Wake Forest™
School of Medicine

Section of Gerontology & Geriatric Medicine

Valued EpiGenetic Glycemic ImprovEments through Weight Loss (VEGGIE) Study
Informed Consent Form to Participate in Research
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# SUMMARY

You are invited to participate in a research study. The purpose of this research study is to see if changes in blood and fat cells during weight loss can help explain the benefits of weight loss. Your participation in this research will involve up to 7 assessment visits and last up to 9 months.

Participation in this study will involve assessments such as vital signs, blood draws, questionnaires, physical function tasks such as hand strength, balance and walking, an oral glucose tolerance test, and a fat sampling. Some participants will be asked to have a DXA or bone density scan. The diet intervention will involve attending weekly dietary group sessions and recording your daily food intake. All research studies involve some risks. The risks to this study that you should be aware of are those associated with the start of a diet program such as changes in bowel function (diarrhea and/or constipation). The risks with physical function testing include a risk of falling. The DXA scan has the risk of 2 millirem of radiation exposure. The oral glucose tolerance test's main risks include dizziness and weakness. The main risks of the fat sampling sampling procedure are bruising, excess bleeding, and infection. Please read the risks section for more information about risks. There is a possibility that you may directly benefit from the participation in this study. A possible benefit is that by losing weight you may reduce your risk for diabetes and heart disease. Because individuals respond differently to diet changes, no one can know in advance if it will be helpful in your particular case.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices include talking with your doctor about a diet and/or exercise program that would be a good fit for you. This can include the products available for this study. You will not lose any service, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Jingzhong Ding, PhD, MD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is: 336-713-8558.

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest School of Medicine at [redacted].

## INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are between the ages of 40-70 years, are not physically active on a regular basis, are not pregnant, and are interested in a healthy lifestyle change. Your participation is completely voluntary. Please take your time in making your decision as to whether or not you wish to participate. You should read, or have read to you, all of the information in this form and ask questions about anything you do not understand before deciding if you want to be in this study. Ask the study doctor or study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

## WHY IS THIS STUDY BEING DONE?

Weight loss improves glucose control (how your body processes sugar) and prevents diabetes. The purpose of this research study is to see if changes in blood and fat cells during weight loss can help explain the benefits of weight loss.

## HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

200 people will take part in this study here at Wake Forest Baptist Health. In order to identify the 200 subjects needed, we may need to screen as many as 800 because some people will not qualify to be included in the study.

## WHAT IS INVOLVED IN THE STUDY?

If you agree to participate in this study by signing this consent form, you will be asked to complete three or four screening visits to see if you qualify for the study. You will then complete a baseline visit before beginning the intervention. After the initial 18 weeks of the study you will complete 2 follow up visits. There are a total of up to 7 assessment visits over a 9 month period. The details about all study visits and procedures are provided below. We will make every effort to follow the visit procedures in the order they are outlined below; however, it may be necessary at times to make changes to accommodate different schedules.

<u>Prescreening Visit</u>

We will ask that you come to Wake Forest Baptist Medical Center for a non-fasting visit. You will learn all the details of the study in a group setting and you will be given time to ask any questions and get satisfactory answers. Then, you will be moved to a confidential room and be asked to sign this informed consent form. After signing the consent form, we will:

- Measure your blood pressure, pulse, height, weight, and BMI (and potentially measure your waist)

If you continue to qualify we will:

- Ask you questions about your physical activity level, memory, and mood
- Review and give you a 3 day food record for you to complete prior to your next visit

This entire visit will take up to 1½ hours to complete. If you qualify for the study, we will schedule you to come back in and complete Screening Visit 1. If you do not, your participation in the study will be over.

Screening Visit 1

We will ask that you come to Wake Forest Baptist Medical Center having fasted for at least 8 hours prior to your appointment time, with nothing to eat or drink except water. You will learn all the details of the study and you will be given time to ask any questions and get satisfactory answers. Then, you will be asked to sign this informed consent form *if you didn't do this at the Prescreening Visit.* After signing the consent form, we will:

- Measure your blood pressure, pulse, height, weight, and BMI (and potentially measure your waist) *if this wasn't done at the Prescreening Visit.*

If you continue to qualify we will:

- Draw blood (approximately 1 tablespoon) from a vein in your arm to collect measurement of lipids (cholesterol), blood counts and chemistries, blood sugar levels, liver and kidney functions for screening purposes
- Provide you with a light snack
- Ask you questions about your physical activity level, memory, and mood *if this wasn't done at the Prescreening Visit.*
- Ask you questions about your background, medical history, review of medications and dietary supplements
- Review and give you a 3 day food record for you to complete prior to your next visit *if this wasn't done at the Prescreening Visit.*
- You will be asked to provide a stool sample for microbiome testing. Microbiome is the collection of microorganisms (such as bacteria, fungi, and viruses) that live in or on the human body. You will be provided instructions and a kit for collection.

This entire visit will take up to 1½ hours to complete. Once we receive your lab work we will let you know if you continue to qualify. If you do, we will schedule you to come back in about a week to continue to Screening Visit 2. If you do not qualify with the blood work collected at SV1, we will send you copies of your lab results and your participation in the study will be over.

Screening Visit 2

We will ask you return to Wake Forest Baptist Medical Center for a non-fasting visit. At this visit we will:

- Measure your weight
- Collect your 3 day food record
- The study staff will go over details about one of the potential diet interventions; you will be given a 3-day trial supply of meal replacements to try for 3 days prior to your next visit. You will also be asked to track your food intake during these 3 days and complete a survey about the meal replacement products

This entire visit will take approximately ½ hour to complete.

Screening Visit 3

We will ask you return to Wake Forest Baptist Medical Center for a non-fasting visit. You will be meeting the Registered Dietician (RD) at this visit. At this visit we will:

- Measure your weight

- Collect your 3 day meal replacement food record, and the meal replacement survey to be reviewed by the RD
- Conduct an interview with the dietician to discuss your eating habits and lifestyle
- Ask you to complete questionnaires about your fatigue, quality of life, social support, memory, and thinking ability.
- Ask you to do a series of physical performance tests including balance tests, chair rise (stand up from a seated position in a chair 5 times), a short-distance (4-meters or 13-feet) walking speed test, and a narrow walk test. We will also measure your hand strength and ask you to walk on a treadmill for 14 minutes at a pace comfortable for you.
- Take a urine pregnancy test (women only)
- Measure your waist and hips

This visit will take approximately 1½-2 hours to complete. We will schedule you to come back in about 1-3 weeks for Baseline Visit 1.

Baseline Visit 1

We will ask you to return to Wake Forest Baptist Medical Center having fasted for at least 8 hours with nothing to eat or drink except water. At this visit we will:

- Measure your blood pressure, pulse, weight
- Take a sample of your urine
- Take a urine pregnancy test (women only)
- Take a sample of your abdominal fat (more details in the risk section below)
- Take a blood sample to measure your blood counts, blood sugar levels, and how your cells may change after losing weight. (This will be taken with other blood prior to you drinking the sugar drink.) If you are age 50 and older, we will draw an additional small tube of blood for additional testing on aging related research.
- You will have an oral glucose tolerance test which tells how well your body uses sugar (glucose) and makes insulin when sugar is consumed. This test may detect diabetes or your chance of developing diabetes. A needle is placed in a vein in your arm at the beginning of the test and will stay there for 2 hours to avoid multiple needle sticks. A blood sample (3.5 Tablespoons to include other blood tests performed) is drawn which will include a sample of blood to check your current sugar level. If your sugar level is within the expected range, you will be asked to drink a sweet sugar drink. After that, blood samples of 1 tsp. each are drawn every 30 minutes for 2 hours (total about 5 Tablespoons for all blood from this visit). At the end of the test you will be given something to eat. You will have your sugar level checked again at the end of the test to make sure it is at a safe level before we remove the needle from your arm. (Please see risks section for more details.)
- Randomize you to an intervention group- this will happen by phone during or after your visit (see Randomization section below for more details)
- Some participants will be randomized to have a DXA (dual energy x-ray absorptiometry) scan. If you are chosen, this is a painless scan of your body that determine the amount of bone, fat, and muscle you have (more details provided in the Randomization and Risks Section of this form)

This visit will take about 3 ½ - 4 ½ hours to complete. You will start your intervention the

following week.

**Randomization**

You will be randomized into one of the study groups listed below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in any group. You must agree to be in any group and cannot pick or change the group that you are placed in.

The groups are:

1. Weight Loss /DXA
2. Weight Loss/ no DXA
3. Delayed Weight Loss/ DXA
4. Delayed Weight Loss/no DXA

**Study Groups (interventions)**

1. Weight Loss Groups

Phase 1 (0-18 weeks)- Participants assigned to the Weight Loss group will follow a specific diet plan given to them by the dietician for 18 weeks. The diet will include sufficient nutrients, but is designed for an approximate weight loss of about 8-10% of your current weight. Four meal replacements per day will be provided for you during the course of this phase. Prior to starting the intervention, you will have an initial meeting with the study dietician to discuss the diet, the meal replacement choices, and all other information you will need prior to attending your first group session. You will be responsible for providing two meals a day and one snack using the guidelines provided by the study dietician. You will also be asked to record all food and drinks each day in a logbook diary. You will also be asked to attend weekly group classes led by the study dietician who will provide instruction in healthy eating and other weight control strategies. You will be weighed at each of these class times. You will be encouraged to interact with others that are in your class during class time as well as potentially outside of class. At the end of the 18-week weight loss phase you will be asked to complete a Program Evaluation form to provide feedback on your experience in the program and the meal replacement products you used.

Phase 2 (8 weeks): After completion of the active weight loss phase, you will have a brief meeting with the dietician to discuss a calorie level to maintain your weight as well as review tracking your activity. During this phase you will be asked to attend group meetings every other week to discuss increasing your activity. Activity logs will be dispensed and topics in regards to activity will be discussed in class. There will be a transition off the structured diet and nutritionists will be available during this time to answer questions. You will be weighed at these group meetings, but the focus will be on maintaining your weight. At the end of this phase, you will be offered an optional session with a staff member at the time of your exit to discuss long term goals and strategies.

2. Control/Delayed Weight Loss Groups

Phase 1 (0-18 weeks)

Participants randomized to the Delayed Weight Loss group will be asked to continue with your normal behavior and habits for 18 weeks in a manner that allows you to keep your weight within 5% of your starting weight over the 18-weeks. During this time, a staff member will call you

monthly or schedule you to come to the clinic for a brief study visit to check in with you. At the end of the 18 weeks you will be scheduled to come in for 2 follow up assessment visits. All participants who are still active in the study and complete these visits will be offered the opportunity to participate in a weight loss program.

Phase 2 (18 weeks)
Participants who elect to continue in this weight loss portion of the study will follow modified Diabetes Prevention Program involving 18 weekly dietary and exercise sessions led by the study staff. This program is designed for an approximate weight loss of 7% of your current weight. Participants will be guided by the dietician on their food purchasing and preparation of their meals, but no meal replacements or supplements will be provided. Prior to starting the program, you will have an individual session with the dietician to introduce you to the program, help set your goals, and review how to track your food and activity.

During weight loss, you will be asked to record all food and drinks each day in a logbook diary and you will have a log to track your activity. You will also be asked to attend weekly group classes led by the study dietician who will provide instruction in healthy eating and other weight control strategies. You will be weighed at each of these class times. You will be encouraged to interact with others that are in your class during class time as well as potentially outside of class. At the end of the weight loss phase, you will then be offered an optional session with a staff member at the time of your exit to discuss long term goals and strategies.

Follow Up Visit 1 (week 17)
We will ask you to return to Wake Forest Baptist Medical Center for a non-fasting visit. At this visit we will:

- Measure your weight
- Dispense your 3 day food record
- Ask you to do a series of physical performance tests including balance tests, chair rise (stand up from a seated position in a chair 5 times), a short-distance (4-meters or 13-feet) walking speed test, and a narrow walk test. We will also measure your hand strength and ask you to walk on a treadmill for 14 minutes at a pace comfortable for you.
- Take a urine pregnancy test (women only)
- Ask you to complete questionnaires about your fatigue, activity level, quality of life, social support, memory and thinking ability.
- If you were in the weight loss group, you will be asked to complete a program evaluation.
- If you were randomized to receive a DXA at BV1, then you will have a second DXA (dual energy x-ray absorptiometry) scan. This scan is a painless scan of your body that determines the amount of bone, fat, and muscle you have (more details provided in the Risks Section of this form), **This scan might be scheduled at your FV2 visit to allow more flexibility.
- Measure your waist and hips

This visit will take approximately 1 ½-2 hours to complete. We will schedule you to come back in about a week for Follow Up Visit 2.

