PRINCIPAL INVESTIGATOR: Jack A. Yanovski, MD, PhD

STUDY TITLE: Phase II Trial of Liraglutide (Saxenda(R), Novo Nordisk) in Adolescents with Obesity After Sleeve Gastrectomy: A Pilot Open-Label Study

STUDY SITE: NIH Clinical Center

Cohort: Young adults and adolescents with obesity 1 year after sleeve gastrectomy

Consent Version: 11/10/2022

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

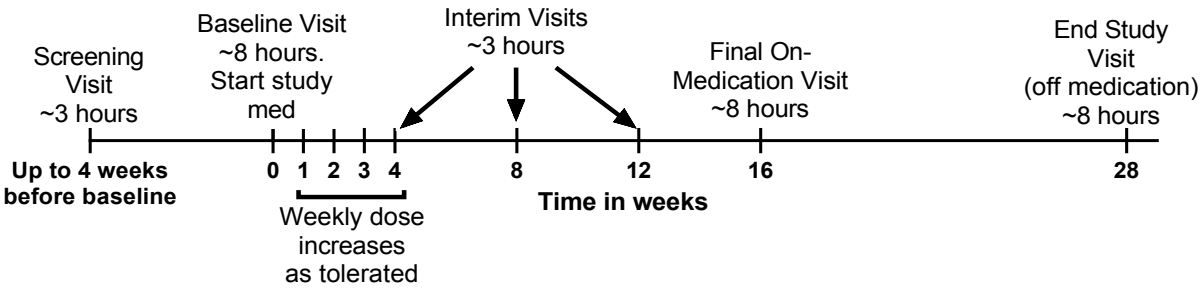
This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

We wish to study adolescents (age 12-20.99y) who continue to have obesity after having the weight-loss surgery called "vertical sleeve gastrectomy." Liraglutide is a weight loss promoting and glucose lowering medication that is FDA-approved to treat obesity in patients age 12 and older and to treat type 2 diabetes in patients 10 years and older, but has not been studied in adolescents who have had prior weight loss surgery. A recent study suggests that use of liraglutide plus lifestyle therapy leads to lowering of body-mass-index (BMI) in adolescents. We will study the effects of giving liraglutide 3.0 mg once daily for 16 weeks in adolescents

who continue to have obesity 1 year or more after vertical sleeve gastrectomy. After a screening visit to find out if you/your child can take part, you/your child will undergo baseline studies including blood draws and x-rays. Afterwards, you/your child will be taught how to give an injection of liraglutide daily under the skin at home. Liraglutide will be started at the lowest dose of 0.6 mg daily and then increased slowly over the first several weeks. The drug will be taken for a total of 16 weeks. Then we will repeat the studies done at baseline to see how weight has changed. Liraglutide may cause gastrointestinal side effects like nausea, diarrhea, vomiting, decreased appetite, indigestion, and constipation, but for most people, these side effects do not make them stop taking liraglutide. If side effects become too bothersome, we may not increase or may even decrease the dose. While on Liraglutide, we will ask that you/your child not take other weight loss medications, insulin, sulfonylureas, or other medications that affect insulin secretion or liraglutide clearance. The effects of liraglutide on the unborn child and on the newborn baby are not known. Because of this, you/your child cannot participate in this study if you/your child are pregnant or breast-feeding or become pregnant during the study.

We will ask you/your child to come to the NIH Clinical Center for outpatient follow-up visits that will include a weight check and physical examination. The final on-medication visit will also involve blood work, collection of urine and stool samples, questionnaires, and an imaging scan to check body composition. While at home, we will ask you/your child to take the study medicine once a day.



The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being enrolled is a minor then the term "you" refers to "you and/or your child" throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Metabolic Bariatric Surgery, including an operation called "vertical sleeve gastrectomy," is currently the most effective weight loss treatment for severe obesity and its associated diseases such as high blood pressure or diabetes. Yet, as many as 75% of adolescents who undergo such surgery, even if they have a good initial response, do not achieve a BMI<30 kg/m^2 (meaning they still have obesity), or subsequently have weight regain after reaching their lowest weight at approximately 1 year after surgery that places them at continued risk for the metabolic consequences of obesity.

This is a research study. The purpose of this research is to find out if a medication called liraglutide can help adolescents who continue to have obesity 1 year or more after vertical sleeve gastrectomy lose additional weight.

Liraglutide is a medication that suppresses appetite and helps the body regulate its blood sugar level. Liraglutide has been approved by the U.S. Food and Drug Administration (FDA) to treat obesity in children age 12 years or older, to treat type 2 diabetes in patients 10 years and older and to treat obesity in adults 18 years and older. We ask you to join our study so we can find out if liraglutide can help teenagers and young adults with obesity after vertical sleeve gastrectomy lose more weight.

WHAT WILL HAPPEN DURING THE STUDY?

If you agree to participate and are found to qualify, you will be one of 40 adolescents assigned to take liraglutide once daily for 16 weeks. Liraglutide is administered subcutaneously (an injection just under the skin) at a starting dose of 0.6 mg daily. The dose will be increased weekly up to 3.0 mg per day as tolerated.

The study consists of seven outpatient visits at the NIH Clinical Center: a **screening visit** to determine eligibility, a **baseline visit** to study your metabolism, body composition, appetite, and mood before you start taking study medicine, **three short visits** during the time you take liragludie to check your weight and how you are feeling, a **final on-medication visit** to repeat blood tests, questionnaires, and body composition scan, and an **End Study off-medication final visit** 12 weeks after you stop taking liraglutide to look for weight change after the intervention.

Outpatient Screening Visit:

This visit will take about 3 hours to complete. You will be seen on a weekday in the Clinical Center at the National Institutes of Health. We ask that you remain fasting for 10 hours before coming to the clinic and have nothing to eat or drink except water that morning. During this visit, we will perform the following:

1. **Protocol review and signing of consent, and, if needed, assent form**. We will go over the study in detail and answer any questions. The consent and assent forms will need to be signed before you can take part in the study.
2. **Complete medical history and physical exam,** with vital signs, weight, and height measurements.
3. **Fasting blood tests** to ensure that you are in good health. The analysis will examine blood cell count, liver and kidney function, cholesterol level, blood sugar level, inflammation level, vitamin D level, and coagulation studies. We will collect about 1 tablespoon of blood (~12 mL) at this visit.
4. **Urine sample collection** for urine analysis and a pregnancy test (for women of childbearing age).
5. **Nutrition counseling.** You will meet with our nutrition staff who will review how to maintain a healthy diet and manage a dietary log.
6. **Testing of how you respond to pictures of appealing foods.** You will be shown a series of images and asked to respond to them on a computer.
7. **Wrist accelerometer set-up.** We will set up an accelerometer (a device like a watch) on your wrist that will help measure your physical activity. You will be asked to wear it during all hours, except when bathing or showering, contact sports, or when swimming. The at-home monitoring period will last for fourteen (14) consecutive days. You will return this accelerometer when you return to the Clinical Center for the Baseline Visit.
8. **Optional stool sample collection set-up**. If you agree, we will ask you to obtain stool samples to save for future experiments that include sequencing of the DNA from the microorganisms in your stool (the "microbiome"). We will send the needed supplies home with you at this visit so you can bring the samples back at your next visit.

Baseline Visit:

If your Screening Visit results suggest you will qualify for participation in the study, you will be scheduled for the Baseline Visit. This visit can be done up to 4 weeks later. For the Baseline Visit, we ask that you remain fasting for 10 hours before coming to the clinic and have nothing to eat or drink except water that morning. You will be seen on a weekday in the Clinical Center at the National Institutes of Health, and the visit will take 6- 8 hours to complete.

During this visit we will perform the following:

1. **Interval medical history and physical exam,** with weight, height, waist circumference, and blood pressure measurement. You will also complete a few **questionnaires** that will ask about your mood and feelings about your weight. Some will be completed on a computer.
2. **Urine sample collection** as described before.
3. **Fasting blood tests** to look at your baseline metabolic, inflammatory, glucose, cholesterol levels, as well as reserve blood samples to be preserved for additional possible research tests. We will insert a small needle into your vein (an intravenous line

or I.V.) to obtain blood samples. We will collect about 2.5 tablespoons of blood (~36 mL) for these tests.

4. **Oral Glucose Tolerance Test (OGTT)** is a procedure that tells us a lot about how sugar is used by your body, how well your insulin works, and how sensitive your body is to insulin. The OGTT study is done while you rest in bed and takes two hours to complete. You will be given specific instructions for your diet for the day prior to testing. Testing instructions will be specific to each individual participant. Generally, the test will include the following procedures:

   After 10 pm the night before the test and on the morning of the test, you should only drink water – no other foods or liquids; this is called "fasting."

   An intravenous (IV) needle and tube will be placed in your arm so that we can do multiple blood draws without having to "stick" you each time. The needle will stay in your arm for the entire length of the test.

   Then you will be asked to ingest a drink containing 75 grams dextrose, which tastes like a very sweet liquid. Blood samples will be drawn at +0, 15, 30, 60, 90, and 120 min after you consume the dextrose drink. We will collect less than 1 tablespoon of blood (~10 mL) at this visit.
5. **Dual energy x-ray absorptiometry** (DXA) to look at your body composition (amounts of muscle, bone, and fat in the body). The test involves lying still on a padded table while a small camera passes over your body. We will do 1 scan of your whole body. The dose of the x-ray is much less than the amount you would get from a normal chest x-ray. The total amount of time to do this test will be about 20-30 minutes.
6. **Buffet meal.** You will be invited to eat as much as you want at a lunch buffet meal at the NIH Clinical Center. We will calculate how much food you ate after you are done. You will be asked to assess your appetite and mood before and after the test meal.
7. **Nutrition counseling**. You will meet with our nutrition staff to learn how to maintain a healthy diet.
8. **Optional return of stool samples:** If you agreed to collect stool samples at home, we will ask you to turn in your stool samples.
9. **Review of food record.** You will go over the record of your diet in person with one of the NIH nutrition staff.
10. **Check of lab results and final determination of study eligibility.** We will review your results and let you know if you qualify for the study.
11. **Injection teaching:** The nurses will teach you how to take the liraglutide study medicine by subcutaneous injection. You will need to be comfortable taking the medicine before you go home.
12. **Dispense study medication**. If you are found eligible, we will give you study medication for you to take at home. You will be given approximately a 4-week supply of study

medication to be taken one time per day. The medication can be taken with or without food. If you would like, we will help set up a reminder alarm to help you remember when to take your medicine. If you forget to take a dose, then take it as soon as you remember. But if it is more than 12 hours since you should have taken the medication, just skip the missed dose and take your next dose as usual the following day. We will ask you to call the research team if you miss your dose of Liraglutide for 3 days or more.

At-home dose adjustment:

As long as you are feeling well, we will increase the dose once a week, starting at 0.6 mg per day and increasing to 1.2, 1.8, 2.4, and at most 3.0 mg per day. If you do not feel well, you should call the study team. We may decide to decrease the dose or not increase it depending on your symptoms.

Interim Visits (weeks 4, 8, and 12):

To make sure that you are doing well taking the medication, you will be seen on a weekday in the Clinical Center at the National Institutes of Health about 4 weeks, 8 weeks, and 12 weeks after you started to take the study medicine. These visits will take about 2 hours to complete. During this visit we will perform the following:

