Study Title for Study Participants: Testing the addition of chemotherapy plus radiation to the usual chemotherapy in pancreatic cancer that was removed by surgery.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: RTOG 0848 A Phase II-R and A Phase III Trial Evaluating Both Erlotinib (Ph II-R)* and Chemoradiation (PhIII) as Adjuvant Treatment for Patients with Resected Head of Pancreas Adenocarcinoma

**PH II-R ERLOTINIB RANDOMIZATION COMPLETED 4/2/14*

What is the usual approach to my pancreatic cancer that was removed by surgery?

You are being asked to take part in this study because you have pancreatic cancer that was removed by surgery. People who are not in a study are usually treated with chemotherapy. There are several FDA-approved chemotherapy drugs that are commonly used. For patients who receive the usual approach for this cancer, about 10-20 out of 100 are free of cancer at five years.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

Why is this study being done? (12-APR 2018)

The purpose of this study is to compare any good and bad effects of using radiation plus a fluoropyrimindine (an FDA-approved chemotherapy drug that may help radiation be more effective) along with usual chemotherapy compared to usual chemotherapy alone. The addition of radiation and fluoropyrimindine chemotherapy could prevent your cancer from returning, but it could also cause side effects. This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach. To be better, the study approach should increase life, on average, by five or six months compared to the usual approach.

In an earlier part of this trial, the purpose of this study is to compare any good and bad effects of adding an investigational drug called erlotinib to usual treatment with the chemotherapy drug gemcitabine compared to treatment with gemcitabine alone. This purpose is being evaluated in patients who entered this study before April 2014. [Please see below "Earlier Group (no longer enrolling)" under What are the study groups?"]

There will be up to 545 people taking part in this study.

What are the study groups?

Patients can currently be treated on this study in two study groups. Both groups will receive the usual chemotherapy used for this type of cancer, as determined by your doctor. After 5 months of treatment, you will be evaluated by CT scans. If you have evidence of cancer, you will no longer receive treatment on this study. If no evidence of cancer is found, a computer will by chance assign you to one of two treatment groups in the

study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the other.

- Group 1
  You will get the usual chemotherapy used for this type of cancer, as determined by your doctor, for one more month.

- Group 2
  You will get the usual chemotherapy as described in Group 1, for one month.

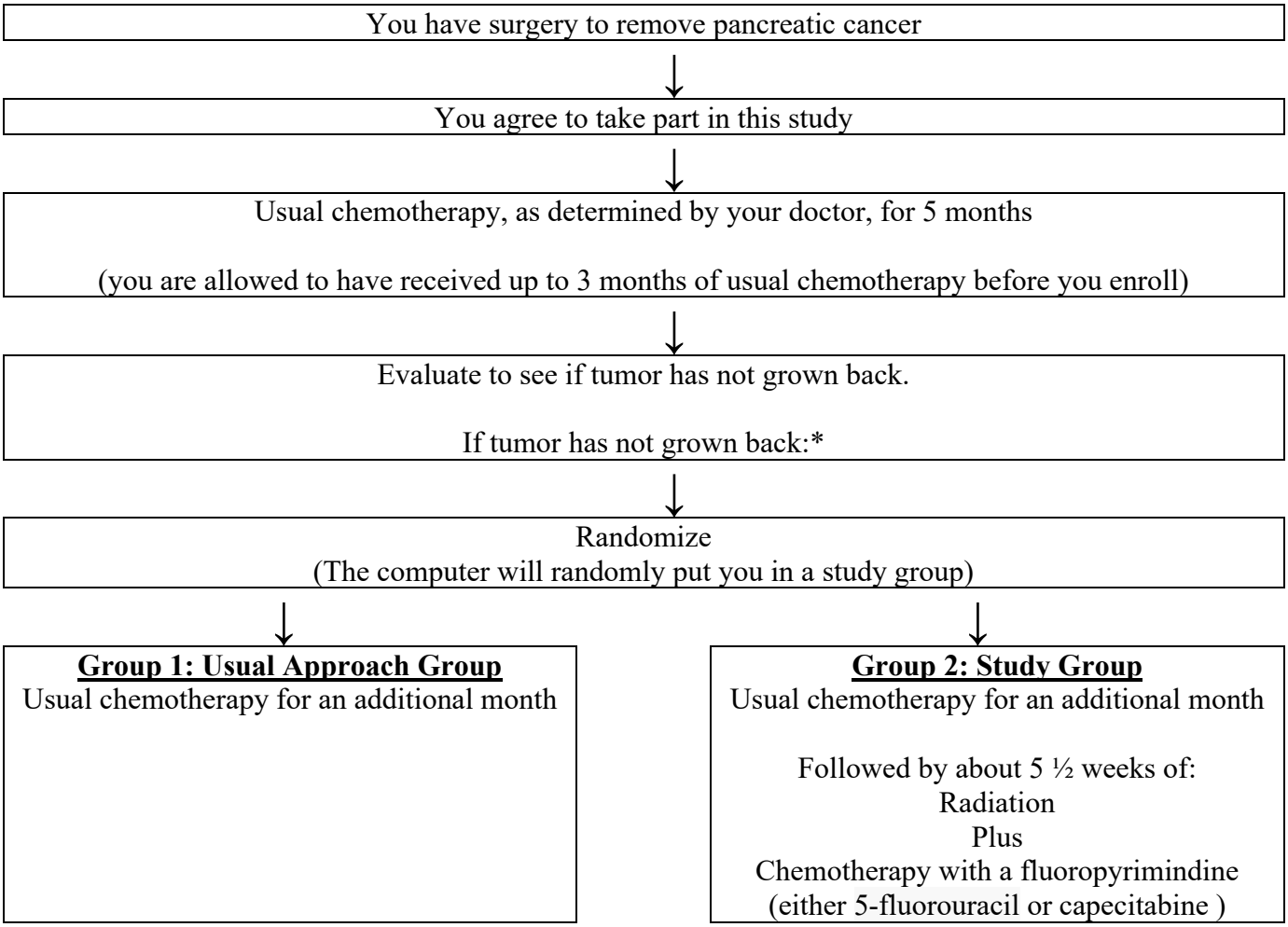
  You will also receive radiation and fluoropyrimindine chemotherapy for 5 ½ weeks as follows:

  - Radiation will be given to the area where your tumor was once a day, Monday through Friday for 5 ½ weeks (28 radiation treatments).

  - Fluoropyrimidine will be given with the radiation. There are two forms of fluoropyrimidine. You may receive a pill form of fluoropyrimidine called capecitabine, which is taken twice a day, Monday through Friday, on radiation days for 28 days. Alternatively, you may receive the intravenous form called 5-fluorouracil, which is given by vein continuously, 7 days per week, for 5 ½ weeks throughout radiation. If you receive the intravenous 5-FU you will need a special tube placed into a large vein in your arm, neck or chest and a small pump to give the drug. This pump weighs about 7 ounces and would be worn by you throughout the 5 ½ weeks. You and your doctor will decide which form of fluoropyrimidine (capecitabine or 5-fluorouracil) is best for you.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the others.

Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



*If tumor has grown back, you will no longer receive treatment on this study, but you will be seen in follow-up visits.

Earlier Group (no longer enrolling)

An earlier group of this study treated patients with erlotinib. In an earlier part of this study, patients were randomized to receive treatment with an investigational drug called erlotinib plus usual treatment with the chemotherapy drug gemcitabine versus treatment with gemcitabine alone. In 2013, after over 250 patients had been entered, new information became available about erlotinib. In a study performed in Europe, the addition of erlotinib to gemcitabine was proven not to be helpful for patients with locally advanced pancreatic cancer (pancreatic cancer that was too advanced to be removed by surgery but had not yet spread to other organs). As a result of this study, the erlotinib part of this study was closed, but data are still still being assessed on patients who had entered the study before the erlotinib part was closed.

How long will I be in this study?

You will receive the usual chemotherapy for 5 months. You may enter the study without having started usual chemotherapy or you may enter the study having received up to 3 months of usual chemotherapy. After 5 months of usual chemotherapy, you will be evaluated by CT scans to see if your tumor has grown back. If it has not grown back you will receive one month of additional chemotherapy with or without 5 ½ weeks of radiation plus chemotherapy with a flouropyrimindine.

After you finish usual chemotherapy with or without radiation plus a fluoropyrimindine, your doctor will continue to watch you for side effects and follow your condition every 3 to 6 months for the first 3 years, then yearly.

What extra tests and procedures will I have if I take part in this study?

All of the exams, tests, and procedures you will have are part of the usual approach for your cancer.

What possible risks can I expect from taking part in this study? (12-APR 2018)

The radiation and chemotherapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

<u>Study Groups 1 and 2: Possible Side Effects of Usual Chemotherapy</u>
Your doctor will address the risks associated with usual chemotherapy as part of your usual care for your panctreatic cancer. You should discuss any concerns you have about about these risks with your doctor.