Follow Up Visit 2

We will ask you to return to Wake Forest Baptist Medical Center having fasted for at least 8 hours with nothing to eat or drink except water. At this visit we will:

- Collect your 3 day food record
- Measure your blood pressure, pulse, weight
- Take a sample of your urine
- Take a urine pregnancy test (women only)
- Remove a sample of your abdominal fat (more details in the risk section below)
- Take a blood sample to measure your blood counts and chemistries, your sugar levels, your cholesterol, and how your cells may change after losing weight. (This will be taken with other blood prior to you drinking the sugar drink.) If you are age 50 and older, we will draw an additional small tube of blood for additional testing on aging related research.
- You will have an oral glucose tolerance test which tells how well your body uses sugar (glucose) and makes insulin when sugar is consumed. This test may detect diabetes or your chance of developing diabetes. A needle is placed in a vein in your arm at the beginning of the test and will stay there for 2 hours to avoid multiple needle sticks. A blood sample (3.5 Tablespoons to include other blood tests performed) is drawn which will include a sample of blood to check your current sugar level. If your sugar level is within the expected range, you will be asked to drink a sweet sugar drink. After that, blood samples of 1 tsp. each are drawn every 30 minutes for 2 hours (total about 5 Tablespoons for all blood from this visit). At the end of the test you will be given something to eat. You will have your sugar level checked again at the end of the test to make sure it is at a safe level before we remove the needle from your arm. (Please see risks section for more details.)

This visit will take about 3 ½ - 4 ½ hours to complete.

As part of this research study, you will be audiotaped during the memory testing. This is being done to ensure we are able to capture your answers and score the tests appropriately. You understand that you may request the recording be stopped at any time during the course of the research study. You can also withdraw your consent to use and disclose the audiotape before it is used. You should also understand that you will not be able to inspect, review, or approve the audiotapes before they are used in this study. The audiotapes will be destroyed once their use in this study is finished.

## Blood Collection

You will have approximately 1 tablespoon of blood drawn at your screening visit and 6 tablespoons drawn at your Baseline Visit 1 and Follow-Up Visit 2 for a total of 13 tablespoons throughout the entire study.

As part of this study, blood samples will be obtained and DNA from your blood sample will be purified. DNA, or deoxyribonucleic acid is the substance in your cells that stores and transmits inherited traits, such as eye color or blood type. Because we do not know how the results of this DNA study relate to your individual health, the results of the research will not be given to you or your doctor. These results will not be placed in your medical records.

## Storage of Biological Tissue/Blood/Urine

If you agree to participate in this study, we will store up to 2.5 tablespoons of blood, up to one tablespoon of urine, and a small amount of fat tissue to use for future research. These samples will be kept and may be used in future research to learn more about health and disease. Your samples will be obtained in the Clinical Research Unit and the Geriatrics Clinical Research Unit at Wake Forest University Baptist Medical Center. The samples will be stored in Dr. Yongmei Liu's Laboratory and in the Biogerontology Laboratory. Stool samples will be stored in Dr. Hariom Yadav's Laboratory. The samples will be given only to researchers approved by Dr. Jingzhong Ding. An Institutional Review Board (IRB) must also approve any future research study using your tissue/urine/blood samples. In order to participate in this study, you must be willing to provide these samples for future research.

Your blood, urine, stool, and tissue samples will be stored with a unique identifier and will not include any identifiable information about you, such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule regulations. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc. will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

The research that may be done with your blood, urine, stool, and tissue samples are not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of this study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research done with your blood, urine, and tissue samples will not be given to you or your doctor. These results will not be put in your medical records. The research using your blood, urine, and tissue samples will not affect your care. Your samples will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of this research.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he will not give your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

## How Long Will I Be in the Study?

You will be in the study for up to 9 months. You can stop participating at any time. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

## What Are the Risks of the Study?

Being in this study involves some risk to you. Risks and side effects related to the intervention program, study diet, and study procedures include:

1. Diet intervention

There are no known serious risks associated with eating a prepared diet to lose weight. Changes in usual bowel function (diarrhea and/or constipation) may occur when beginning the new diet due to differences between this diet and your usual diet. During the active period of weight loss, you may feel hungry or fatigued. Under conditions of rapid weight loss (more than 5 pounds per week), there is a very small chance of developing gallbladder disease.

2. Questionnaires

During the clinic visits we will ask you a variety of questions that you may feel are boring or wonder why we need this information. Please know that we only collect information that we feel may be useful. You may become tired during the questionnaires or memory testing and if this occurs, we can take a break until you are ready to continue.

3. Physical function tests

Your ability to perform certain physical activities will be measured before and after the intervention. There is a slight risk of falls while participating in the balance test. However, you will be positioned beside a step or wall that can be reached immediately if you feel that you are going to lose your balance. Additionally, the person conducting the test will stand next to you at all times. There is a small possibility that you may stumble, fall or aggravate one of your joints/muscles during the walking test.

