least one (1) hour after you apply the study drug.

After you have applied the cream during this visit, the physician will examine the area where the cream was applied.

Do not drive or operate machinery until you have determined how the cream will affect you. You doctor will ask about symptoms such as sleepiness and how the cream affected you.

In addition to the study cream and materials, you will be given a diary to document any skin symptoms you experience after applying the cream. You will complete this daily during the entire study.

Visit 3 and 5 Telemedicine (Visits will last about 1 hour)

You will talk to the study team to the UVA Hand Center via videoconference a week after you have stopped applying the study cream. The study doctor will ask you the same questions about suicide that you were asked in the previous visit. You will be asked questions about your current pain level and questions about your activity level.
The study doctor will examine the area you applied the Study Cream during this video conference. You doctor will ask about symptoms such as sleepiness and how the cream affected you. You will be asked about any new medications you are taking.

Study Schedule

Visit	Visit 1 (Screening and Baseline)	Visit 2	Visit 3 Telemedicine	Visit 4	Visit 5
Study Day	0	14	21	35	49
Informed Consent	X				
Review study eligibility/ medical history	X				
Blood Draw	X	X		X	

Urine Pregnancy Test (if applicable)	X	X		X	
Vital Signs	X	X		X	
VAS Pain Score	X	X	X	X	X
SANE Score	X	X	X	X	X
Patient Reported Outcome Measures		X	X	X	X
Physician Skin Monitoring		X	X	X	X
Suicide questions	X	X	X	X	X
Monitor for sleepiness			X	X	X
Study Medication Dispensed		X		X	
Diary dispensed		X		X	
Diary Review			X	X	X
Study Medication Collected			X	X	X
Side Effects		X	X	X	X

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety.

These responsibilities are listed below:

- You must attend each study visit.

- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Ensure that the study cream is applied as instructed, keep it in a safe place away from children, return any unused study cream at each visit, and report any lost or missed applications.
- Ensure that the study cream is applied only on you.
- Answer all of the study-related questions completely.
- Inform the study doctor or study staff as soon as possible if you have to take any new medications, including anything prescribed by a doctor or those that you can buy without a prescription (over-the-counter), including herbal supplements and vitamins. The study doctor will let you know if you can take these medications.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Because this CBD Cream is investigational, we do not know all of the risks of the cream. A possible risk is skin irritation. However, use of Cannabidiol (CBD) topically does have risks.

Risks and side effects related to the Cannabidiol (CBD) include:

- nausea
- diarrhea
- fatigue, sleepiness
- change in appetite
- weight gain/loss

CBD use may affect how the drug Coumadin works in your body. If you are currently taking Coumadin, you will be asked not to participate in the study.

Do not drive or operate machinery until you have determined how the CBD Cream will affect you.

Risks of having your blood drawn:

Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often), and
- ✓ infection (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:

- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

Risks of Sharing the Drug

Do not share the study drug with anyone. It is prescribed only for you and could hurt someone else. Keep it out of reach of children and people not able to read or understand the label.

Blood Donation

If you participate in this study it may affect your ability to donate blood. If you have any questions call the organization where you donate blood and talk to one of their nurses.

Risks from Completing Questionnaires

- Some of the questions asked may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and to the next question
- Some of the questions asked may make you angry, emotionally upset or stressed out not or at a later time. If this occurs, you may contact the following person for help: Dr. Brent DeGeorge. If you do not wish to answer a question, you may skip it and to the next question.
- There could be a risk of discomfort and harm (to psyche, reputation, employability, insurability, social status, criminal or civil liability) that may occur as a result of

participation. If you do not wish to answer a question, you may skip it and to the next question.

Risks for women:

Pregnancy and Contraception

The drug(s) used in this study can harm an unborn or nursing baby. Therefore, you cannot be in this study if you are pregnant or nursing a baby. A pregnancy blood test will be done about **7** days before starting this study if you are a woman able to become pregnant. You MUST NOT become pregnant while on this study or for up to 30 days after your last dose of drug.

You and your partner must use an approved form of birth control during this study. Examples of birth control you may use are

- Norplant
- IUD (intrauterine device)
- Depo-Provera
- Birth Control Pills
- Birth Control Patch
- Sterilization

The birth control methods listed below are less effective. They may be used if combined with other birth control methods.

- Condoms
- Jellies or foam
- Withdrawal
- Sponge
- Diaphragm
- Rhythm
- Cervical cap

Ask your doctor for more details about the proper birth control method for you. If you become pregnant during this study, you must tell your doctor right away. Your doctor will discuss your treatment and the effect on the pregnancy.

Risks for men:

We do not know the effects of these drugs on male sperm. If you are a male, you should not father a baby while you are in this study and for 90 days after your last dose of the drug. You should also not donate to a sperm bank during this time. To do so may hurt your unborn baby. You must use an effective method of birth control during this time.

If your partner becomes pregnant during this study or for 90 days after the study ends you must tell the study team right away.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You may or may not benefit from being in this study. Possible benefits include potential pain relief and gain of hand function**.** In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- Standard of care for joint arthritis

If you are an employee of UVA your job will not be affected if you decide not to participate in this study. If you are a student at UVA, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will not get any money for being in this study.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance:

- Blood and urine tests
- Study visits
- Vitals signs
- Study drug

- Physical examination of skin where study drug is applied
- Questionnaires

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required. You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
c) The side effects of the study drug are too dangerous for you
d) New information shows the study drug is not safe for you
e) You do not follow your doctor's instructions

If you decide to stop being in the study, we will ask you to let us know as soon as possible. You will be required to return all unused study creams, as well as all empty containers as soon as possible.

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

How will your personal information be shared?

The UVA researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study. Information obtained from you during this study will not be used in future research.

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.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part of this form and return it to the researchers. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your medical records will be able to find out that you are in this study. This is done so your regular doctors will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

Your information, collected for this study, will be protected by a Certificate of Confidentiality from the federal government. If UVA receives a subpoena or court order demanding information from the study records that would identify you, we will use the Certificate to resist the demand. However, UVA will not use it in the following cases.

- You have agreed in writing to allow UVa to share the information with your employer, your insurance company for billing purposes, or someone else
- Reports to authorities where there is a danger that you may harm yourself or others, or if there is evidence of probable child or elder abuse or neglect.

In addition, the Certificate does not prevent government authorities who oversee research from reviewing this study. This Certificate does not mean that the government either approves or disapproves of this study. It just helps protect your privacy.

Please contact the Principal Investigator listed earlier in this form to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished

- Express a concern about the study

Brent DeGeorge MD, PhD
Department of Plastic Surgery
University of Virginia
415 Ray C. Hunt Dr.
Charlottesville VA 22903
434-760-3297
bd6u@virginia.edu

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908

Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

You may also report a concern anonymously by calling the UVA Compliance Hotline phone number at 1-800-235-8700.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Please indicate below whether you want us to notify your health care provider that you have agreed to take part in this study.

_____ Yes, I want the study doctor to notify my health care provider that I have agreed to take part in this study.

Health Care Provider Name:
Health Care Provider Address:
Study team will send a copy of the consent form to the health care provider.

_____ No, I do not want the study doctor to notify my health care provider that I have agreed to take part in this study or I do not have a health care provider.

Leaving the Study Early

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention part of this study but agree to continue to have follow up information about me collected by the study team.

The follow up information will be collected by:

- In person follow up visit, so that the study doctor may examine the study cream application site and I may return the study cream to the study team.

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE