INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH

Effects of Dietary Phosphorus Restriction on Whole-Body Calcium and Phosphorus Balance and Kinetics in Patients with Moderate Chronic Kidney Disease

ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions that might help change or improve the way we do things in the future.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

TAKING PART IN THIS STUDY IS VOLUNTARY

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with Indiana University Health, Indiana University, or Purdue University.

Research studies only include people who want to take part in the study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

Study Summary

Summary: The following document is a consent form regarding research for which you may be eligible. Your participation in this study in completely voluntary. You do not have to consent to this study.

Purpose: The purpose of this study is to determine how a low phosphorus diet affects the calcium and phosphorus in the body in patients with moderate chronic kidney disease (CKD). Phosphorus is a mineral that your body uses for cell function and to build bones.

Duration: There is a two-week period leading up to the study where you will take a vitamin D supplement. You will follow a special diet at home for 7 days and then go to the research center to stay overnight for 7 days/7 nights. After completing the 7-day overnight stay, you will then return home to your normal diet and come for a final blood draw visit one week later. You will then have a 1-3 week break from the study at home on your normal diet, continue to take the vitamin D supplement, and then repeat the same process (special diet at home for 7 days, followed by a 7-day overnight stay and 1 week follow up blood draw).

Procedures: We will ask you to follow a special diet. You will be asked to come to the research center for testing. We will collect blood, urine and stool samples. You will be asked to spend the night for 7 nights, on two different dates.

Please review the rest of this document for more details about this study and the things you should know before making a decision about whether to participate in this study.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to determine how low phosphorus in the diet affects calcium, phosphorus, and magnesium in the body in patients with moderate chronic kidney disease (CKD). Phosphorus, calcium, and magnesium are essential nutrients with many important functions in the body including bone health and energy metabolism. However, some people, like those who have kidney problems, may need to limit how much phosphorus they consume from the foods they eat because the kidneys may not be able to control how much is kept in the body versus put out in the urine. Calcium and magnesium are important minerals that interact with phosphorus in the body. It is important for us to know how low phosphorus diets that are prescribed to patients with CKD affect calcium, phosphorus, and magnesium handling in the body.

You were selected as a possible subject because you are an adult with moderate chronic kidney disease.

The study is being conducted by Dr. Kathleen Hill Gallant in the Department of Nutrition Science at Purdue University, in collaboration with Dr. Sharon Moe in the Department of Medicine at Indiana University School of Medicine. It is funded by Departmental funds of the Purdue University Department of Nutrition Science and funding from the National Institutes of Health.

HOW MANY PEOPLE WILL TAKE PART?
If you agree to participate, you will be one of up to 6 subjects taking part in this research.

WHAT WILL HAPPEN DURING THE STUDY?
If you agree to be in the study, you will do the following things:

- Participate in a screening visit: This visit will take approximately 60 minutes to make sure you can participate. This visit will be conducted at the IU Clinical Research Center at University Hospital in Indianapolis or at your clinic visit if time allows. You may need to have blood (about ½ tablespoon) and urine collected for screening if you have not recently had the needed labs checked. If you do need blood and urine collected for screening, you will be asked to not eat anything (fast) from midnight the morning of your visit. You will be able to drink water during the time you are fasting. You will also be asked about your medical history and current diet. You will also learn how to keep a record of the food you eat, and how to collect a stool sample at home prior to your first study visit.

- If you qualify for the study based on your screening visit, and choose to enroll in the study, you will be assigned by chance (like a coin toss) to determine the order in which you will complete two study diets given in two different time frames called SESSIONS. Diet 1: low calcium, high phosphorus diet or Diet 2: low calcium, low phosphorus. You and/or your doctor cannot choose the order of the diets. All subjects who complete their assigned diet group will then return to their normal diet for 1-3 weeks before starting the next diet group. Thus you will be in your assigned diet group for up to 14 (7 in the hospital) days, return to normal diet for 1 week at home, return for a final blood draw 1 week later, and then have 1-3 week break from the

study. Then you will go on the other diet group for the another 14 days. Each of the 14 day periods are described in detail in the next section.

SESSION 1:

- Two weeks prior to starting study diet: you will be asked to take Vitamin D for 14 days and keep a 4-day food record so we can determine how much phosphorus, calcium, and magnesium you usually eat. You will also be asked to collect one home stool collection to bring with you to your first inpatient study visit.