1. **Interval medical history and physical exam,** with weight, height, and vital signs measurements at each visit.
2. **Urine sample collection** with pregnancy test as described before for females at each visit.
3. **Collection of Used Liraglutide pens**. We will collect your used liraglutide pens from the previous 4 weeks and give you a new 1-month supply of medication at each visit.
4. **Wrist accelerometer set-up (At the 12-week visit only).** We will set up an accelerometer on your wrist that will help measure your physical activity, as you did at the Screening Visit. You will be asked to wear it during all hours, except when bathing or showering, contact sports, or when swimming for fourteen (14) consecutive days.
5. **Repeat testing of how you respond to pictures of appealing foods,** the same tests you did at your Screening visit will be done at the 12-week visit only.
6. **Nutrition counseling**. You will meet with our nutrition staff to learn about various nutrition topics and for measurements at each visit.
7. **Optional stool collection materials (At the 12-week visit only)**. If you agreed to collect stool, we will give you the needed materials to take home and bring the sample back at your final visit.

Final On-Medication Visit (16 weeks after starting study medication):

For this visit, we ask that you remain fasting for 10 hours before coming to the clinic and have nothing to eat or drink except water that morning. You will be seen on a weekday in the Clinical Center at the National Institutes of Health, and the visit will take 6- 8 hours to complete.

During this visit we will repeat the tests you did at the Baseline Visit:

1. **Interval medical history and physical exam,** with weight, height, and blood pressure measurement. You will also complete a few questionnaires that will ask about your mood and feelings about your weight. Some will be completed on a computer.
2. **Urine sample collection** as described before.
3. **Fasting blood tests** to look at your baseline metabolic, inflammatory, glucose, cholesterol levels , as well as reserve blood samples to be preserved for additional possible research tests. We will insert a small needle into your vein (an intravenous line or I.V.) to obtain blood samples.
4. **Oral Glucose Tolerance Test (OGTT)**. Blood samples will be drawn at +0, 15, 30, 60, 90, and 120 min after you consume the dextrose drink
5. **Dual energy x-ray absorptiometry (DXA)** to look at your body composition.
6. **Lunch Buffet meal.**
7. **Nutrition counseling**. You will meet with our nutrition staff to learn about various nutrition topics.
8. **Optional return of stool samples** as described before.
9. **Review of food intake record.** You will go over a 1 week record of your diet in person with one of the NIH nutrition staff.

Final Off Medication Visit:

This visit takes place 28 weeks after you started the study medicine. You will be seen on a weekday in the Clinical Center at the National Institutes of Health, and the visit will take 1-2 hours to complete. During this visit we will perform the following:

1. **Interval medical history and physical exam,** with weight, height, waist circumference, and blood pressure measurement. If this evaluation suggests any medical problems, blood or other tests may be obtained at this visit.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for approximately 7 months. As described above, the 7 required visits last from 2 to 8 hours each.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 50 people participate in this study at the NIH.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

a. Physical examination and measurement of vital signs by a health care provider involves no known risk but does take time. A limited physical examination will be performed in a concise but thorough manner with appropriate measures taken to provide your privacy. Body circumference measurements of the waist will be done with a flexible tape measure; this involves

no risk and is not painful.

b. Questionnaires and interviews are also without significant risk but may be inconvenient because of the time required to complete. It is also possible that you may experience slight discomfort as a result of being asked to fill out questionnaires or respond to queries about stress and mood.

Procedures: We will ask you to complete five questionnaires that will take approximately 30-60 minutes to complete. The questionnaires will ask you about your general feelings regarding your own appearance, your perception of other's evaluation about your body and appearance, weight satisfaction, mood, suicidal ideation, and quality of life.

Risks: Some of the questions in the questionnaire may be upsetting or make you feel uncomfortable. You can skip any of the questions you do not want to answer, and you can stop at any time.

c. Surveys and food records

You will be taught how to keep a log of your dietary intake. Surveys and food records are without significant risk but may be inconvenient because of the time required to complete.

d. Buffet Meal

You will be asked to eat a lunch buffet meal during your study visit. The buffet meal is without significant risk, but you may feel uncomfortable if you eat too much or too quickly.

e. Accelerometer testing. You will be asked to wear an accelerometer on your wrist for 2 weeks at a time to measure your physical activity. It is an unobtrusive device without known risks and requires no maintenance by you. You may find it mildly inconvenient to wear the accelerometer during all hours, except when bathing or showering and for contact sports. If you develop irritation at the site of the wrist strap you should take it off and contact the research study team.

f. DXA scanning. You will have a DXA (Dual energy X-Ray Absorptiometry) scan to measure your bone density. This procedure will take place at the NIH Clinical Center and will take about 20 minutes to complete. During that time, you will need to lie still on a padded table while the instrument scans your body. We will do 1 scan of your whole body at two of your visits.

g. Blood withdrawals

Procedures: You will have a blood drawn from a vein. This may require a needle stick in your arm or hand, or if you already have an IV catheter in place, we may be able to draw through that. The amount of blood we will draw is about 1 tablespoon at the screening visit and about 3 tablespoons at Visits 1 and 5.

Risks: Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint or even throw up. The study team member may apply numbing cream to the area so that the needle stick won't hurt as much.

Blood withdrawals will remain well within the NIH guideline.This guideline is based upon body weight; for adults the maximum amount of blood that can be taken is 10.5 mL/kg or 550

mL, whichever is smaller, over any eight-week period. For children, no more than 5 mL/kg may be drawn for research purposes in a single day, and no more than 9.5 mL/kg may be drawn over any eight-week period. Any child weighing more than 58 pounds can participate safely in this study.

h. Urine collection for pregnancy testing

For girls and women, urine collections for pregnancy check are without significant risk, but they do take time and you may find them uncomfortable to collect.

i. Stool samples are also without significant risk, but some subjects may find them uncomfortable to collect.

j. Oral glucose tolerance test (OGTT)

The only risks from this kind of study are those described for any blood draw, as well as developing nausea from the sugar drink. You may develop temporary high blood sugar levels from the sugar drink, but it should normalize within a few hours and should not be clinically significant.

k. Liraglutide: the most common side effects of the medication used in this study are nausea, diarrhea, vomiting, decreased appetite, indigestion, and constipation. Possible serious side effects include: pancreatitis (swelling and inflammation of the pancreas), hypoglycemia (low blood sugar), kidney failure in patients who have kidney disease, serious allergic reaction, and acute gallbladder disease, including gallstones. Liraglutide comes with a black box warning for a risk of thyroid C-cell tumors as it causes thyroid C-cell tumors at clinically relevant exposures in both sexes of rats and mice. It is unknown whether Liraglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (a rare type of thyroid cancer) in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined. If you or a family member has a history of medullary thyroid cancer, or a genetic condition called multiple endocrine neoplasia type 2 that places you at risk for this cancer, you may not participate in the study.

We will monitor you for all adverse effects. If severe adverse effects develop, we will decrease the dose, temporarily stop, or discontinue the medication. If you experience any of the following, contact our team right away:

- Severe abdominal pain, diarrhea or vomiting
- Allergic reaction to the medicine that is severe, such as swelling or difficulty breathing

Keep the medication out of the reach of children.

What are the risks related to pregnancy?

The effects of liraglutide on the unborn child and on the newborn baby are not known. Because of this, you can not participate in this study if you are pregnant or breast-feeding. It is also important that participants do not become pregnant during the course of the study. Females with child-bearing potential will be required to undergo a pregnancy test prior to starting and at every study visit. Males should not to father a child during the study and for at least 6 months after completion of the study. Those who are sexually active and not surgically sterile must use effective contraception.

You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

What are the risks of radiation from being in the study?

DXA scanning is not painful but may be inconvenient because of the time needed to complete the study. DXA scanning involves radiation exposure for research purposes only.

During your participation in this research study, you will be exposed to radiation from two DXA scans. This is considered a low exposure. The risk of this exposure is too low to be reliably measured. The amount of radiation you will receive is less than the NIH Radiation Guidelines of 0.5 rem per year for participants less than 18 years old.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called "background radiation". No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The radiation you will get by participating in this study is less than the average yearly background radiation in the United States.

