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
Signed copy to be provided to subject or authorized representative

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: Effect of Tocotrienols on Bone Health: A Pilot Study

INVESTIGATOR: Leslie Shen, PhD, CCRP

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CONTACT TELEPHONE NUMBERS: Clinical Research Institute: 806-743-4222
Dr. Leslie Shen: 806-743-2815
(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 # 6 of this form or if you have any unexpected complications.)

INSTITUTION: Texas Tech University Health Sciences Center, Lubbock

1. **Why is this study being done?**
   After menopause, women have a higher risk of bone deterioration. This increases the chance of bone fractures. Recent studies suggest that tocotrienol supplements (vitamin E isomers) might be good for bone health. However, no study has been done to show how this supplement affects bone health in postmenopausal women. The purpose of this study is to learn about how taking tocotrienol supplements with daily calcium + vitamin D supplements affects bone health in women who are at least one year post-menopause.

2. **How many people will take part in this study?**
   About 78 people will take part in this study.

3. **Why am I being asked to take part in this research study?**
   You are being asked to take part in this study because you are a female who is at least 40 years old, and it has been 1 year or longer since your last period.

4. What will happen during this study? What will be done that is different from my usual care? (Research procedures are indicated by bold text)

Visit 1: Clinical Research Institute

- **Meet with a research coordinator to discuss the study and give informed consent.**
- **Complete a questionnaire about your age, medical history, health status, current medication (if any), menstrual history, physical activity, etc.**

Visit 2: Lubbock Wellness Center

- **Complete a bone scan (DXA)**

Based on the result of your bone scan, if you still qualify to be in this study, you will be notified to come for visit 3. You will be given the results of your bone scan at the end of the study. However, if you no longer qualify to be in the study, you will be mailed your bone scan results at the time of exclusion.

Visit 3: Clinical Research Institute

- **Complete a food-fasted blood draw (4 teaspoons). With this blood sample, we will do a blood chemistry screening.**

Based on the results of your blood tests, if you still qualify to be in this study, you will be notified to come for visits 4-6. If you are excluded from the study because of bone scan or blood screening results, you will be notified by phone and referred to your primary care physician. You will also receive a letter that includes your vitamin D and TSH levels. If your doctor prescribes vitamin D supplements or thyroid medication, please let us know after taking the vitamin D supplement or thyroid medication for 2 months. You may be invited back for a second blood test to recheck your vitamin D and TSH levels. If they are within normal ranges, you will be eligible to take part in the study.

Visit 4 (Baseline Visit): Clinical Research Institute

- **Have a 4 tsp. blood draw and give a urine sample.**
- **Measure body weight and height.**
- **Complete a quality of life survey.**
- **Complete a physical activity survey.**
- **Complete a diet questionnaire.**
- **You will be randomly assigned-like flipping a coin- to one of three treatment groups and you will not know which group you are assigned to.**
    1. **Placebo group: 430 mg olive oil softgel twice daily**
    2. **Low T3 group (low-dose Tocotrienols): 430 mg olive oil softgel in the morning and 300 mg tocotrienol softgel in the evening daily**
    3. **High T3 group (high-dose Tocotrienols): 300 mg tocotrienol softgel twice daily. One in the morning and one in the evening.**
- **You will be given a 6-week supply of the pills, along with verbal information about the pills. You will also be given a 6-week supply of calcium + vitamin D tablets Supplements.**

- **You will be asked to report any problems, issues, or concerns that have occurred since your last visit.**

You will take 1 morning pill after breakfast and 1 evening pill after dinner each day for 6 weeks. You will also take one calcium + vitamin D supplement each day.

Visit 5 (After 6 weeks): Clinical Research Institute.

- **Have a 4 tsp. blood draw and give a urine sample.**
- **You will be given a 6-week supply of the pills, along with verbal information about the pills. You will also be given a 6-week supply of calcium + vitamin D Supplements.**
- **Bring any leftover study drug softgels and calcium + vitamin D tablets to be counted by research staff.**
- **Report problems, issues, or concerns, if any.**

You will take 1 morning pill after breakfast and 1 evening pill after dinner each day for 6 weeks. You will also take one calcium + vitamin D supplement each day.

Visit 6 (After 12 weeks-End of Study): Clinical Research Institute

- **Have a 4 tsp. blood draw and give a urine sample.**
- **Measure body weight and height**
- **Complete a quality of life survey.**
- **Complete a physical activity survey.**
- **Complete a diet questionnaire.**
- **Bring any leftover study drug softgels and calcium + vitamin D tablets to be counted by research staff.**
- **Report problems, issues, or concerns, if any.**

****In addition to the procedures listed above, a small subgroup of participants will be invited to have an additional blood test during visits 4, 5, and 6. If you choose to be a part of this subgroup, you will sign an Informed Consent Addendum that describes the purpose of the subgroup and the additional procedures that will occur.**

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

This study consists of 6 visits. Each of the first three visits will take 1-2 hours to complete. The fourth visit will take 2-3 hours to complete. After the fourth visit, you will take the study drug and Ca+vitamin D supplement each day for 12 weeks. It will take no more than 5 minutes each morning and evening to take these pills. The two follow-up visits at weeks 6 and 12 will take about 1 hour. All six visits should take no longer than 7 months to complete.

Some of the information that is identifiable to you might be kept indefinitely.