- During the study (Days 1-7 of the first 10 day period): you will be given all of your meals, snacks, and beverages to eat and drink at home/work for 7 days. You will be asked to pick up your meals as carry outs at the IU Health University Hospital in Indianapolis. You will do this twice and be given food for 3 days at a time, or if this does not work for your schedule, you can ask to make a more convenient pick-up(s) arrangement(s) with the study staff. The day of the first meals pick-up you will also have an additional fasting blood draw and urine collection and will bring in your stool collection and diet record from home; this visit will take about 30-60 minutes. You will need to fast (not eat anything) from midnight the night before. The second meal pick-up day will not involve any other study measurements. You will be expected to consume all the food, and only the food, you are given during the 7-day research study. The diets will be designed to meet your energy needs, and food preferences will be honored when possible. You will need to be able to consume milk and dairy for this study as well as other animal foods.
- 2-day Phosphorus, Calcium, and Magnesium Absorption Test (Days 8-9 of the 14 day period): After 7 days of eating the study diet at home, you are asked to participate in a two-day phosphorus and calcium absorption test at the clinical research center at IU Health University hospital. For the first day, you will be asked not to eat anything (fast) from about midnight, but you can drink plain water. You will then be admitted to the clinical research center at University Hospital by 8:15AM. You will have your height, weight, blood pressure, heart rate and breathing rate measured. Fasting blood and urine will be collected. If you are a person of child-bearing potential, you will have your urine tested to confirm you are not pregnant. You will have an IV placed by a trained member of the clinical research team. You will be given a special type of phosphorus, calcium, and magnesium to drink in the form of milk with your breakfast. This liquid contains a small amount of radioactivity. Over the next six hours, you will have your blood drawn several times using your IV, and you will also be asked to collect all urine and stool. You will continue to be provided your meals, snacks, and beverages. You will be monitored by medical and research staff during the entire testing time. You may watch TV, use a computer, read, or do other similar leisure activities while the test is being conducted but cannot leave the center. You will fast again at approximately midnight the morning of day two in the clinical research center. The second day is similar to the first day, but instead of a special phosphorus and calcium drink, you will have the special form of phosphorus, calcium, and magnesium in salt water ("saline") given by IV injection. This is to see how fast your body gets rid of phosphorus, calcium, and magnesium in your blood. You will again have your blood drawn over 6 hours by IV and you will continue to collect all your urine and stool. You will continue to eat the study food and collect all your urine and stool through the following morning (day 10). The morning of day 10, you will have your weight, blood pressure, heart rate, and

breathing rate measured, a final blood draw, IV removed.

- 12-day study that determines complete calcium, phosphorus, and magnesium handling in the body (Days 10-15 inpatient, and Day 21 outpatient visit): after you have completed your two-day phosphorus, calcium, and magnesium absorption testing, **and if you follow the diet and study procedures up until this point**, you will remain at the clinical research center for an additional 7 days. You will continue to eat the study food, take the vitamin D, the capsules of the non-absorbable stool marker and collect all your urine and stool through the entire length of your stay. Blood samples will be drawn each morning. On Day 15, you will have a fasting blood drawn and urine collected and then sent home. At home, you will follow your usual diet until Day 21, when you will return for a final blood draw.

SESSION 2:

- You will be asked to return to your normal diet for 1-3 weeks prior to starting the next diet group. During this time, you will be asked to continue taking the vitamin D supplement. After the 1-3 weeks, you will return to the Research Center to obtain your study diet and testing as Days 1-21 above for Session 2. This will end your participation in this research study.

- If you have diabetes, you will be asked to monitor your blood sugar by fingerstick at home during the study and report any blood sugars lower than 100 mg/dL to the study staff.
- The total amount of blood collected during each session is about 17 tablespoons. For comparison, when someone donates blood, they give approximately 17-20 tablespoons

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

While participating in the study, the risks, side effects, and/or discomforts include:

- Risk of blood draw and IV: The risk involved with blood draw and IV placement in this study may include pain, discomfort, fainting, bruising, and infection. Precautions will be taken to minimize these risks by using sterile technique and applying pressure to the site after the needle or IV is withdrawn. IVs will only be placed, and blood will only be drawn by skilled blood-drawing personnel or research nursing staff.