4. Body measurements

Several methods will be used to determine the amount of fat, muscle and bone and the location of body fat. A tape measure will be used to measure the size of your waist and hips. A dual energy X-ray absorptiometry machine (DXA) will measure the amount of your muscle, bone and fat. This machine uses photons (energy) which scan across your body while you are lying quietly on a padded table. The DXA scan is painless.

The DXAs involve exposure to radiation. The radiation dose that you will receive as a result of participating in this study includes radiation from DXA scans. The amount of radiation you will receive from all the DXA scans is 2 millirem. This is equal to 0.01 times the amount of natural background radiation that the average person in the United States receives each year (300 millirem).

The risk of these procedures is small and is similar to that received from a clinical x-ray. Please be aware that this radiation exposure is necessary for this research study only and is not essential for your medical care. The Wake Forest University/Baptist Medical Center's Radiation Safety Committee, a group of experts on radiation matters, has reviewed the use of radiation in this research study and has approved this use as being necessary to obtain the research information desired. The potential long-term risk from these radiation doses is uncertain, but these doses have never been associated with any definite adverse effects. Thus, the risk to you, if any, is estimated to be slight.

5. Oral glucose tolerance test

We will ask you to undergo an oral glucose tolerance test before and after the intervention. This test tells how well your body uses sugar (glucose). This test may detect diabetes or your chance

of developing diabetes. After an overnight fast, a blood sample (1 teaspoon plus other laboratory tests) is drawn and your current blood sugar level is determined to ensure it is safe to continue with this test. Then you will be asked to drink a sweet sugar drink. Your blood will then be drawn after 30, 60, 90, and 120 minutes have passed. For your comfort an IV will be placed in your arm at the first blood draw to avoid multiple needle sticks. The staff can then get blood directly from the catheter at the desired times without having to do another needle stick. You may experience discomfort, bruising and/or bleeding where the IV is inserted. Occasionally, some people become dizzy, lightheaded or feel faint. Infection may occur on rare occasions. At the end of the test you will be given something to eat. There is a small risk of developing low blood sugar (hypoglycemia) when you drink the sugar (glucose) drink for this test. Signs of low blood sugar include feeling sweaty, dizzy, weak, and having a fast heartbeat. This is easily corrected by giving you a sugar drink to raise your blood sugar. Your blood sugar will be tested after you have a snack to make sure it has come up to a normal level and it is safe for you to leave.

6. Fat Sampling

To reduce the chance of bleeding, you cannot take aspirin, certain other pain relievers (like ibuprofen, Motrin™, Advil™, Aleve™) or other medications that may affect bleeding, platelets, or bruising for 5 days before and for 3 days after the procedure. It is OK to use acetaminophen (Tylenol™ or Extra-strength Tylenol™). You will also be asked to avoid strenuous physical activity for 36 hours before and after the procedure. You will be asked to fast (nothing to eat or drink except water for 8 hours before your visit).

The fat sample will be used to isolate specific cell types, including fat cells, and levels of specific genes in these cells will be analyzed. The entire procedure takes less than 45 minutes to complete and a snack will be provided after the sampling. The fat sampling will be performed before and after the initial 18 weeks of the study interventions. The skin in an area of your abdomen will be thoroughly cleaned with an iodine solution (betadine) and a local anesthetic (numbing medicine similar to what a dentist uses) will be used to numb your skin first and then your abdominal fat. You may feel a burning sensation from this medication for a short period of time. After the numbing medicine takes effect, a very small incision (approximately 1/2 inch to 1 inch long) will be made. Using surgical forceps and scissors, a small piece of fat (about the size of a large grape) will be removed. The clinician may make several attempts to obtain enough samples for testing. You may feel pressure or discomfort during this portion of the procedure. After the fat tissue is removed, the clinician will apply pressure to your abdomen to prevent bleeding into the tissue and will close the incision with absorbable sutures, then steri-strips and a gauze dressing will be applied.

