IRB APPROVAL
Approval Date: 01/28/2014
Expiration date: 07/29/2014

	Human Research Protection Program Institutional Review Board **Authorization to Participate in a Research Project and Permission to use or Release Protected Health Information (PHI)**	

STUDY TITLE: Vitamin D and type 2 diabetes study (**D2d** study).

CONSENT VERSION DATE: January 13, 2014

HOSPITAL OR INSTITUTION: Maine Medical Center Research Institute

INVESTIGATOR: Irwin Brodsky, MD, MPH (Principal Investigator), Clifford Rosen, MD, John Devlin MD (Co-Investigators)

SUBJECT'S NAME (printed):_____

You are being asked to volunteer for a research study. Research studies include only people who choose to take part. In order to decide whether you should agree to be part of this research study, you should understand enough about its risks and benefits to make an informed judgment. This process is known as informed consent. Please take your time to make your decision.

You are being asked to take part in this research study to evaluate the effect of taking vitamin D on the prevention of diabetes in persons at high risk for diabetes.

WHY IS THIS STUDY BEING DONE?
This research is being done because diabetes is a serious condition affecting about 1 in 10 people in the United States. Lifestyle changes, such as healthy eating, exercise and weight loss, can decrease the chances of developing diabetes. However, many people still develop diabetes despite trying to change their lifestyle. The goal of this study is to see whether taking vitamin D can lower the risk of getting diabetes in people with a high risk for diabetes. As a food ingredient or dietary supplement, vitamin D is generally recognized as safe. However, we do not know if vitamin D is effective in preventing diabetes. Taking vitamin D to prevent diabetes is considered experimental.

HOW MANY PEOPLE WILL TAKE PART IN THE RESEARCH STUDY?
The study takes place at many cities in the United States. There will be a total of 2,382 participants in the D2d study nationwide. Maine Medical Center is one of those sites. There will be approximately 125 participants enrolled in this study at Maine Medical Center.

WHAT IS INVOLVED IN THE STUDY?

You will participate in this study for approximately 4 years to see whether taking vitamin D alters the risk of developing diabetes during the approximately 4 years of the study. Your visits and testing will be done at the clinical offices of the Maine Medical Partners Endocrinology and Diabetes Center, located at 175 US Route 1, Scarborough, ME 04074.

You will be "randomized" into one of the 2 study groups, either vitamin D or placebo, described below. Randomization means that you are put into a group by chance. It is like flipping a coin. Which group you are put in is done by computer. Neither you nor the researcher will choose what group you will be in. You will have an equal 1 in 2 chance of being placed in either group.

The groups are: Vitamin D 4000 IU (International Units) per day or no vitamin D supplement. During the study, you will be instructed to take 1 pill every day by mouth in the morning with breakfast. The study pill contains either vitamin D 4000 IU or a placebo with no vitamin D (that does not have a medical effect). Both types of pills have other ingredients (soybean oil, gelatin, glycerin and water). The two different types of pills will look exactly the same and you will not know whether the pill you are taking has vitamin D or not. The research staff will also not know which pill you are taking. You will be assigned to take the vitamin D or placebo pill by chance (like tossing a coin). There is a 50 percent chance you will receive vitamin D pills. Before starting the study, you will be asked what dietary supplements (minerals and vitamins, including vitamin D and calcium) you are taking. During this study, you will be asked not to take more than a certain amount of vitamin D and calcium on your own and you will be provided with recommendations for sensible sun exposure. During the study, you will also be asked not to start any new supplements (vitamins and minerals), especially vitamin D or calcium, without first discussing it with the investigator, study doctor, or the study's research coordinator because taking additional vitamin D or calcium may lead to side effects.

Participation in the study will require up to 13 scheduled visits to Maine Medical Partners Endocrinology and Diabetes Center, as shown below. Additional visits, possibly requiring blood tests, may be needed as determined by the research team. Between visits, you will receive phone calls, emails or texts to see how you are doing, to remind you of your next visit and to share important news about the study.

Your cooperation with all study procedures is essential for your safety and the success of the study.

