FORT HAYS STATE UNIVERSITY
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INSTITUTIONAL REVIEW BOARD FOR HUMAN SUBJECTS RESEARCH

NEW IRB SUBMISSION

I. Project Title and Research Team Members

Project Title:

Effects of Acute Estrogen Therapy on Bone Formation

Principal Investigator Name:

Jon Snow, Robb Stark

Faculty Research Supervisor (If student is the PI):

Dr. Eddard Stark

Additional Team Members:

N/A

This form must be used to submit an application through the IRBNet system.
No other methods of submission will be accepted.

Access the system here: www.irbnet.org
Student and Adjunct Faculty researchers: Please note that Faculty Research Supervisor approval is required prior to submission to IRB. The Faculty Research Supervisor signature in IRBNet indicates approval and agreement with section XII.
For faster processing, ensure all research team members have completed all required CITI training through https://www.citiprogram.org/ prior to submitting this application.

II. Type of investigator and nature of the activity: (Check all appropriate categories.)

A. Faculty/Staff at FHSU:
- ☑ Submitted for extramural funding to:
- ☐ Submitted for intramural funding to:
- ☐ Project unfunded
- ☐ Quality improvement/program evaluation
- ☐ Quality assurance
- ☐ Other (Please explain)

B. Student at FHSU: ☑ Graduate ☐ Undergraduate ☐ Independent Study
☑ Thesis ☐ Specialist Field Study ☐ Graduate Research Paper

C. Class Project (Course Number and Course Title), explain activity:

N/A

D. Other than faculty, staff, or student at FHSU (Unaffiliated with FHSU)
Please explain:

N/A

III. Human Subjects Research Ethics Training: The IRB will not review submissions without verification of appropriate CITI training. The Principal Investigator and all members of the research team must complete the appropriate CITI training modules. Faculty Research Advisors, when listed above, must also complete CITI training. If the PI is not affiliated with FHSU, documentation of CITI or other comparable training must be provided.
Date completed CITI training:

Jon Snow: July 2017; Robb Stark: May, 2017; Dr. Eddard Stark: April 2017

IV. Project Information

A. Expected study period from: 8/21/2017 To: 8/20/2018

B. Describe the purpose of the research. Explain what is intended to be discovered, including goals, aims, and objectives and/or state the hypothesis to be tested. Background: provide a brief scientific or scholarly rationale for the research activities, and address gaps in current knowledge.

Estrogen (E) deficiency is the major cause of postmenopausal osteoporosis. Understanding the mechanisms by which E regulates bone metabolism is critical for developing novel approaches to prevent and treat this disorder. We will use novel methods we have developed to examine gene expression in highly purified bone marrow osteoblastic cells. We will test whether the increase in bone formation previously observed following acute E treatment in women is associated with an increase in markers of Wnt/BMP signaling and/or production and in other genes related to bone formation by osteoblastic cells.

We will study 20 post-menopausal women, all of whom will be at least 10 years postmenopausal (in order to avoid confounding effects of early postmenopausal changes in bone turnover) and meet the other inclusion/exclusion criteria described below. If the subjects have not had a negative mammogram in the past year, we will obtain a digital screening mammogram and document a negative mammogram prior to entering them into the study. The participants will be treated with a transdermal E2 patch (0.1 mg/d) for 3 weeks. At baseline, they will have fasting, 8 am bloodwork drawn for bone formation (OCN and PINP) and resorption (CTx and TRAP 5b) markers. Three weeks later, they will have the fasting blood samples redrawn to assess changes in bone turnover following E treatment, additional peripheral blood will be drawn for the cell analyses, and bilateral bone marrow aspirate and biopsy performed for the analyses described below.

☐ Investigators NOT currently affiliated with FHSU will collaborate on this project.

C. (If checked above) Identify any cooperating institutions by name.

N/A

D. This study is being/has been reviewed by another IRB. Yes ◯ No ◉
If yes, please attach relevant documentation.

V. Subject Information

A. Number of subjects:

Approximately 20 post-menopausal women.

B. Subject Age (Check all that apply):

- ☐ 1-7
- ☐ 8-17
- ☐ 18-65
- ☑ 65+

C. Special Populations (Check all that apply):

- ☐ Minors
- ☐ Non-English speaking
- ☐ Prisoners
- ☐ Individuals with impaired decision-making capacity
- ☐ Individuals who are economically or educationally disadvantaged
- ☐ Individuals with Legally Authorized Representatives
- ☐ Individuals who are vulnerable to coercion or undue influence

D. Describe target demographic of proposed subjects; explain how you will ensure that selection is equitable and that all relevant ethnic groups, genders, and populations have access to the study.

At least 10 years postmenopausal; Menopause is defined as no menses for at least 1 year (or documented ovariectomy) and a serum FSH above 30 IU/L.

E. Describe any specific populations targeted for inclusion or exclusion: Justify criteria based on age, gender, race, ethnicity, sexual orientation, or origin.

Exclusion criteria include the following: 1) Clinically significant abnormality in any of the following screening laboratory studies (to be reviewed and determined by PI or CI): serum 25-hydroxyvitamin D (see below); phosphorus (minor change outside of normal guidelines is acceptable and does not impact the study); alkaline phosphatase and aspartate transaminase (AST) (minor change outside of normal guidelines is acceptable but not to exceed 50% above normal or ineligible); Creatinine (Cr) (minor change outside of normal guidelines is acceptable but not to exceed a value of 1.2 or ineligible); serum calcium must not exceed upper limits of normal guidelines or subject ineligible; FSH needs to be ≥30; TSH needs to be above 0.3 and not > 10; 2) Presence of significant liver disease, renal disease, malignancy (including breast cancer and myeloma), malabsorption syndrome, hypoparathyroidism, hyperparathyroidism, acromegaly, Cushing's syndrome, hypopituitarism, severe chronic obstructive pulmonary disease, untreated gallbladder disease, history of MI or stroke, or history of thrombophlebitis or deep venous thrombosis; 3) Undergoing treatment with any of the following drugs: adrenocorticoid steroids (3 months

VI. Recruitment

A. Describe the recruitment process for the study. Explain in detail how you will gain access to and recruit participants for participation in this project. Upload scripts, emails, letters, advertising, and all marketing materials with your application. Provide a step-by-step description of how potential participants will be recruited.

We will recruit from previous participants and volunteers from the community. Screening laboratory studies will be performed as outpatients in the CRU at Hays Med. If a subject is found to have low body stores of Vitamin D as assessed by the serum 25-hydroxyvitamin D of <20 ng/ml, they will be treated with 1000 units/day of Vitamin D for 8 weeks and then have their level rechecked. If the level is still < 20 ng/ml, they will receive a second course of treatment; if the level is still < 20 ng/ml after the second course, they will not continue in the study and will be referred to their primary physician for further evaluation. If it is 20 ng/ml or greater they will then continue with the study.

If they have not had a negative mammogram in the past year, they will undergo a screening mammogram. A negative mammogram is one that is read as such by the radiologist, although minor abnormalities such as fibrocystic disease, benign calcifications, etc., which are judged by the radiologist as benign changes will not preclude the subjects from participating.

B. Identify all applicable recruitment methods. (Please provide copies of materials).

- [x] Flyers
- [ ] Purchased Sample List
- [ ] Email
- [x] Telephone
- [x] Newspaper
- [ ] Poster
- [ ] Class Announcement
- [ ] Departmental Communication
- [ ] Third Party (Professional or Charitable Organization)
- [ ] Internet
- [x] Letter
- [ ] Personal or Professional Contacts
- [ ] Amazon MTurk
- [ ] Social Media
- [ ] SONA
- [ ] Snowball method (if used, must describe process in detail)
- [ ] Other (describe)

C. Are you recruiting students from a class you teach or for which you have responsibility? ◯ Yes ◉ No

D. Are you recruiting employees who directly or indirectly report to you? ◯ Yes ◉ No

E. If yes to either VI C or D, please explain why this population is necessary and describe what precautions have been taken to minimize potential undue influence or coercion.

N/A

VII. Compensation

- [x] Participants will not receive compensation
- [ ] Students will receive extra credit or course credit
- [ ] Participants will receive monetary compensation
- [ ] Participants' names will be entered into a drawing for a prize

Describe the compensation or credit, including amount, scheduling and method. Explain what will happen if participants withdraw from the study.

Participants will not be directly compensated for their participation.

VIII. Risks and Benefits

A. Describe the anticipated benefits of the research for individual subjects.

Through participating in this research, participants may gain more insight about their condition. Participants may also gain more knowledge about changes in bone formation.

B. Describe the anticipated benefits of the research for society or the discipline. Explain how the benefits outweigh the risks.

The discipline will gain insight and knowledge in relation to how different treatments for women post-menopause impact medical conditions. The results from this study may help lead to the development of novel approaches to prevent and treat this disorder.

C. Does this study involve any of the following? (Check all that apply.)

- ☐ Deception
- ☐ Omission
- ☐ Misleading Information/false feedback
- ☐ Physical or mental stress
- ☑ Collection of fluids or tissue
- ☑ Substances taken internally or applied externally
- ☐ Information pertaining to illegal activity
- ☐ Information relating to sexual attitudes, orientation or practice
- ☐ Private identifiable information
- ☐ Personal or sensitive information
- ☐ Private records (academic or medical)
- ☐ Social or economic burden to participants
- ☐ Mechanical or electrical device applied to subjects
- ☐ Information pertaining to substance use
- ☐ DXA Scan, X-RAY, MRI
- ☐ Information that, if released, could damage an individual's financial standing, reputation, employability, or cause social stigmatization, discrimination, or embarrassment
- ☐ Other
- ☐ **None of these**

D. Describe the nature and degree of the risk or harm checked above. If using deception, include a justification for the deception.

Venipuncture: The risks of venipuncture for blood drawing include pain, bleeding, bruising, infection and inflammation at the site. The total amount of blood withdrawn will not exceed 550 ml over an eight week period. Hemoglobin measurements at the screen visit must be greater than 11.5 g in females in order to participate. All subjects will refrain from giving blood or being on other research studies for eight weeks prior to the study, during the study, and for 8 weeks after completion of the study.

Intravenous access: The risks of intravenous access are as above for venipuncture. There is also the potential risk for blood borne infection through the catheter site.
Bone marrow aspirates and biopsies: These are routine procedures associated with minimal or no complications. Possible side effects include pain, bleeding, bruising and infection at the site where the bone marrow is removed. Pain is minimized by the use of local anesthesia, and moderate sedation is offered to the subjects. Bleeding at the site may occur at the time of procedure; to minimize this, pressure is applied to the area until bleeding stops. This can be a painful procedure, and the discomfort may last for several days.

Medications used: Estradiol dermal patch is used at a dose that approximates normal circulating estradiol levels in premenopausal women and will be administered for only 3 weeks. The patches may cause a topical allergic type reaction. This may cause vaginal bleeding in women with intact uteri. However, it has been our experience in a number of other studies that for postmenopausal women who have been amenorrheic for >1 yr that bleeding is uncommon when E administration is given for only 3 weeks. Other E related symptoms such as mastodynia, premenstrual syndrome symptoms, and pedal edema are very unlikely with such a short period of treatment. The Women's Health Initiative, a large prospective trial of an average of 5.2 yrs with Prempro reported the following adverse effects (difference from controls): heart attacks, 7 per yr per 10,000 patients studied;

E. What steps will be taken to minimize risks or harm and to protect the subject's welfare (when risk is greater than minimal)?

It should be noted that the PI and research team have extensive prior experience conducting research of this kind. In order to reduce and minimize risks, the researchers will complete extensive background checks on the participants' medical conditions in order to exclude participants who should not complete this study. The researchers also will be in contact with the participant's primary care physician if emergencies/unexpected adverse events occur. A researcher will be present when all data and specimens are collected in order to answer questions posed by participants as well as direct the participant to the appropriate person/organization should they feel discomfort and/or distressed from participating in this study.

IX. Emergencies

How will emergencies or unanticipated events related to the research be handled if they arise? (Please note that this refers to an emergency situation associated with the research activity not an emergency such as a fire alarm.)

The investigator's thesis chair, the Department Ethics Chairperson, and the FHSU IRB will be contacted immediately should emergencies occur. Also, the researchers will be in contact with the participant's primary care physician.

X. Data Collection and Security

A. Procedures: Describe the setting and tasks subjects will be asked to perform. Describe the frequency and duration of procedures, tests, and experiments. Include a timeline or a step-by-step description.