- Risk of study diet: You will be eating a fixed diet at home and in the hospital. We will give you study food to meet your needs, but you may feel hunger or fullness on the study diet compared to what you normally eat.

  The amount of phosphorus, calcium, and magnesium in the study diet is similar to the amount that a typical American eats each day. On the low phosphorus diet, the amount of phosphorus is the level recommended by the clinical guidelines for patients with kidney disease. The amount of phosphorus, calcium, and magnesium in the absorption test drink is small and not expected to cause any discomfort. All meals, snacks, and the radioactive phosphorus and special calcium and magnesium drink will be made up by trained study staff who will follow safe food handling methods.

If you have diabetes, there is increased risk for hypoglycemia while on the study diet because it may be different than your usual diet you eat. Symptoms of hypoglycemia include shakiness, sweating, tiredness, dizziness, hunger, irregular heartbeat, anxiety, irritability, tingling feeling around the mouth. Severe symptoms of hypoglycemia include confusion, blurry vision, seizures, or loss of consciousness. If you have diabetes, then we will ask you to write down everything you eat prior to the start of the study. We will then use that information to adjust your diabetic medications. If you use a sliding scale insulin at home to adjust with each meal, we will ask you to bring in your glucose monitor and self-manage while in the hospital. You will be asked to notify the study physician if you experience a hypoglycemic episode (any blood sugar lower than 100 mg/dL or if you have symptoms of hypoglycemia) while at home during the study while you are monitoring your blood sugar by fingerstick.

If you experience low blood sugar at home, you should treat it by having 15 grams of carbohydrate, waiting 15 minutes, then check your blood sugar again. If your blood sugar is still low (below 70 mg/dL), repeat these steps. Some good choices of 15 grams of carbohydrate include: a glucose tablet or gel,, ½ cup of juice or regular soda pop (not diet), 1 tablespoon of sugar, honey, or corn syrup, 15 small jelly beans or skittles, 3 pieces of hard candy such as round peppermints or jolly ranchers. **In the case of severe hypoglycemic symptoms, or when in doubt, call 911.**

- Risk of Radiation Exposure: The special form of phosphorus that you get in this study is radioactive and will expose you to low amounts of radiation (the special forms of calcium and magnesium are not radioactive). Every day, people are exposed to low levels of radiation that come from the natural environment and man-made radiation sources around them. This type of radiation is called "background radiation." The amount of radiation you will get from the phosphorus drink in this study is approximately, or less than, 1 years' worth of background radiation. The probability of harm from participating in this study is low compared to other everyday risks. Certain diseases or conditions may affect your sensitivity to radiation. For more detailed information on the risks of radiation or if you wish to have a more detailed dose estimate, please ask your study doctor.

  If you have had radiation (like x-rays, CT or radiation therapy) in the past year before this study, or you participated in a different study where you were exposed to radiation, please tell us now. We want to make certain that the probability of harm from the amount of radiation you will be exposed to in this study continues to be low when combined with the radiation you have received within the past year.

  If you are pregnant, you cannot take part in this research study. If you are able to have a baby, are not pregnant and wish to take part in this study, you will need to take a pregnancy test prior to enrollment. If you get pregnant while taking part in this study, or think you are pregnant, please tell Dr. Hill Gallant, Dr. Moe, or other study staff right away. You may not be able to continue this study if you become pregnant.

- Risk of loss of confidentiality: Every research study carries the risk for loss of confidentiality. However, precautions will be taken to avoid this possibility.

- There also may be other side effects that we cannot predict.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?
We do not expect you to receive any benefit from taking part in this study, but we hope to learn things which will help patients with kidney disease in the future.

WILL I RECEIVE MY RESULTS?
We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, this information will be provided to you. You may need to meet with professionals with expertise to help you learn more about your research results. The study team/study will not cover the costs of any follow-up consultations or actions.

HOW WILL MY INFORMATION BE PROTECTED?
Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, the Indiana University Institutional Review Board or its designees, the Indiana Clinical Research Center (ICRC) and any state or federal agencies who may need to access your medical and/or research records (as allowed by law). State and federal agencies may include the Office for Human Research Protections (OHRP), and/or National Institutes of Health (NIH).

The University of Minnesota and representatives of the University of Minnesota and its affiliates, including those that have responsibilities for monitoring or ensuring compliance, such as the Quality Assurance Program of the Human Research Protection Program (HRPP).