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Study Visit	Visit 1 Screening	Visit 2 Baseline	Visit 3 Randomize	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12	End of Study
Schedule	1-4 weeks before visit 2	1-3 weeks before visit 3	Day 0	Month 3	Month 6	Month 12	Month 18	Month 24	Month 30	Month 36	Month 42	Month 48	Varies
Duration	1- 1.5 hours	3 hours	15-30 min.	30 min.	1 hour	3 hours	1 hour	3 hours	1 hour	3 hours	1 hour	3 hours	1 hour
Stipend	$25	$50	$25	$25	$25	$50	$25	$50	$25	$50	$25	$50	$25

Visit 1 – Screening: To prepare for the visit you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visit. Please take any medications you normally take in the morning. During this visit, we will find out if you meet the study requirements and are eligible to participate. During the visit:

1. You will first review these Informed Consent Forms and discuss them with research staff. If you decide that you want to participate, you will be asked to sign the forms.
2. You will be asked questions about your health, medications, dietary supplements or other pills you may be taking.
3. You will have your weight, height, blood pressure and heart rate measured.
4. If your medical history, weight, blood pressure are within the study requirements, then you will have:
    a. Blood collection (about 2 tablespoons of blood), while fasting, for the following tests: complete blood cell count, liver tests, calcium, creatinine (kidney test), glucose (sugar), hemoglobin A1c (a test for diabetes) and pregnancy test (for women of reproductive potential)
5. A snack will be provided.

Within a few days after the visit, the investigator will review the results of your laboratory tests. If the results are within the study requirements, you will be asked to return within four weeks for the baseline visit, as described below.

Visit 2 – Baseline: To prepare for the visit you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visit. Please take any medications you normally take in the morning. During the visit:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking.
2. You will have your weight, height, waist, blood pressure and heart rate measured.
3. You will have a physical examination. The examination may be postponed to the next visit.
4. You will complete questionnaires about your diet and physical activity.
5. You will be provided with information on a healthy lifestyle (eating and exercise) to lower your risk of getting diabetes.
6. You will have:
   a. Urine sample collected to measure calcium and creatinine (kidney test).
   b. Blood collection (about 2 tablespoons of blood), while fasting, for the following tests: glucose (sugar), hemoglobin A1c (a test for diabetes), 25-hydroxyvitamin D (a test for vitamin D level), and insulin (test for pancreas function).
   c. After fasting blood collection is done, you will have an oral glucose tolerance test (OGTT), which measures how your body uses glucose. You will drink a 10 oz. glucose (very sweet sugar) drink and blood will be collected at 30 minutes (about 1 tablespoon of blood) and two hours (about 1 tablespoon of blood) after the glucose drink, to test for glucose and insulin.
7. A snack will be provided.
8. You have the option to complete a pre-test questionnaire related to National Diabetes Education Programs as part of an ancillary study to test the effectiveness of the GAME Plan tool kit. I will be given the tool kit and do a follow-up questionnaire at month 3, after reading the materials.

I agree to participate in the ancillary study. Circle yes or no.

YES NO Participant's Initials _____

Note: The investigator may combine visits 1 (Screening) and 2 (Baseline) into one visit. If this is planned the research staff will explain the order of procedures.

Within a few days after the visit, the investigator will review the results of your laboratory tests. If the results are within the study requirements, you will be asked to continue in the study and return within three weeks for the next visit, as described below.

Visit 3 – Randomization: This visit can occur at any time of the day. There is no special preparation for this visit. During this visit:

1. You will get a 6-month supply of the study pills and receive verbal and written instructions on how to take them (one pill daily in the morning with breakfast).
2. With your permission, a letter will be sent to your physicians (e.g. primary care physician, endocrinologist) informing him/her of your participation in the study.

Visit 4 (month 3): To prepare for the visit you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visit. Please take any medications you normally take in the morning, including the study pill. During the visit:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will have:
   a. Urine sample collected to measure calcium and creatinine.
   Blood collection (about 1 tablespoon of blood), while fasting, for the following tests: calcium, creatinine.
4. A snack will be provided.
5. If you agreed to participate in the ancillary study, you will complete the post-test questionnaire.