The numbing medicine injected into your skin and adipose tissue will anesthetize the tissue to effectively reduce and eliminate discomfort during the fat sampling. Very rarely, this numbness can persist. In addition, bruising and excess bleeding can occur. You may feel pain or soreness in the area of the sampling after the local anesthetic wears off. There is a slight risk of delayed or residual bleeding into the tissue (hematoma) and a slight risk of infection. Although it is very rare, infection (presenting as redness, pus from wound, increasing pain) can occur. You will be given instructions on how to care for the incision and treat any pain or discomfort before you leave the clinic. A very small scar (approximately 1/2 inch to 1 inch) may persist. If you are

allergic to the local anesthetic, you may experience dizziness, anxiousness, numbness of the lips and tightness of the throat. Medications to treat your reaction are kept close by if needed. If you are allergic or sensitive to the adhesive tape, you may experience skin irritation or a rash where the tape was applied. A very small number of individuals feel lightheaded or dizzy during, or immediately following, the procedure. If this should occur, we will stop the procedure and provide appropriate treatment.

7. Blood sampling, storage and analyses
Blood samples will be drawn from a vein in your arm after an overnight fast before and after the intervention. You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally, some people become dizzy, lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

8. Stool Sample
There is minimal risk associated with stool collection. Be sure to wear gloves provided when you collect the sample. Wash your hands before and after collection and dispose of gloves in the trash. This will help protect you from spreading bacteria and cross-contamination.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks. There also may be other side effects that we cannot predict. You should tell the research staff about all mediations, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

## Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

## ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study include receiving information about your risk factors for heart disease including cholesterol, blood pressure, blood sugar, body fat amount and location, and physical fitness status. These tests will help you to know how healthy you are compared to others your age and whether or not you have an immediate health concern. A possible benefit is that by losing weight you may reduce your risk for diabetes and heart disease. Because individuals respond differently to diet changes, no one can know in advance if it will be helpful in your particular case.

## WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study. The meal replacement products used in this study are also commercially available.

## What Are the Costs?

There are some costs to you for taking part in this study. There will be no cost to you for the four daily meal replacements (if assigned to the Weight Loss group). The procedures related directly to the study will be paid for by the study. The two lean and green meals plus one snack per day (Weight Loss Group) and the cost related to food for the Delayed Weight Loss Group will be your responsibility. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

## WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de-identified information might be re-identified.

Only the following people or organizations will be granted access to your research records:

- The study investigator and his/her staff, or others at Wake Forest University Health Science who oversee the research
- Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest Baptist Medical Center
- Medifast®, who is providing the products for the study
- Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not

connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Diabetes and Digestive and Kidney Diseases which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. 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 YOU BE PAID FOR PARTICIPATING?

If eligible, you will be paid up to $100 if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be paid $50 for each of the following completed study visits (BV1 and FV2). Payments will be made by check or gift card and will be mailed to you.

To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

## WHO IS SPONSORING THIS STUDY?

This study is being sponsored by National Institute of Diabetes and Digestive and Kidney Diseases and the Claude D Pepper Older American Independence Center. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. Medifast® is providing the meal replacements being used in this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

## WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

If you have a serious side effect during the study, and require immediate medical attention, you should call 911. If you have a side effect that does not require immediate medical attention, you should discuss it with the study staff.

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of

such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the Wake Forest Baptist Health, Incorporated does not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted]

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call [redacted] at [redacted] during normal business hours or [redacted] after hours and identify yourself as a VEGGIE Weight Loss study participant.

## What About My Health Information?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** health history, your family health history, how you respond to study activities or procedures, laboratory and other test results, and information from study visits, phone calls, surveys, and physical examinations.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products. Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and Wake Forest Baptist Health; Medifast®, who is providing the meal

replacements for the study; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly contacted by Medifast® for any commercial purpose. You will not be identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups, it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished. You can tell [redacted] you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form, you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest Baptist Health will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial 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 Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and Wake Forest Baptist Health. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A Wake Forest Baptist Health (WFBH) electronic medical record will be created for all study participants. Information about your participation in the study will be placed in the WFBH medical record, along with any routine medical test results that were obtained at WFBH as part of this study.

## WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Prior to being randomized, you will be given a 3-day trial period in which to follow the meal replacement diet plan based on the study guidelines. You will be asked to record all food and drink consumed each day. If after this trial period you decide that you do not want to participate, for any reason, you may withdraw from the study without consequence to you and will not be asked to continue in the study.

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study, we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because:

- your study doctor feels it is in your best interest;
- you may not be following the instructions properly;
- you do not later consent to any future changes that may be made in the study plan;
- or for any other reason.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

## WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, [redacted] during normal business hours or [redacted] after hours and identify yourself as a VEGGIE weight loss study participant.

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted]. You will be given a copy of this signed consent form.

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm