D2d Protocol Appendix A
Vitamin D and Type 2 Diabetes (D2d) study
Informed Consent to Participate in Research

Collaborating Clinical Site Principal Investigator: *[insert name]*
Collaborating Clinical Site Co-Investigators: *[insert names]*
Collaborating Clinical Site Study Telephone Number: *[insert telephone number]*

INTRODUCTION

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

Taking part in this research study is entirely your choice. You may decide not to participate in this study or may decide to stop taking part in this research study at any time for any reason. If you decide not to participate in the study or stop being in this research study after you agree to participate, your decision will not affect your care or treatment outside this study, payment for your health care, or your health care benefits.

If you decide to take part in this research study, you will be asked to sign this form. You will be given a copy of the signed form. You should keep your copy for your records. The form has information, including important names and phone numbers, to which you may wish to refer in the future.

Please read all the information in this form carefully. Please ask the Principal Investigator, study doctor, or (*his/her*) representative, to explain any words, terms or sections that are unclear to you. You should also ask any other questions that you have about this research study. Do not sign this consent form unless you understand the information in it and have had your questions answered to your satisfaction.

New things might be learned during this study that you should know about. The investigators will tell you about any new information that may affect your willingness to continue in this study.

If you are eligible to participate and agree to be in the study, the investigator or study doctor may still choose to not allow your participation or to stop your participation in this study if *s/he* thinks it is in your best medical interest.

As a participant in the D2d study, your identity, medical records, and data relating to this research will be kept confidential, except as required by law. Representatives from the U.S. Food and Drug Administration, National Institutes of Health, (the study sponsor), D2d study Coordinating Center, and representatives from Tufts Medical Center may look at records that identify you.

If you have questions about your rights as a research study participant, please call the *(insert official name of site IRB)* Institutional Review Board (IRB) at *###-###-####.* The IRB is a group of researchers, doctors, nurses and non-medical people who review human research studies for safety and protection of people who take part in the studies. Federal law requires the IRB to review and

approve any research study involving humans. This must be done before the study can begin. The study is also reviewed frequently while it is in progress.

This research study has been reviewed and approved by the *(insert official name of site IRB*) IRB*.* Also, an external monitoring committee is watching the study for information on safety.

PURPOSE OF STUDY

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. 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. There will be *(insert expected # of local participants)* participants in this study *in/at (insert name of D2d collaborating clinical site institution).*

PROCEDURES TO BE FOLLOWED

Your participation in the study will last approximately 4 years, depending on when you begin participating. 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 international units) or no vitamin D (i.e. placebo pill that does not have a medical effect). ~~(i.e. placebo, which is a soft-gel pill containing lactose, cellulose and magnesium 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 (insert name of D2d collaborating clinical site institution),* 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.

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	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD	$TBD

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 this 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. A small tube inserted in a vein in your arm for blood draw. To avoid repeated sticks, the small tube will stay in your vein for the entire test and all blood samples will be drawn from the same tube.
   c. 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).
   d. 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 (about 1 tablespoon of blood) after the glucose drink, to test for glucose and insulin.
7. 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 continue in the study and return within three weeks for the next visit, as described below.

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.

Visit 3 – Randomization: This visit can occur at anytime 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.
   b. Blood collection (about 1 tablespoon of blood), while fasting, for the following tests: calcium, creatinine.

4. A snack will be provided.

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. A small tube inserted in a vein in your arm for blood draw. To avoid repeated sticks, the small tube will stay in your vein for the entire test and all blood samples will be drawn from the same tube
    c. Blood collection, (about 2 tablespoons of blood), while fasting, for the following tests: calcium, creatinine, glucose, hemoglobin A1c, 25-hydroxyvitamin D, and insulin.
    d. 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 (about 1 tablespoon of blood) after the glucose drink, 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 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 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 1/2 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 any 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 1/2 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 (about 1/3 tablespoon of blood), 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 *(insert site name or location of meetings)*, to discuss specific topics about prevention of diabetes.

You may need to come for additional visits to evaluate health issues that may be related to the study,

which should 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.

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.

RISKS

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.

BENEFITS

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.

ALTERNATIVES

The choice to take part in this study is yours. The alternative to participation in this study is not to participate.

WHOM TO CONTACT

If you have any problems or questions about the study, you may call the principal investigator *(and study physician)*:

(Insert Site Principal investigator's name)	Phone Number	*###-###-####*
	(Insert after hours #)	*###-###-#### (24 hours a day)*

If you have any problems or questions about the study, you may call one of the following members of the research team:

(Insert Site Research Coordinator name)	Phone Number	*###-###-####*
	(Insert after hours #)	*###-###-#### (24 hours a day)*

Other people you may call with questions are:

(Insert name(s) and phone number(s) of other members of the research team [e.g. co-investigator, study physician, research coordinator]).

RESEARCH RELATED INJURY

Emergency medical treatment will be given to you if you are hurt or get sick as a direct result of taking part in this research study. Any needed medical care is available at the usual cost. 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. The institution where this research is being conducted has not set aside any money to pay for a research-related injury or illness.

COSTS

There are no costs associated with participation in this study.

PAYMENT

You will be given a stipend to reimburse you for your time and efforts while participating in this research study. *(Describe the: amount /per visit, how frequently the participant will receive the stipend and how the participant will receive it {e.g. cash, check}). (Add information if participants will have transportation or parking covered separately)*

PRIVACY AND 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 *(insert official name of site IRB and name of D2d collaborating clinical site institution)*, 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.

DOCUMENTATION OF CONSENT

I have been given a copy of this form. I have read it or it has been read to me. I understand the information and have had my questions answered to my satisfaction. I agree to take part in this study, as noted below.

I understand that I will be informed of any new findings developed during the course of this research study that may affect my willingness to stay in this research study.

_____	_____
Date	Participant's Signature

I have fully explained to *[insert name of participant]* _____ the nature and purpose of the above-described study and the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____	_____
Date	Principal Investigator or Representative's Signature