Visit 5 (month 6), visit 7 (month 18) and visit 9 (month 30), visit 11 (month 42): To prepare for these visits, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During these visits:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will complete a questionnaire about your physical activity.
4. You will have:

a. Blood collection (about 1/2 tablespoon of blood), while fasting, for the following tests: glucose and hemoglobin A1c.
5. A snack will be provided.
6. You will return your bottle with the study pills, whether or not there are any pills left.
7. You will get a new 6-month supply of the study pills and receive verbal and written instructions on how to take them (one pill daily in the morning with breakfast).

Visit 6 (month 12), visit 8 (month 24) and visit 10 (month 36), visit 12 (month 48): To prepare for these visits, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During these visits:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will complete a questionnaire about your physical activity.
4. You will complete a questionnaire about your diet (at the month 12 and 36 visits only).
5. You will have:
   a. Urine sample collected to measure calcium and creatinine.
   b. Blood collection, (about 2 tablespoon of blood), while fasting, for the following tests: calcium, creatinine, glucose, hemoglobin A1c, 25-hydroxyvitamin D, and insulin.
   c. After fasting blood collection is done, you will have an oral glucose tolerance test (OGTT), which measures how your body uses glucose. You will drink a 10 oz. glucose drink and blood will be collected at 30 minutes (about 1 tablespoon of blood) and two hours after the glucose drink (about 1 tablespoon of blood), to test for glucose and insulin.
6. A snack will be provided.
8. You will return your bottle with the study pills, whether or not there are any pills left.
9. At the month 12, month 24 and month 36 visit, you will get a 6-month supply of the study pills and receive verbal and written instructions on how to take them (one pill daily in the morning with breakfast).

Visit 13 (end of study): To prepare for this visit, you must not have anything to eat or drink (other than water) for 8 hours before arriving for your morning visit. You also must not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During the visit:

1. You will be asked if you have had any changes, since the last visit in your health or medications, dietary supplements or other pills you may be taking.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will have a physical examination
4. You will have:
   a. Urine sample collected to measure calcium and creatinine
   b. Blood collection (about 1 and ½ tablespoons of blood), while fasting, for the following tests: calcium, creatinine, glucose and hemoglobin A1c
5. A snack will be provided
6. You will return your bottle with the study pills, whether or not there are pills left

Additional Visits: You may need to come for additional visits to determine whether you meet the criteria for diabetes. To prepare for these visits, you must not have anything to eat or drink (other than water) for the 8 hours before arriving for your morning visit. You must also not participate in vigorous physical activity for 24 hours before the visits. Please take any medications you normally take in the morning, including the study pill. During these visits, which will last 30 minutes or 3 hours, depending on whether an OGTT is done:

1. You will be asked if you have had any changes, since the last visit, in your health or medications, dietary supplements or other pills you may be taking. You may have a physical examination, if needed.
2. You will have your weight, height, blood pressure and heart rate measured.
3. You will have:
   a. Blood collection, (about 4 tablespoon of blood), while fasting, for the following tests: glucose and/or Hemoglobin A1c.
   b. After fasting blood collection, you may have an oral glucose tolerance test (OGTT), which measures how your body uses glucose. You will drink a 10 oz. glucose drink and blood will collected at two hours after the glucose drink, to test for glucose. The research team will tell you, before the visit, if an OGTT needs to be done so you can plan your time.
4. A snack will be provided.

You will be asked to join the D2D support and education program. As part of this program, you will attend group meetings, held twice yearly at Maine Medical Partners Endocrinology and Diabetes Center to discuss specific topics related to the prevention of type 2 diabetes.

You may need to come for additional visits to evaluate health issues that may be related to the study, which would last about 30-60 minutes.

If the results of your blood tests meet the study criteria for diabetes, we will refer you to your health care provider for additional testing and treatment. You will remain in the D2d study, continue taking the study pills, and return for all scheduled visits. Your continued participation is important to the study. At the annual visits (at 12, 24, 36, and 48 months) you will have blood drawn fasting, but will not have the oral glucose tolerance test, or blood collection for insulin.

HOW LONG WILL I BE IN THE STUDY?
We think you will be in the study for approximately 4 years depending on when you begin participating. The researcher may decide to take you off this study if it is in your best interest.

With your permission, we will provide the results of your laboratory tests and medical examinations to your health care provider. We will also ask you to give your provider(s) permission to share medical information related to the diagnosis of diabetes with the D2d study doctor. Blood and urine samples that remain after all planned tests have been completed will be destroyed, unless you agree to have your samples stored in the research repository (storage of your blood specimens for special tests for which you must give separate consent).

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first.

WHAT ARE THE RISKS OF THE STUDY?
While taking the study pill, which may be vitamin D, there is a very small risk of developing kidney stones or a high level of calcium in your blood and urine. A high calcium level may give you symptoms of stomach pain, nausea, vomiting, headache, and fatigue. Persons who are at risk for high calcium levels or kidney stones will not be allowed to participate in the study. Blood and urine tests will be done during the study to monitor for high calcium level. We will permanently stop the study pills and refer you to your primary care provider if your blood calcium rises above a certain level or if you get a kidney stone. During the study, there is also a very small risk of developing a metallic taste in your mouth, nausea, vomiting, decreased appetite, anemia (low blood count), high level of phosphorus (a mineral) in your blood, fatigue, weakness, difficulty sleeping, frequent urination, headache or kidney damage. During the oral glucose tolerance test, there is a very small risk of nausea and vomiting or developing symptoms of low blood sugar level, which include rapid heartbeat, sweating and headache. If you stop taking the pills because of a medical condition, you will not re-start the pills. However, you will be asked to stay in the study and complete the scheduled visits and all procedures.

There may be slight discomfort during the blood draw and there is the possibility of a small bruise at that skin area of the blood draw. There is a small risk of skin infection at the area of the blood draw. There is also a very small possibility of vein inflammation. There is also a very small possibility of anemia from repeated blood collections.

There is potential loss of privacy. We will protect your information by labeling your research records with a code, and keeping the key to the code in a password protected database.

For women, if you are pregnant or nursing a baby or intend to become pregnant during the study, you should not participate in the study and you should notify the investigator(s). If you become pregnant or you miss a period during the study, you should notify the research team.
A pregnancy test will be performed if you report missing two periods in a row. Prior to the start of the study, women who can get pregnant will be instructed to use a birth control method of their choice.
For more information about risks and side effects, ask the researcher.

ARE THERE BENEFITS TO TAKING PART IN THE RESEARCH STUDY?
We do not know whether you will receive any benefit from participating in this study. However, during the study, you will have the opportunity to learn how healthy eating and exercise can lower your risk of getting diabetes. During the screening, we will provide you with the results of your medical examination and laboratory results. You will be advised to contact your personal physician if any unexpected medical condition or problem is identified. During the study, you will receive testing for diabetes. The information we learn from this study may help people in the future who are at high risk for getting diabetes.

WHAT OTHER OPTIONS ARE THERE?
The choice to take part in this study is yours. The alternative to participation in this study is not to participate. Please talk to your regular doctor about these and other options.

WHAT ABOUT CONFIDENTIALITY?
If you agree to take part in this research study, your personal information will not be given to anyone unless we get your permission in writing. Your personal information will only be given if the law requires it. Your personal information will also only be given for regular hospital treatment, payment, and hospital management activities. Study results will be published, but your identity will not be revealed in any articles or scientific presentations. We will make every effort to keep your information private, but it cannot be completely guaranteed. Certain government agencies (the Office for Human Research Protections, U.S. Food and Drug Administration), the National Institutes of Health, the *Maine Medical Center IRB*, MMP Endocrinology and Diabetes Center or representatives of the D2d study Coordinating Center may check records that identify you. This might include your medical or research records and the informed consent form you signed. The records of this study might also be reviewed to make sure all rules and regulations were followed.

A description of this study 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 for all participants. You can search this web site at any time.

WHAT ARE THE COSTS?
You or your insurance company will not be charged for any tests or services specifically required by this research study. You will still be responsible for the cost of your usual ongoing medical care,

including procedures, non-study medications, and tests that your study doctor or regular doctor requires during this study as part of your usual medical care.

PAYMENT
You will be given a stipend to reimburse you for your time and efforts while participating in this research study. Compensation will be provided in the form of a check, at a rate of $25 per completed study visit scheduled for 1 hour or less and $50 for each completed study visit scheduled for more than 1 hour (example: 3 hour annual visits), plus travel stipend to reimburse you for the cost of traveling to our study office for visits, at an amount determined by the standard federal rate for mileage.

