HSPP USE ONLY
IRB Protocol Number: 11-0270-04
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SUBJECT'S CONSENT FORM

Study Title: Pilot Study on the Bioactivity of Vitamin D in the Skin after Oral Supplementation

Principal Investigator: Steven A Palmer, M.D., Ph.D.

Sponsor: National Cancer Institute

Introduction

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part in the research. Please take your time to make your decision about volunteering. You may discuss your decision with your friends and family. You can also discuss this study with your health care team. If you have any questions, you can ask your study doctor for more of an explanation. You should only agree to participate in this study when you are comfortable enough with the information so that you can make an informed decision.

Why is this study being done?

The purpose of this study is to find out if taking a high dose of a form of Vitamin D, called cholecalciferol, could help prevent skin cancer in people who have sun damaged skin and low blood levels of Vitamin D. The researchers will determine if Vitamin D can get to the skin in areas that are usually protected from the sun as well as areas that are exposed to the sun, and if the high-dose Vitamin D supplementation improves the nature of the skin cells to prevent skin cancer.

How many people will take part in the study?

About 25 people will take part in this study.

What will happen if I take part in this research study?

Before you begin the study…
You will need to have the following exams, tests, or procedures to find out if you can be in the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

Screening Visit

- A blood sample will be collected for routine laboratory tests (6 teaspoons). Routine blood tests include a. complete blood cell count, metabolic panel and tests to assess major organs such as the kidneys and liver.
- The study staff will record your vital signs (blood pressure, pulse and temperature), weight, and height.
- You will complete a questionnaire about your medical history, and medications, vitamins and herbal supplements that you take.

- A urine pregnancy test will be done if you are a woman who could become pregnant.
- A study doctor will examine your skin and review your medical history questionnaire.
- You will be given a symptom and sun exposure diary to write down any illness or injury you may have and to record time spent outside each day and whether sunscreen or sun protective gear is used when going outside. You will start the diary from this visit and throughout the study. A study coordinator will show you how to use the diary.
- You will be asked to minimize sun exposure and avoid tanning during the study. You may not participate in any other study or clinical trial during this study.
- Starting at this visit, and continuing until the end of your participation in the study, you will be asked to take no more than one standard multivitamin a day. This may not contain more than 600 IU of Vitamin D or more than the recommended daily allowance of calcium for your age and sex.

Age	**Male**	**Female**
40-50 years	1,000 mg calcium	1,000 mg calcium
51–70 years	1,000 mg calcium	1,200 mg calcium
71+ years	1,200 mg calcium	1,200 mg calcium

If you have two or more normal moles, located in areas of the body not usually exposed to sunlight and easily accessible to be biopsied, the study doctor may ask if you will allow those to be photographed and collected for the study. The researchers will look for chemical changes in the cells of the moles that may occur during the study. Please indicate if you consent to these procedures by checking the box and initialing the statement below. Approximately 10 to 15 of the study participants will undergo these procedures. You may decline the photographs and collection of the normal moles and still participate in the study if you are otherwise eligible.

Two of my normal moles may be photographed and biopsied for use in this study.

- Yes ____ - No ____

<u>Baseline Visit:</u>
If the exams, tests and/or procedures show that you can be in the study, you will return to the clinic for a Baseline Visit (within approximately 4 weeks from the Screening Visit) to undergo the following procedures:

- Review your symptom diary, as well as what medications/supplement you are taking.
- A urine pregnancy test if you are a woman who could become pregnant.
- Two areas of normal skin on the left buttock and two areas of sun damaged skin on the right forearm and will be removed (biopsied) by the study doctor. At each biopsy site the study doctor will first inject lidocaine (a numbing medicine or painkiller) and then a 1/8" or a 3/8" diameter circle of skin will be removed, sutured closed (stitched), and covered with a bandage.
- If applicable to you, 1 of the selected moles will be photographed and removed (biopsied) by the study doctor. Lidocaine will be injected at the beginning of the

procedure to numb the mole and the skin surrounding it. The biopsy site will be sutured closed (stitched), and covered with a bandage.
- You will be asked to complete a questionnaire about your previous history of sun exposure and other topics related to skin cancer risk. This will take about 10 minutes.

Study Agent Dispensation Visit:
You will return to the clinic about 2-4 weeks after the Baseline Visit to have the stitches removed. You will be given a supply of Vitamin D study capsules and be asked to take one capsule with food and a full glass of water two times a week for 8 to 9 weeks. You will take one capsule on Monday and one capsule on Thursday of each week. The study coordinator will give you complete instructions for taking the capsules both in person and in writing. You will continue to keep the symptom and sun exposure diary while you are on the study. You will also be given a study calendar to write down when you take the Vitamin D during each week. If necessary, a urine pregnancy test will be done before the study capsules are given to you. In addition to the Vitamin D study capsules, you may continue to take no more than one standard multivitamin a day. The multivitamin may not contain more than 600 IU of Vitamin D or more than the recommended daily allowance of calcium for your age and sex.