Screening laboratory studies will be performed on outpatients in the CRU at Hays Med. If a subject is found to have low body stores of Vitamin D as assessed by the serum 25-hydroxyvitamin D of <20 ng/ml, they will be treated with 1000 units/day of Vitamin D for 8 weeks and then have their level rechecked. If the level is still < 20 ng/ml, they will receive a second course of treatment; if the level is still < 20 ng/ml after the second course, they will not continue in the study and will be referred to their primary physician for further evaluation. If it is 20 ng/ml or greater they will then continue with the study.

If they have not had a negative mammogram in the past year, they will undergo a screening mammogram. A negative mammogram is one that is read as such by the radiologist, although minor abnormalities such as fibrocystic disease, benign calcifications, etc which are judged by the radiologist as benign changes will not preclude the subjects from participating.

We will study 20 post-menopausal women, all of whom will be at least 10 years postmenopausal (in order to avoid confounding effects of early postmenopausal changes in bone turnover) and meet the other inclusion/exclusion criteria described below. If the subjects have not had a negative mammogram in the past year, we will obtain a digital screening mammogram and document a negative mammogram prior to entering them into the study. The participants will be treated with a transdermal E2 patch (0.1 mg/d) for 3 weeks. At baseline, they will have fasting, 8 am bloodwork drawn for bone formation (OCN and PINP) and resorption (CTx and TRAP 5b) markers. Three weeks later, they will have the fasting blood samples redrawn to assess changes in bone turnover following E treatment, additional peripheral blood will be drawn for the cell analyses, and bilateral bone marrow aspirate and biopsy performed for the analyses described below.

Biospecimen (types, number, volume, processing, storage):
Screening visit: blood sample for the following-CBC, serum calcium, phosphorus, alkaline phosphatase, creatinine, AST, FSH, 25(OH)D, and TSH.
Baseline: blood draw of 50 ml for bone formation markers (OCN and PINP) and bone resorption markers (CTx and TRAP 5b)

3 weeks after baseline draw: blood draw of 50 ml for bone formation markers (OCN and PINP) and bone resorption markers (CTx and TRAP 5b) and cells for RNA
Bilateral bone marrow aspirate and biopsy: These procedures are as routinely performed clinically in Hematology. These will be performed by the Transfusion Therapy Center (TTC) nurses or our study coordinator, Louise McCready, RN, who has been trained by the TTC nurses, under the supervision of Dr. Khosla. This will provide up to 80 ml of marrow. 2 ml of fresh, unprocessed bone marrow will be used for analysis of apoptosis. The remaining bone marrow aspirate and all of the peripheral blood will be depleted of the red blood cells and most of the platelets and granulocytes by density-gradient centrifugation over Ficoll-Paque. The mononuclear cells (MNCs) will then be harvested from the interface, washed, and cell number and cell viability with trypan blue will be measured. Following

B. Describe the steps that will be taken to secure the data during storage, use, and transmission. How and where will the data be stored, for how long will it be kept, when will it be destroyed, what safeguards are in place for data with identifying information? Include a description of physical and electronic security.

Data will be stored electronically and only the research team will have access to the data. If data is presented at a conference, it will be stored for up to five years electronically and then destroyed. Names will not be included on the electronic records, only ID numbers. A list of names and ID numbers will be stored under lock and key. After the completion of data collection, the list of names and ID numbers will be destroyed.

C. Identify any direct identifiers like name, unique identifier, address, email, etc. that will be kept with the records. Explain why it is necessary to record the identifiers and describe the coding system to be used.

A list of names and ID numbers will be kept in a locked room within the clinic to protect participant's identity and only the research team will have access to the lists in order to identify participants and match their results over time.

D. If retaining a link between study code numbers and direct identifiers after data collection is complete, please explain why this is necessary, how long the link will be kept, how it will be stored, and when it will be destroyed.

Once the data is collected and all the data is matched to the correct participants, the names will be kept in case participants must be contacted again. However, the list of participant names and ID numbers used in the analyses will be destroyed.

E. Data collection methods (check all that apply)

- ☐ Observation
- ☐ Interviews
- ☐ Focus groups
- ☑ Surveys/Questionnaires
- ☐ Psychological tests
- ☐ Educational tests
- ☑ Blood draw, saliva swab, or other biological sampling
- ☐ Audio recording (see section X. F)
- ☐ Video Recording (see section X. F)
- ☐ Previously collected data (no individual identifiers)
- ☐ Previously collected data (with individual identifiers)
- ☐ Internet-based methods
- ☐ Other (describe)

F. If using audio or video recording, describe how the recordings will be used, how confidentiality will be maintained, who will have access, and how and when the recordings will be destroyed or completely deidentified.

N/A

G. Protected data to be collected (check all that apply)
☑ Protected health Information (see Section X, Part H)
☐ Unique ID number (e.g. employee ID, driver's license number, student ID number, etc.)
☐ Academic records
☐ Social security number
☐ Other personally identifiable information

H. If the research involves protected health information, it must comply with the HIPAA Privacy Rule.
Select one:

☐ The research does not involve protected health information

Do you plan to use or disclose identifiable health information outside FHSU?
◯ Yes ◉ No

If yes, the consent form must include a release of protected health information.

The IRB may make a waiver of authorization for disclosure if criteria are met under the HIPAA Privacy Rule. *If a waiver of authorization is being requested, the researcher must contact the IRB administrator prior to submitting this application.*

Will the protected health information to be used or disclosed be deidentified, or will a limited data set be used or disclosed? *Please describe*:

The protected health information will be de-identified. Results of the study will be aggregated and no names or identifiable information will be included in future conference presentations and publications.

I. Sharing results with subjects (Indicate if results, like tests or incidental findings, will be shared with the subject or others, and if so, indicate how it will be shared.)

If the study is presented at a conference or published, results will be aggregated and no identifiable information will be included.

J. Withdrawal of subjects (Describe the procedures to be followed when subjects withdraw from research or under what circumstances subjects may be withdrawn without their consent.)

Participants will not be compensated for completing this study. Participation in the study is voluntary, and participants may choose to withdraw at any point during the study. If participants decide to withdraw from the study, their materials will not be used (any completed surveys and specimen samples will be destroyed).

XI. Informed Consent

A. Specify the type of informed consent you will use with this research project.

☑**Signed Consent**

Consent forms included with this submission:

☑Adult ☐Assent Script/Procedures ☐Parent/Guardian
☐Foreign Language Version ☐Agency Consent

☐**Oral Consent** (Waiver of documentation of consent, include script with application)

☐Signed consent form would be the only record linking the subject to the research, and the principal risk of signing a consent form would be the potential harm resulting from a breach of confidentiality.

☐The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context.

☑**Information Statement** (include with application)

☑**Debriefing Statement** (include with application)

B. Describe any potential concerns with obtaining informed consent (Foreign language, minimizing possibility of coercion, etc.)

There are no anticipated concerns for obtaining informed consent. In order to minimize the possibility of perceived coercion, the researcher will reiterate that the study is voluntary and participants may withdraw at any time without penalty. If participants decide to withdraw, all materials will be destroyed and their data will not be used in future analyses.

C. Describe the process you will follow to obtain consent and/or assent. Include names of individuals on the research team who will obtain consent, where and when the process will take place, and how you will ensure the subject's understanding.

The PI will talk to the participants about potential risks and benefits of the study. The PI will highlight important information from the consent statement and will give the informed consent to the participants to read; this will give participants the opportunity to ask any questions they may have prior to signing the consent. The PI also will let the participants know that the research team will be in contact with the participant's primary care physician in the event of any emergencies and/or unanticipated adverse events.

All materials related to this study must be uploaded into your IRBNet study workspace. Instructions for using IRBNet are located at the FHSU IRB website. Required materials may include, but are not limited to:

- Completed application
- Copies of all recruiting materials, including scripts, emails, letters, posters, advertising, etc.
- Copies of all measurements, instruments, surveys, interview questions being used, etc.
- All consent forms and assent forms or scripts (for children).
- Debriefing materials, if used.

Please note that all materials and scripts to be used for this study need to be reviewed and approved by the IRB.

XII Certifications:

I am familiar with the policies and procedures of Fort Hays State University regarding human subjects in research. I subscribe to the university standards and applicable state and federal standards and will adhere to the policies and procedures of the Institutional Review Board for the Protection of Human Subjects. I will comply with all instructions from the IRB at the beginning and during the project or will stop the project.

AND

I am familiar with the published guidelines for the ethical treatment of human subjects associated with my particular field of study.

Statement of Agreement:

By electronically signing and submitting this application package, I certify that I am willing to conduct and /or supervise these activities in accordance with the guidelines for human subjects in research. Further, I certify that any changes in procedures from those outlined above or in the attached proposal will be cleared through the IRB.

If the Principal Investigator is a student, the electronic signature of the Faculty Advisor certifies:
1) Agreement to supervise the student research; and, 2) This application is ready for IRB review. The Student is the "Principal Investigator". The Faculty Research Advisor is the "Advisor". Designees may not sign the package. It is the student's responsibility to contact their Faculty Research Advisor when the study is ready for the Advisor's signature.

I certify the information provided in this application is complete and correct.
I understand that I have ultimate responsibility for the conduct of the study, the ethical performance of the project, the protection of the rights and welfare of human subjects and strict adherence to any stipulations imposed by the IRB.
I agree to comply with all FHSU policies, as well as all federal, state and local laws on the protection of human subjects in research, including:

- Ensuring all study personnel satisfactorily complete human subjects research training.
- Performing the study according to the approved protocol.
- Implementing no changes in the approved study without IRB approval.
- Obtaining informed consent from subjects using only the currently approved process and form.
- Protecting identifiable health information in accordance with HIPAA Privacy rule.
- Promptly reporting significant or untoward adverse effects or unanticipated problems to the IRB.

Example of Adult Informed Consent Statement

Name of the Study: Effects of Acute Estrogen Therapy on Bone Formation

INTRODUCTION

The Department of Nursing at Fort Hays State University supports the practice of protection for human subjects participating in research. **You are being asked to participate in a research study. It is your choice whether or not to participate.** The following information is provided for you to decide whether you wish to participate in the present study. You may refuse to sign this form and not participate in this study. You should be aware that even if you agree to participate, you are free to withdraw at any time. If you do withdraw from this study, it will not affect your relationship with this unit, the services it may provide to you, or Fort Hays State University.

PURPOSE OF THE STUDY

The purpose of this study is to examine the effectiveness of a novel method we have developed to examine gene expression in highly purified bone marrow osteoblastic cells and test whether the increase in bone formation previously observed following acute E treatment in women is associated with an increase in markers of Wnt/BMP signaling and/or production and in the genes related to bone formation by osteoblastic cells.

PROCEDURES

Screening laboratory studies will be performed as outpatients in the CRU at either Charlton 7 or Domitilla 5, Saint Mary's Hospital. If you are found to have low body stores of Vitamin D as assessed by the serum 25-hydroxyvitamin D of <20 ng/ml, you will be treated with 1000 units/day of Vitamin D for 8 weeks and then have your level rechecked. If the level is still < 20 ng/ml, you will receive a second course of treatment; if the level is still < 20 ng/ml after the second course, you will not continue in the study and will be referred to your primary physician for further evaluation. If it is 20 ng/ml or greater you will then continue with the study.

If you have not had a negative mammogram in the past year, you will undergo a screening mammogram and document a negative mammogram prior to you entering the study. A negative mammogram is one that is read as such by the radiologist, although minor abnormalities such as fibrocystic disease, benign calcifications, etc. which are judged by the radiologist as benign changes will not preclude you from participating.

You will be treated with a transdermal E2 patch (0.1 mg/d) for 3 weeks. At baseline, you will have fasting, 8 am bloodwork drawn for bone formation (OCN and PINP) and resorption (CTx and TRAP 5b) markers. Three weeks later, you will have the fasting blood samples redrawn to assess changes in bone turnover following E treatment, additional peripheral blood will be drawn for the cell analyses, and bilateral bone marrow aspirate and biopsy performed for the analyses comparing treatments.

If you decide to participate in this research study, you will be asked to sign this consent form after you have had all of your questions answered and understand

what will happen to you. The length of time of your participation in this study is approximately one hour at the baseline blood draw and at the follow-up draw after three weeks of treatment. We ask that you refrain from giving blood or participating in other research for an eight-week period prior to the baseline blood draw and for an eight-week period following the follow-up blood draw.

Approximately 20 participants will be in this study.

RISKS

Venipuncture: The risks of venipuncture for blood drawing include pain, bleeding, bruising, infection and inflammation at the site. The total amount of blood withdrawn will not exceed 550 ml over an eight week period. Hemoglobin measurements at the screen visit must be greater than 11.5 g in females in order to participate. All subjects will refrain from giving blood or being on other research studies for eight weeks prior to the study, during the study, and for 8 weeks after completion of the study.

Intravenous access: The risks of intravenous access are as above for venipuncture. There is also the potential risk for blood borne infection through the catheter site.

Bone marrow aspirates and biopsies: These are routine procedures associated with minimal or no complications. Possible side effects include pain, bleeding, bruising and infection at the site where the bone marrow is removed. Pain is minimized by the use of local anesthesia, and moderate sedation is offered to you. Bleeding at the site may occur at the time of procedure; to minimize this, pressure is applied to the area until bleeding stops. This can be a painful procedure, and the discomfort may last for several days.

Medications used: Estradiol dermal patch is used at a dose that approximates normal circulating estradiol levels in premenopausal women and will be administered for only 3 weeks. The patches may cause a topical allergic type reaction. This may cause vaginal bleeding in women with intact uteri. However, it has been our experience in a number of other studies that for postmenopausal women who have been amenorrheic for >1 yr that bleeding is uncommon when E administration is given for only 3 weeks. Other E related symptoms such as mastodynia, premenstrual syndrome symptoms, and pedal edema are very unlikely with such a short period of treatment. The Women's Health Initiative, a large prospective trial of an average of 5.2 years with Prempro reported the following adverse effects (difference from controls): heart attacks, 7 per year per 10,000 patients studied; stroke, 8 per year per 10,000 patients studied; venous thromboembolism, 8 per year per 10,000 patients studied; breast cancer, 8 per year per 10,000 patients studied. About 25% of American postmenopausal women are still taking E therapy chronically, and we do not believe that this short exposure will prove to produce problems. Nonetheless, the study nurse will remain in regular contact with the you and any adverse effects will be investigated. Vitamin D has little risk. Side effects that may occur are abdominal cramping, headache weight gain, nausea, vomiting, constipation.

Moderation sedation: Possible complications include drowsiness, a fall in blood pressure, or a slowing of the breathing rate. Minor complications may also include fainting, nausea, or vomiting.

Radiation: The amount of radiation you will receive has a low risk of harmful effects.

BENEFITS
Through participation in our study, you may gain more insight to your condition and tracking changes in bone formation. The discipline may also gain insight in terms of how different treatments for women post-menopause impact medical conditions. The results of this study may also help researchers develop new approaches to prevent and treat this disorder.

PAYMENT TO PARTICIPANTS
You will not be directly compensated for your participation.

PARTICIPANT CONFIDENTIALITY (HOW WILL PRIVACY BE PROTECTED)
Your name will not be associated in any publication or presentation with the information collected about you or with the research findings from this study. Instead, the researcher(s) will use a study number or a pseudonym rather than your name. Your identifiable information will not be shared unless (a) it is required by law or university policy, or (b) you give written permission.

Permission granted on this date to use and disclose your information remains in effect indefinitely. By signing this form you give permission for the use and disclosure of your information for purposes of this study at any time in the future.

OTHER IMPORTANT ITEMS YOU SHOULD KNOW

- **Withdrawal from the study:** You may choose to stop your participation in this study at any time. Your decision to stop your participation will have no effect on the quality of your treatment.

INSTITUTIONAL DISCLAIMER STATEMENT
In the event of injury, the Kansas Tort Claims Act provides for compensation if it can be demonstrated that the injury was caused by the negligent or wrongful act or omission of a state employee acting within the scope of his/her employment.

REFUSAL TO SIGN CONSENT AND AUTHORIZATION
You are not required to sign this Consent and Authorization form and you may refuse to do so without affecting your right to any services you are receiving or may receive from Fort Hays State University or to participate in any programs or events of Fort Hays State University. However, if you refuse to sign, you cannot participate in this study.

CANCELLING THIS CONSENT AND AUTHORIZATION
You may withdraw your consent to participate in this study at any time. You also have the right to cancel your permission to use and disclose further information collected about you, in writing, at any time, by sending your written request to: Jon Snow, Department of Nursing, 600 Park St., Fort Hays State University, Hays, KS 67601.

If you cancel permission to use your information, the researchers will stop collecting additional information about you. However, the research team may use and disclose information that was gathered before they received your cancellation, as described above.

QUESTIONS ABOUT PARTICIPATION
Questions about procedures should be directed to the researcher(s) listed at the end of this consent form.

PARTICIPANT CERTIFICATION:
I have read this Consent and Authorization form. I have had the opportunity to ask, and I have received answers to, any questions I had regarding the study. I understand that if I have any additional questions about my rights as a research participant, I may call (785) 628-4349, write the Office of Scholarship and Sponsored Projects (OSSP), Fort Hays State University, 600 Park St., Hays, Kansas 67601, or email irb@fhsu.edu.

I agree to take part in this study as a research participant. By my signature I affirm that I am at least 18 years old and that I have received a copy of this Consent and Authorization form.

_____ _____
Type/Print Participant's Name Date

_____
Participant's Signature

RESEARCHER CONTACT INFORMATION:

Jon Snow
Principal Investigator
Department of Nursing
600 Park St.
Fort Hays State University
Hays, KS 67601
(785) 628-5555

Robb Stark
Principal Investigator
Department of Nursing
600 Park St.
Fort Hays State University
Hays, KS 67601
(785) 628-5555

Eddard Stark, Ph.D.
Faculty Supervisor
Department of Nursing
600 Park St.
Fort Hays State University
Hays, KS 67601
(785) 628-5555

Recruitment Message: Effects of Acute Estrogen Therapy on Bone Formation

Hello,

We are Jon Snow and Robb Stark. We are graduate students in the Nursing Department at Fort Hays University. We would like to invite you to participate in a new treatment for bone growth for women with postmenopausal osteoporosis.

If you choose to participate, you will be asked to refrain from participating in any other research projects for eight weeks prior to the start of our study. You will be asked to have blood drawn for a baseline and then be asked to wear an acute dose Estradiol dermal patch for three weeks before a follow-up blood draw.

Participating in this study might help you gain new knowledge about your condition and a treatment that may be beneficial for you. If you would like to participate you will be asked to fill out a consent form related to the study. You will have an opportunity to ask questions about the study before you begin as well as throughout the study process. If you agree to participate, you will be asked to undergo a screening mammogram. The study may take ~30 minutes at the baseline and follow-up blood draws with three weeks of treatment between the blood draws.

Please do not hesitate to contact us and/or our faculty supervisor (Dr. Stark) with questions about this study. Thank you!

Jon Snow
jesnow3@mail.fhsu.edu

Robb Stark
restark3@mail.fhsu.edu

Dr. Eddard Stark
enstark@fhsu.edu
(Faculty Supervisor)

Debriefing Form: **"Effects of Acute Estrogen Therapy on Bone Formation"**

You have just completed a study titled the "Effects of Acute Estrogen Therapy on Bone Formation." The purpose of this study was to examine a new method for testing bone formation in women using an Estradiol dermal patch. You were asked to refrain from participating in other research projects for eight weeks prior to the start of our study, when we did a baseline blood draw. For three weeks you wore the E patch as a form of treatment before coming back for a second blood draw to see how bone formation was impacted through the treatment along with regular blood work comparisons from the beginning to the conclusion of the study. The information provided will help researchers to better understand how this new method for your condition may be treated compared to previous treatment plans used. This information could also aid in further development of treatments.

The research team greatly appreciates your help with this project! If you feel distressed after your participation in this project, you can contact local counseling services (please let us know if you would like recommendations/referrals for counseling services), or the Office of Scholarship and Sponsored Projects at 785-625-4349 if you have questions about the process of this research project. For more information about the research project, you can contact the principal researchers, Jon Snow and Robb Stark. You may also contact the faculty sponsor, Dr. Stark.

Sincerely,

Jon Snow
jesnow3@mail.fhsu.edu

Robb Stark
restark3@mail.fhsu.edu

Dr. Eddard Stark
enstark@fhsu.edu
(Faculty Supervisor)