WHAT IF I AM INJURED DUE TO MY PARTICIPATION IN THIS STUDY?
If you become sick or injured as the result of participation in this study, Dr. Brodsky, the principal investigator, will arrange or provide medical care. All needed facilities, emergency treatment, and professional services are available to you, just as they are to the general public. You or your medical insurance company will pay for any such medical care. There are no plans to pay for your treatment if you get hurt or sick as part of this study.

Maine Medical Center has no policy or plan to pay for any injuries that you might receive as a result of your participation in this study. However, this does not take away your rights to seek or collect compensation for injury related to malpractice, fault, or blame on the part of those involved in the research, including the hospital.

You or your insurance company will be responsible for any costs resulting from underlying disease or treatments provided to you outside of this research study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?
Taking part in this study is your choice. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled.

We will tell you about new information that may affect your willingness to stay in this study.

PERMISSION TO USE OR RELEASE IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH PURPOSES

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written permission. If you sign this form, it will provide that permission. This section of the consent document is intended to inform you about how your health information will be used or disclosed in this study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law.

WHY AM I BEING ASKED TO RELEASE THIS INFORMATION?
As part of this research study, you are being asked to allow Dr. Brodsky collect health information about you from your primary care provider regarding changes in your medical condition that might affect your participation in the study. This may include his/her determination that you have developed

diabetes or that you have been placed on medication for diabetes. It may include information about his/her determination that you have developed a new medical condition that makes participation in the study riskier.
This information will be collected, entered onto a database with the health information from others taking part in this research study. Dr. Brodsky may also need to obtain copies of any medical records you have with other health care providers to document the items listed above.

WHAT AM I BEING ASKED TO RELEASE?
For this research study, the following information will be collected:

- Information about your developing diabetes or being placed on medication for diabetes
- Information about new conditions or medications that make participation in the D2d study riskier than when you enrolled

WHO WILL SEE THIS INFORMATION?
Personnel or members of the Maine Medical Center Institutional Review Board, personnel from the Office of Human Research Protections or any regulatory agency may see parts of your medical records related to this research study and, therefore, will see your name and other personally identifiable information about you. The information collected is the property of investigator, and you will not be able to get it back. In the event of any publication regarding this study, your identity will not be disclosed.

A description of this research study will be available on http://www.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.

WILL THE INFORMATION COLLECTED AS PART OF THIS STUDY BE DESTROYED WHEN IT IS NO LONGER NEEDED?
The study records will be stored for a minimum of 7 years. If important research information can be obtained from the records after 7 years, they may be stored longer. There is no expiration date after which it will be discarded.

CAN I STOP MY INFORMATION FROM BEING USED?
If you leave the study, and do not wish to have any more of your personal data collected, you must notify Dr. Brodsky in writing. You may also call Dr. Brodsky at 207-662-2208 and your request to stop collecting information will be honored, but you must also notify Dr. Brodsky in writing. To notify Dr. Brodsky in writing, send your request to: Irwin Brodsky MD, MPH, Clinical Outcomes Research and Evaluation, 509 Forest Ave. , Portland, ME, 04101-1512. Any data that has already been collected will continue to be seen and used as described previously.

WHAT IF I DO NOT AUTHORIZE YOU TO COLLECT AND RELEASE MY HEALTH INFORMATION?
If you agree to be in this research study, you are authorizing the release of your health information as part of the trial. If you do not want to release your health information, you may not take part in this

research study (do not sign this form if you do not want to take part in this research study, or you do not want to release your health information).

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury contact

Dr. Irwin Brodsky at (207)662-2208 or after hours at (207)741-6056
For questions about your rights as a research participant, contact the Maine Medical Center Institutional Review Board (which is a group of people who review the research to protect your rights) at (207) 396-8183.

I have read, or have had read to me, the above information before signing this consent form. I agree to participate in this research study. I also authorize use or disclosure of my personal health information for the purpose of this research. I have been offered ample opportunity to ask questions and have received answers that fully satisfy those questions.

_____ _____
Signature of Patient or Authorized Representative Date/24 hour time

_____
Printed Name of Patient or Authorized Representative

_____ _____
Signature of the Person Obtaining Consent Date/24 hour time

_____
Printed Name of the Person Obtaining Consent

A signed copy of this consent form must be given to each subject entering the study.