This consent form is not valid without a TTUHSC IRB stamp in the lower left corner of each page.

CONSENT TO TAKE PART IN A RESEARCH STUDY

This is a research study for people who voluntarily choose to take part. Please take your time to make a decision, and discuss the study with your personal doctor, family and friends if you wish.

STUDY TITLE: Dual benefits of Vaginal Estriol: improved urogenital health and re-myelination in relapsing remitting multiple sclerosis (RRMS)?

INVESTIGATORS: Mirla Avila, MD; Smathorn Thakolwiboon, MD; Alan Peiris MD, PhD; Charles Thompson, MD, Dargelis Chi, MD

CONTACT TELEPHONE NUMBERS:
Neurology Department: 806.743.2391
Clinical Research Institute: 806.743.4222 (Office) or 806.543.8994 (Cell)
You may contact the investigator(s) at the number(s) listed above during normal business hours if you develop any of the conditions listed in Question # 7 of this form or if you have any unexpected complications.

INSTITUTION: Texas Tech University Health Sciences Center, Lubbock, TX

1. **Why is this study being done?**
   The purpose of this study is to evaluate vaginal estriol as a treatment for urogenital symptoms in relapsing remitting multiple sclerosis (RRMS) patients and to see how it might help increase the material in the brain that helps transmit signals to other brain cells.

2. **How many people will take part in this study?**
   About 20 people will take part in this study.

3. **Why am I being asked to take part in this research study?**
   You're being asked to participate because you are a female RMSS patient.

4. **What will happen during this study? What will be done that is different from my usual care?**
   These visits will occur during your regularly scheduled clinic visits.
   - There will be four study visits (today, at 3 months, 6 months and at 9 months). At each of these four visits, we'll be collecting up to a teaspoon of blood via needle stick. We will be measuring your hormone levels with these samples.
   - You'll be given two noninvasive eye tests at three of the four visits:
     - **Visual Evoked Potential (VEP) Test:** You will be asked to look a checkerboard pattern while a technician is measuring the time it will take for the image to reach your brain. To measure this, we will attach an electrode to your scalp that will give us this information.

        - **Optical coherence tomography (OCT) Test:** You will be asked to stay still and focus on a small light while we take a picture of your retina with a device you will look into.
    - You'll be asked to complete a questionnaire about your quality of life with MS as well as one asking you about your bladder control at this visit, 3-month visit and final visit.
    - You will have Magnetic Resonance Imaging (MRI) once at the beginning of the study and once at the final visit. A MRI scan will be done by you laying down and going into a machine. It will show images of your brain so we can see the status of your RRMS. This is performed on your follow up MRI schedule, per your standard of care.
    - Today you will be given estriol cream and instructed on how to use the estriol cream. You will apply the cream. You will draw 1mg of estriol vaginal cream with the provided applicator and apply it intra-vaginally once a day. After application you should lay on your back for 30 minutes. You will do this every day until your final study visit.
        - You will be given more cream at each visit excluding your final visit. We will also verify if you've been using the cream as instructed.
    - We will collect some data from your medical chart such as demographic data, such as age, race and information related to your RRMS.

5. How much of my time will this study take? How long will I be in the study?

This study will require a minimum of 30 minutes every day. You'll also have four study visits, including today, each will last about 1.5 - 2 hours. These will take place during your regularly scheduled clinic visits. The OCT test will be done in the Ophthalmology department.

You'll be in the study for about nine months. A member of the study team may call or text you to remind you of your appointments.

6. Are there any benefits to <u>me</u> if I take part in this study?

It is possible that urogenital symptoms or MS symptoms may improve. Sexual function could also improve. It is also possible that no improvements in your symptoms may occur.

7. What are the risks and/or discomforts to me if I join this study?

Risks associated with venipuncture for blood draws include: discomfort, pain, bleeding, bruising, infection where the needle enters the skin; feeling lightheaded or fainting at the site of the needle or blood.

No physical risk with VEP or OCT, these are noninvasive procedures.

Estriol Cream: There is a low risk of thromboembolism (blood clot). Using the applicator or cream may cause vaginal discomfort or infection.

You will be asked about vaginal discomfort or vaginal infections and encouraged to call if you are experiencing these symptoms. If you experience these symptoms you may be referred to your PCP or Gynecologist for appropriate management.

There is a potential loss of confidentiality; we are taking appropriate precautions to minimize this risk.

There may be other risks that are unknown.

8. Will there be any added risks to me from this study if I am a female?
No.

9. What other choices do I have if I do not take part in the research study?
You do not have to take part in this study.

10. What about confidentiality and the privacy of my records?
We will keep your involvement in this research study confidential to the extent permitted by law. In addition to the staff carrying out this study, others may learn that you are in the study. This might include federal regulatory agencies such as the Food and Drug Administration (FDA) and the Office for Human Research Protection (OHRP), Texas Tech University Health Sciences Center (TTUHSC) representatives, representatives from any hospital or site where the research takes place, and the TTUHSC Institutional Review Board (a committee that reviews and approves research). These people may review and copy records involving your participation in this research. A copy of this document may be placed in your medical record.

Study results that are used in publications or presentations will not use your name.

11. Who is funding this study?
With assistance from the Laura W. Bush Institute for Women's Health and University Medical Center Women's Health Research Scholar Fund the department of Neurology is providing the space and supplies for this study. No one on the research staff will receive anything of value from other agencies, organizations, or companies to carry out this research.

12. Will it cost me anything to take part in this research study?
No. You will not be required to pay for any of the tests conducted solely for purposes of the research and the estriol cream will be provided free of charge.

13. Will I receive anything for taking part in this research study?
No.

14. Does anyone on the research staff have a personal financial interest in this study?
No.

15. What if I am hurt by participating in this study?
Texas Tech University Health Sciences Center does not offer to pay for or cover the cost of medical treatment for research related illness or injury. No funds have been set aside to pay or reimburse you in the event of such injury or illness unless specifically stated.

16. What are my rights as a voluntary participant?

Taking part in this study is your choice. If you sign this form, it means that you choose to be in the study.

You may also choose not to be in this study. If you decide not to be in the study, it will not affect any medical care, benefits or rights to which you are entitled.

If new information becomes available during the study that may affect your willingness to take part in the study, you will be told.

17. Can I stop being in the study?

You may leave the study at any time. If you leave the study, we cannot remove any information we have collected to that point.

If you decide to leave the study, discuss it with the investigator who will help you do so in the safest way. If you leave the study, your right to standard medical care will continue.

18. Can someone else end my participation in the study?

Under certain circumstances, the investigators, TTUHSC, or the study sponsor may decide to end your participation in this research study earlier than planned.

19. What if I have questions?

For questions about this study, contact the Investigator, Dr. Avila at 806.743. 2391

If you would like to speak to someone who is not involved in the study about your rights as a participant, research-related injuries, or any other matter related to the study, you can call the TTUHSC EthicsPoint Hotline: 1-866-294-9352. Or, you can file an EthicsPoint report online: https://secure.ethicspoint.com/domain/media/en/gui/12958/index.html. Please choose the "Regulatory Compliance" option when making an online report.

A description of this clinical trial will be available on https://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.

[*SIGNATURE PAGE FOLLOWS*]

Your signature indicates that:

- **this research study has been explained to you;**
- **you have been given the opportunity to ask questions and have received answers;**
- **you accept your responsibility to follow the instructions given to you by the research team regarding study participation and, if applicable, research medication;**
- **you agree to take part in this study.**

You will be given a signed copy of this form.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date Time

_____ _____
Signature of Parent/Guardian or Authorized Representative Date Time

_____ Subject was unable to read and understand the written consent.

The elements of informed consent required by 45 CFR 46.116 and 21 CFR 50 have been presented orally to the subject or the subject's authorized representative in a language understandable to the subject or representative.

_____ _____
Signature of Witness to Oral Presentation Date Time

I have discussed this research study with the subject and his or her authorized representative, using language that is understandable and appropriate. I believe I have fully informed the subject of the possible risks and benefits, and I believe the subject understands this explanation. I have given a copy of this form to the subject.

_____ _____
Signature of authorized research personnel who conducted the informed consent discussion Date Time

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER
AUTHORIZATION TO USE AND/OR DISCLOSE YOUR PROTECTED HEALTH INFORMATION for a RESEARCH STUDY

STUDY TITLE: Dual benefits of Vaginal Estriol: improved urogenital health and re-myelination in relapsing remitting multiple sclerosis (RRMS)?

This form is intended to tell you about the use and/or disclosure (sharing) of your personal **Protected Health Information** (PHI) if you decide to participate in the research study described on the previous pages. The health information about you that may be used or disclosed is described below. This information is usually found in your medical records. Only the health information about you that is needed for this research study will be used or disclosed. When you consider taking part in this research study, you are also being asked to give your permission for your Protected Health Information to be released from your doctors, clinics, and hospitals to the research personnel approved for this research study. This Authorization specifically relates to the research study described in the attached Informed Consent document.

1. This Authorization is valid indefinitely or until such time as legal requirements will allow this Authorization to be destroyed.

2. If you choose to cancel this Authorization, please give notice in writing to:
   Institutional Privacy Officer
   Office of Institutional Compliance
   3601 4th St MS 8165
   Lubbock TX 79430

If you sign this Authorization, the following persons, groups or organizations may rely on this Authorization to disclose your Protected Health Information to the Principal Investigator and other research personnel who are conducting this Study:

- your treating physicians and healthcare providers and their staff,
- associated healthcare institutions and hospitals where you have or may receive care.

While this research study is in progress, the Principal Investigator or research personnel working on this study will inform you whether or not you will be allowed to see the research related health information that is created about you or collected by the research personnel prior to the end of the study. After the study is finished you may request this information as allowed by the TTUHSC Notice of Privacy Practices.

The Protected Health Information that you authorize to be used or disclosed for research purposes may include your current or future health information from some or all of your health records, including:

• hospital records and reports • admission history, and physical examination • X-ray films and reports; operative reports • laboratory reports, treatment and test results (including sexually transmitted diseases, HIV or AIDS)	• immunizations • allergy reports • prescriptions • consultations • clinic notes

• any other Protected Health Information needed by the research personnel listed above. (*use separate form for disclosure of psychotherapy notes)	• mental health records • alcohol / substance abuse records

For the purposes of this study, your Protected Health Information may need to be reviewed or disclosed to individuals or organizations within and/or outside of TTUHSC who sponsor, approve, assist with, monitor or oversee the conduct of research studies. This includes, but is not limited to, the TTUHSC Institutional Review Board, TTUHSC compliance reviews, the US Food and Drug Administration (FDA) or governmental agencies in other countries. Some of these individuals or organizations may share your health information further, and your health information may not be protected by the same privacy standards that TTUHSC is required to meet.

If you choose to sign this Authorization form, you can change your mind about this later. If you change your mind, send a letter to the person identified above telling us to stop collecting and sharing your Protected Health Information. When we receive your request, you may be asked to leave the research study if all the necessary information has not been collected. We may still use the information about you that we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

You have the right to refuse to sign this form. If you choose not to sign this form, your regular health care will not be affected. However, not signing this form will prevent you from participating in this research study and prevent you from receiving research related health care services provided under this study.

I have had the opportunity to review and ask questions regarding this Authorization to use or disclose my personal health information, and I will receive a copy of this form. By signing this Authorization, I am confirming that it reflects my wishes.

_____
Printed Name

_____ _____
Signature of Individual or Authorized Representative Date

_____
If applicable, Relationship of Authorized Representative or Authority to Sign