Mid-Study Visit:
You will come to clinic about 3-5 weeks after you begin taking the Vitamin D study capsules. The following tests and procedures will be done:
- You will bring the bottle(s) of unused Vitamin D study capsules.
- You will get a new supply of study capsules.
- The staff will review your symptom diary and study calendar with you as well as the sun exposure diary.
- A urine pregnancy test will be done if you are a woman who could become pregnant.
- Your weight will be measured.
- A blood sample will be collected to measure calcium and Vitamin D (4 teaspoons).

A study coordinator will contact you by telephone about 2 weeks and 6 weeks after you begin taking study capsules to follow up on your progress in the study.

When you are finished taking the Vitamin D study capsules…
You will return to clinic the day after you finish taking the study drug for 8 to 9 weeks. The following tests and procedures will be done:
- You will bring the bottle(s) of study capsules, even if they are empty.
- The staff will review your symptom and sun exposure diary as well as the study calendar with you.
- A urine pregnancy test if you are a woman who could become pregnant.
- A blood sample (about 10 teaspoons) will be collected for routine laboratory tests and for research tests.
- Two areas of normal skin on the left buttock and two areas of sun damaged skin on the right forearm and will be removed (biopsied) by the study doctor, next to the areas where samples were removed at the baseline visit.
- If you are a study participant who had normal moles selected for the study at the

baseline visit, the study doctor will take regular and close-up photographs of the 1 remaining selected study mole. Then that mole will be removed (biopsied) by the study doctor.

About 10-14 days after completing the study drug you will come back to the clinic to have your stitches removed. The study staff will ask whether you had any side effects.

Study Plan

The study calendar below shows what will happen to you during the study. The study may involve 6 visits to the clinic, lasting between 20 minutes to 1½ hours each.

Study Calendar

Screening Visit	Undergo exams, tests or procedures to find out if you can be in the study.
Baseline Visit	Clinical evaluation and collection of skin biopsy samples.
Study Agent Dispensation Visit	Return to clinic to have stitches removed and receive Vitamin D study capsules. Begin taking study capsules twice a week for 8-9 weeks. Keep study diaries. Throughout the study, contact the study team if you experience side effects.
3-5 weeks after start of study capsules	Return to clinic for evaluation of side effects and use of study capsules. Bring diary, calendar and your bottle(s) of study capsules.
End of 8 to 9 weeks of study capsules	Return to clinic for evaluation of side effects and clinical evaluation/removal of the study moles. Bring diaries, calendar and your study drug.
10-14 days after final biopsies	Return to clinic to have stitches removed and for evaluation of side effects.

How long will I be in the study?

You will spend about 16 weeks enrolled in the study. You will be asked to take Vitamin D study capsules for 8 to 9 weeks and be followed for 2 weeks after you stop.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or if you decide to stop. He or she will tell you how to stop safely. If you decide to stop taking the study agent, you may still participate in other parts of the study, such as collection of biopsy or blood samples or a final clinic visit. You may be asked if we can still use your medical information, such as age, gender or medical history, to determine what characteristics are common in people who are interested in cancer prevention studies. You can also decide that you do not want us to use your information.

The study doctor may stop you from taking part in this study at any time if he/she believes stopping is in your best interest; if you do not follow the study rules; or if the study itself is stopped.

What side effects or risks can I expect from being in the study?

You may or may not have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Many side effects go away soon after you stop taking the study agent. In some cases, side effects can be serious, long lasting, or may never go away. You should talk to your study doctor about any side effects that you have while taking part in the study.

Possible risks and side effects related to taking Vitamin D capsules include those which are:

Likely (*occurring in greater than 20% of general population)*

- None expected

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Less Likely (*occurring in less than or equal to 20% of general population)*

- High levels of calcium in the blood
- Dry mouth
- Constipation
- Headache
- A metallic taste
- Weakness
- Nausea, vomiting, or decreased appetite

Rare but Serious (*occurring in less than or equal to 2-3% of general population)*

- Vitamin D may increase calcium levels and increase the risk of "hardening of the arteries" in people who have serious kidney disease.
- Vitamin D may increase calcium levels in people with diseases such as sarcoidosis, histoplasmosis, atherosclerosis, hyperparathyroidism, and lymphoma. This could lead to kidney stones and other health problems.
- An allergic reaction (difficulty breathing; closing of the throat; swelling of the lips, tongue or hives).

Reproductive risks: You should not become pregnant while on this study because it is not known if the study drug can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that women who could become pregnant need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. For more information about risks and side effects, ask your study doctor.

Effects of other drugs you may be taking:
It is important to tell the doctor or study staff if you are taking any prescription or over the counter drugs or herbal supplements. We will need this information to make sure that there is no interaction with the study drug.

Some discomfort may be felt when the painkiller (lidocaine) is injected before the skin biopsies; however, it is usually minimal. There is a slight chance of infection following

the biopsy, and there is a slight risk of an allergic reaction to the numbing medicine (lidocaine). You will have a scar at the biopsy site(s), which could be from ½" to 1", depending on the size of the biopsy sample from your forearm/buttock and if indicated the mole that is removed. There is a chance that the scar will be permanent, or it may fade over time.

There is a slight chance of developing an infection (1%) or bruise at the site of a blood sample collection. You may experience discomfort or bleeding during the procedure.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope that Vitamin D will be useful in cancer prevention, there is no proof of this yet. We do know that the information from this study will help doctors learn more about Vitamin D as an agent in cancer prevention. This information could help improve the public health.

What other choices do I have if I do not take part in the study?

You may obtain Vitamin D (over the counter) even if you do not take part in the study. Please talk to your personal doctor for information about options that would be appropriate for you.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. A study identification number will be used instead of your name or other identifiers on the paper study forms, which will be filed in locked file cabinets at the research clinic. The study information collected on the forms will be entered into a computer database, with access protected by the use of a password known only to the individuals conducting the study. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Office for Human Research Protections, the Food and Drug Administration, or other federal, state, or international regulatory agencies involved in keeping research safe for people
- The Institutional Review Board or Office of Responsible Research Practices
- Authorized Cancer Center Representatives and the Cancer Center study team including your study doctor, his associates, and other study personnel
- The sponsor supporting the study, the National Cancer Institute, Division of Cancer Prevention, including their agents or study monitors

What are the costs of taking part in this study?

You will not be responsible for the costs of any clinic appointment or laboratory test associated with your participation in this study (including blood tests, skin biopsies, and biopsy analysis). The Vitamin D study capsules will be provided to you free of charge. You will receive $300 at the end of the study, upon completion of all the required visits and tests. If for any reason you are unable to complete the entire study, the amount of reimbursement will be less and divided up based on the duration of your participation in the study.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Steven A. Palmer, M.D., Ph.D.., if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him at (240) 822-2429.

You can request medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. Neither the study nor the University has funds set aside for the payment of treatment expenses for this study.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you choose to participate in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from the institution conducting the study.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study. In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form or release the institution from liability for negligence.

Who can answer my questions about the study?

You can talk to your study doctor about any question or concerns you have about this study. Contact your study doctor, Steven A. Palmer, M. D., Ph.D., at (240) 822-2429.

If you think you are having a side effect, especially if it lasts more than 24 hours or interferes with your usual activity, contact the study staff at (240) 822-2429. In case of emergency, call (240) 822-2429.and ask the operator to page the dermatologist on call.

If you have questions concerning your rights as a research participant, have questions, complaints, or concerns about the research and cannot reach the Principal Investigator, or want to talk to someone other than the Investigator, you may call the Human Subjects Protection Program office at (240) 822-2429. If you would like to contact the Human Subjects Protection Program via the web, please visit the following website

www.HumanSubjectsProtectionProgram.com

Consent for use of excess specimens for research purposes:

There may be some specimens (blood and skin biopsies) remaining once the study is complete. If I am willing to allow the excess specimens to be used for future research studies, I will specify my consent below. They may be used to learn more about skin cancer and its prevention. These studies will only be done after review and approval by the Institutional Review Board. Remaining skin and blood samples will be stored in the laboratory of the Cancer Center study investigator. The same level of privacy and confidentiality as the main study will be maintained for these remaining samples. The samples may be stored for up to 10 years. Consent for future use of my stored samples is entirely voluntary and may be withdrawn at any time. Please read the sentences below and circle "Yes" or "No" with your initials for each. If you have any questions, please talk to the study staff or the study Principal Investigator.

1. My skin tissue may be kept for use in future skin cancer research. • Yes___ • No ___

2. My blood may be kept for use in future skin cancer research. • Yes___ • No ___

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615
You may also visit the NCI Web site at http://cancer.gov/
For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
For NCI's general information about cancer, go to http://cancer.gov/cancertopicsinfo

A description of this clinical trial will be available on http://www.clinical.com, as required by US law. This website will not include information that can identify you. At most, the website will include a summary of the study results. You can search this website at any time.

Signature

I have been given a copy of all 9 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

_____

Printed name of subject

_____ _____

Subject's Signature **Date**

Investigator/Research Staff

I have explained the research to the participant or the participant's representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or to the participant's representative.

_____

Printed name of person obtaining consent

_____ _____

Signature of person obtaining consent **Date**