A description of this clinical trial will be available on **ClinicalTrials.gov**, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

For the protection of your privacy, this research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers may not disclose or use any information, documents, or specimens that could identify you in any civil, criminal, administrative, legislative, or other legal proceeding, unless you consent to it. Information, documents, or specimens protected by this Certificate may be disclosed to someone who is not connected with the research:

(1) if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases);
(2) if you consent to the disclosure, including for your medical treatment;
(3) if it is used for other scientific research in a way that is allowed by the federal regulations that protect research subjects;
(4) for the purpose of auditing or program evaluation by the government or funding agency.

A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself. If you want your research information released to an insurer, medical care provider, or any

other person not connected with the research, you must provide consent to allow the researchers to release it.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?
Information or specimens collected from you for this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

WHAT WILL YOU DO WITH MY GENETIC INFORMATION?
We will not use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA.

WILL I BE PAID FOR PARTICIPATION?
You will receive payment for participating in this study according to the following schedule:

Screening Visit: $25

Session 1:
Day 1 Visit: $25
First day in the hospital clinical research center; 1st Absorption test day (Day 8): $50
Second day in the hospital clinical research center; 2nd Absorption test day (Day 9): $200
Inpatient stay (Day 14): $300
Outpatient visit (Day 21): $500

Session 2:
Day 1 Visit: $25
First day in the hospital clinical research center; 1st Absorption test day (Day 8): $75
Second day in the hospital clinical research center; 2nd Absorption test day (Day 9): $300
Inpatient stay (Day 14): $400
Outpatient visit (Day 21): $600

Total for study completion (with two 7-day inpatient stays and 1-week follow-ups): $2500

You will also receive parking passes.

A check for each completed visit and/or test days will be sent to the address given by you when you either complete the study or withdraw from the study. Your name, social security number and address will be provided to the business office at Purdue University for the purpose of facilitating payment for participating in this study.

If you receive $600 or more in one calendar year from Purdue University, you will be required to provide your Social Security number or tax identification number to Purdue University. You will receive a 1099 tax form the following January and will need to report this payment as income on your federal and state tax returns. You are responsible for paying any state, federal, or Social Security taxes. If you

have questions regarding how this affects your tax return, please contact a tax professional to assist you. If you do not have a social security number or tax identification number, the Internal Revenue Service (IRS) requires Purdue University to deduct 30% from your compensation to pay required taxes on your behalf.

WILL IT COST ME ANYTHING TO PARTICIPATE?
You will not be responsible for study-specific costs: these include study meals, study visits, study related laboratory tests, and parking for study visits.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?
In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury during the study, you should contact the researcher, Kathleen Hill Gallant, PhD, at 765-494-0101. If you cannot reach the researcher during regular business hours (i.e., 8 a.m. to 5 p.m.), please call the IU Human Subjects Office at 317-278-3458 or 800-696-2949.

In the event of an emergency, call 911 or go to the emergency department and tell the study doctor as soon as possible. If you get emergency care or are hospitalized, please tell the doctor treating you that you are in a research study being conducted by Dr. Sharon Moe. After hours you may call IU Health University Hospital at 317-944-5000 and ask for the Nephrologist on call.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

To share feedback privately with the University of Minnesota Human Research Protection Program (HRPP) about your research experience, call the Research Participants' Advocate Line at 612-625-1650 (Toll Free: 1-888-224-8636) or go to z.umn.edu/participants. You are encouraged to contact the HRPP if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

The University of Minnesota HRPP may ask you to complete a survey that asks about your experience as a research participant. You do not have to complete the survey if you do not want to. If you do choose to complete the survey, your responses will be anonymous. If you are not asked to complete a

survey, but you would like to share feedback, please contact the study team or the University of Minnesota HRPP.

CAN I WITHDRAW FROM THE STUDY?

If you decide to participate in this study, you can change your mind and decide to leave the study at any time in the future. The study team will help you withdraw from the study safely. If you decide to withdraw, notify the study team.

Your participation may be terminated by the investigator without regard to your consent in the following circumstances: if you are unable or unwilling to follow the study procedures.

You will be told about new information that may affect your health, welfare, or willingness to stay in the study.

PARTICIPANT'S CONSENT

In consideration of all of the above, I give my consent to participate in this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____ **Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____ **Date**:_____