If you would like more information about radiation and examples of exposure levels from other sources, please ask a study member for a copy of the pamphlet called *An Introduction to Radiation for NIH Research Subjects.*

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

We are hopeful that your participation in this study will provide evidence as to whether liraglutide will help promote additional weight loss in individuals with obesity following vertical sleeve gastrectomy. However, you might not benefit directly from participating in this study. Should we find abnormalities in any of your test results, you will be notified and receive a copy to assist you in seeking further medical evaluation. This information may or may not improve your health.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because if liraglutide reduces body mass index of patients with refractory obesity after vertical sleeve gastrectomy, it might give them a new drug option to treat obesity and help reduce the chance of developing complications of obesity.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could continue or intensify behavioral management strategies for obesity, or possibly using one of the FDA-approved treatments for obesity in adolescents, including liraglutide, the medication we are studying. Other medications you could possibly use are orlistat, approved for those ≥12 years old and phentermine or phentermine plus topiramate that are approved for those age 17 years and older. These medications have not been approved by the FDA for use specifically in adolescents who have undergone bariatric operations. The other main alternative to this study is not to participate.

You may be eligible for other studies at the NIH. You may learn more about them through www.clinicaltrials.gov.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

After all participants have completed the study and once the study is fully analyzed, we will let you know if liraglutide seemed to help with weight loss and improving metabolic markers of obesity. There is no general plan to share your individual test results with you. However, if any findings suggest you have a medical issue, we will provide this information to you and your primary care provider. You may request a copy of your routine laboratory tests if you desire.

EARLY WITHDRAWAL FROM THE STUDY

You will be asked to end your participation in the study if you become pregnant, are unable to receive liraglutide for 1 week or more, and/or start a different obesity or diabetes medication like insulin. You may also be asked to end your participation in this study at any time if we believe that continuation is not in your best medical interest or if you are unable to comply with the requirements of the study.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding obesity, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of

whether your data will be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will be compensated for the time and inconvenience associated with participation according to NIH research volunteer guidelines.

Compensation per visit- to be given at the end of each visit

1. Outpatient screening visit:	$50
2. Baseline evaluation visit:	$200
3. Interim Safety Visits (three total):	$75
4. Optional baseline stool collection:	$25
5. Visit 5	$200
6. Optional end-treatment stool sample	$25
7. Final Visit:	$50
Total=	$575, up to $625

Payments will be sent after the visit either by check or direct deposit.

Guardians accompanying minors will be compensated $40 per visit x 7 visits: $280 which will be paid as a lump sum at the completion of the study.

If you are unable to finish the study, you will receive full compensation for the parts you completed.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A “Form 1099-Other Income” will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

This study does not offer reimbursement for, or payment of, travel, lodging or meals.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The NIH reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial will be available on http://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. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Information on your medical history and laboratory results will be kept in the electronic record system (CRIS) of the Clinical Center as well as in special research files in the Section on Growth and Obesity. Samples of your blood taken during this study will be kept stored in secure locked freezers. Before storing the samples, all identifying information, including your name, date of birth and the hospital medical record number, will be removed. The samples will be labeled with a code number but no other identifying information. The key to this code along with all other private information will be kept confidential and your privacy protected by keeping them in secure, locked places. Study documents and pertinent hospital or clinical records may be reviewed by qualified monitors within the NICHD quality assurance program. You will be asked to supply your social security number in order to be compensated for participation, but your social security number is not retained by the protocol study team after it is entered in the NIH payment system. You can participate in research but cannot be compensated without supplying a social security number.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from NICHD who audit the study.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy

Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Jack A. Yanovski, MD, PhD; Building 10-CRC Room 1-3330, Telephone: 301-496-0858 Another researcher you may call is: Sheila M. Brady, NP, Telephone: 301-451-3783.. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Parent/Guardian of a Minor Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I give permission for my child to take part in this study.

Signature of Parent/Guardian	Print Name of Parent/Guardian	Date
Signature of Parent/Guardian	Print Name of Parent/Guardian	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.