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

Tocotrienol is available over the counter at many stores. It is generally recognized as safe (GRAS). However, there have been reports of the following potential side effects:

- Rashes
- Trouble breathing

- Facial Swelling
- Itching
- Chest Pain
- Headaches

Additionally, the risks of a blood draw may include:

- Lightheadedness, dizziness or fainting at the sight of blood
- Pain or discomfort, bleeding, bruising at the puncture site; and
- Rarely, infection or redness at the puncture site

Potential DXA related risks:
The technique of dual energy x-ray absorptiometry (DEXA) is a well-established method for the determination of bone mineral density. The total amount of radiation you receive during this research is about 45.7 μSv or less than the natural background exposure of 10 days.

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

8. Are there any benefits to <u>me</u> if I take part in this study?
No.

9. What other choices do I have if I don't take part in the research study?
This study does not involve treatment. 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, and the TTUHSC Institutional Review Board (a committee that reviews and approves research). These people may review and copy records involving this research. A copy of this document may be placed in your medical record.

The sponsor of the study, American River Nutrition Inc., can also review the study records, but the sponsor is not allowed to remove or copy information that identifies you by name.

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

11. Who is funding this study?
American River Nutrition Inc. (ARN) is funding this research study. This means that TTUHSC is being paid by ARN to support the activities that are required to carry out the study. **No one on the research staff will receive anything of value from** ARN **for carrying out this study.**

12. Will it cost me anything to take part in this research study?
No, the DEXA scan and blood tests done just for this study will be paid for by the study. You will also be given the calcium and vitamin D supplement and the study drug at no cost.

13. Will I receive anything for taking part in this research study?

You will be given thirty dollars ($30) to help with transportation costs. You will be mailed half of this amount after Visit 4 is completed, and the other half after visit 6 is completed.

Payment for participation in this research is considered taxable income. In order for you to receive payment for this research, we will need to collect your name, address, and social security number. If you are not able to provide this information, 30% of the amount being paid for this research study will be automatically deducted and sent to the Internal Revenue Service (IRS).

If you receive payments that total more than $600 in one calendar year, Texas Tech University Health Sciences Center is required to report this information to the IRS. A Miscellaneous Income form (1099-MISC) will be sent to you and to the IRS.

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 and its affiliates do 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.

If you have a research related illness or injury, care will be available to you as usual, but you and/or your medical or hospital insurance company will be responsible for the cost of treatment. Before entering this study, you should check whether your insurance company might limit your insurance coverage if you take part in a research study.

16. What are my rights as a voluntary participant?

- Taking part in this study is your choice. You may choose not to be in it. 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 you sign this form, it means that you choose to be in the study. 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 do, discuss it with the investigator, who will help you leave the study in the safest way.
- If you leave the study, your right to standard medical care will continue.
- If you leave the study, we cannot remove any information we have collected to that point.

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. This might happen if the investigator decides you are no longer eligible to participate or if the investigator or sponsor decides to end the study for any reason.

19. What if I have questions?

For questions about this study, contact the Investigator, Dr. Leslie Shen, at 806-743-2815.

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 Research Protection Hotline: 1-800-396-0918.

A description of this clinical trial will be available on 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.

Your signature indicates that

- **this research study has been explained to you;**
- **you've been given the opportunity to ask questions;**
- **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

(Investigator: Witness is to sign below ONLY if subject is unable to read the written consent form. If they or authorized representative can read the consent form, leave this section BLANK)

_____ 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

(Investigator: The following is to be signed for ALL consent forms)

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 (TTUHSC)

AUTHORIZATION TO USE AND/OR DISCLOSE
YOUR PROTECTED HEALTH INFORMATION for a RESEARCH STUDY

STUDY TITLE: Effect of Tocotrienols on Bone Health: A Pilot Study

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:

   Office of Institutional Compliance
   3601 4th St MS 8165
   Lubbock TX 79410

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	• immunizations • allergy reports

• X-ray films and reports; operative reports • laboratory reports, treatment and test results (including sexually transmitted diseases, HIV or AIDS) • any other Protected Health Information needed by the research personnel listed above. (*use separate form for disclosure of psychotherapy notes)	• prescriptions • consultations • clinic 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 Time

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

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CONSENT FORM ADDENDUM
Signed copy to be provided to subject or authorized representative

STUDY TITLE: Effect of Tocotrienols on Bone Health: A Pilot Study

INVESTIGATOR: Leslie Shen, PhD, CCRP

In addition to the main study, we would like to collect data from a small subset of study participants on how the body processes the study supplement. About 45 participants will take part in this subgroup. If you choose to take part in this subgroup, the following will occur during visits 4, 5, and 6, after your fasting blood draw:

- A meal will be provided to you after your fasting blood draw.
- After your meal, you will be asked to take the full daily dose of the study supplement (both softgels). You will not take any study supplements for the rest of the day.
- Two hours after taking the study supplement, you will have 2 teaspoons of blood drawn and give a urine sample.

Taking part in this sub-study will not change your participation in the main study; you can still be in the main study without being in this part. Participation in this part of the study is voluntary. Taking part in this sub-study will add about 3 hours to Visits 4, 5, and 6. You will receive an additional $30 after each sub-study visit.

By signing this form, you agree to participate in this sub-study.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date Time