Study Group 2: Possible Side Effects of Radiation Therapy

Possible Side Effects of Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, more than 20 may have one or more of the following:
• Stomach and intestinal discomfort, which usually occur during the last three weeks of radiation and generally go away within 2 months after the treatment is finished • Nausea • Vomiting • Diarrhea • Fatigue • Tanning, redness of skin, and hair loss within the radiation area, which is temporary • Permanently dry skin in the radiation treatment area • Low blood counts, which could lead to an increased risk of infection, weakness, and/or in bleeding and bruising easily • Loss of appetite and weight loss • Mild muscle aches in the area treated

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, from 4 to 20 may have one or more of the following:
• Infection • Stomach pain

RARE, AND SERIOUS In 100 people receiving radiation therapy, 3 or fewer may have one or more of the following:
• Change in liver or kidney function, which is unlikely to cause symptoms. • Bowel obstruction, which could result in abdominal pain, nausea and vomiting and may require surgery. • Gastric, duodenal or small-bowel ulcer formation that can result in abdominal pain, nausea and vomiting, perforation and bleeding, and may require surgery.

Study Group 2: Possible Side Effects of Fluoropyrimindines (Capecitabine and 5-fluorouracil)

You and your doctor will decide whether it is best for you to receive the pill form of fluoropyrimidine (capecitabine) or the IV form (5-fluorouracil). The leaders of this study believe the effectiveness of the IV and pill forms are the same. The general side effects of the pill (capecitabine) and IV (5-fluorouracil) forms of fluoropyrimidine are similar. However, in some patients, capecitabine may cause more diarrhea and nausea. These potential gastrointestinal side effects of capecitabine are balanced by the inconvenience of a continuous 5-fluorouracil infusion and the need for the minor surgical placement of a special type of intravenous (PICC line or port-a-cath) and the need to carry a small pump for 5 ½ weeks.

Possible Side Effects of Capecitabine (Table Version Date: September 30, 2015)

COMMON, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, more than 20 and up to 100 may have:
• Swelling of the body • Blisters on the skin • Redness, pain or peeling of palms and soles • Pain • Diarrhea, loss of appetite, nausea, vomiting • Sores in mouth which may cause difficulty swallowing • Anemia which may require blood transfusions • Infection, especially when white blood cell count is low • Bruising, bleeding • Feeling of "pins and needles" in arms and legs • Tiredness • Fever

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Capecitabine, from 4 to 20 may have:
• Blurred vision, dry or itchy eyes • Muscle spasms, body aches • Abnormal heartbeat • Restlessness, irritability • Swelling of face, fingers and lower legs • Constipation • Difficulty with balancing

RARE, AND SERIOUS In 100 people receiving Capecitabine, 3 or fewer may have:
• Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Difficulty speaking, walking or seeing • Internal bleeding which may cause blood in vomit or black tarry stools • Damage to the heart

Possible Side Effects of 5-Fluorouracil (Table Version Date: November 9, 2016)

COMMON, SOME MAY BE SERIOUS In 100 people receiving 5-Fluorouracil, more than 20 and up to 100 may have:
• Hair loss • Redness, pain or peeling of palms and soles • Rash, increased risk of sunburn, itching • Diarrhea, nausea, vomiting, loss of appetite • Difficulty swallowing • Sores in mouth • Heartburn • Headache

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving 5-Fluorouracil, from 4 to 20 may have:
• Chest pain • Blood clot • Belly pain • Internal bleeding which may cause black tarry stools • Infection, especially when white blood cell count is low • Anemia which may require blood transfusions • Bruising, bleeding • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Confusion • Abnormal eye movement, blurred vision, watering eyes • Discomfort from light • Difficulty with balancing • Skin changes • Tiredness

RARE, AND SERIOUS In 100 people receiving 5-Fluorouracil, 3 or fewer may have:
• Damage to the heart which may cause shortness of breath • A new cancer resulting from treatment of a prior cancer

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks: You should not get pregnant, breastfeed, or father a baby while in this study. The chemotherapy and radiation therapy used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study and for what time period after treatment ends.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study approach is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the _____ *(insert name of center)* Institutional Review Board at _____ *(insert telephone number). (Note to Local Investigator: Contact information for patient representatives or other individuals at a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can also be listed here.)*

What are the costs of taking part in this study?

You and/or your health plan/insurance company will need to pay for the usual chemotherapy, radiation therapy, fluoropyrimindine, and other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study.

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information? (12-APR 2018)

Your privacy is very important to us. The study doctors will make every effort to protect it. The study doctors have a privacy permit to help protect your records if there is a court case. However, some of your medical information may be given out if required by law. If this should happen, the study doctors will do their best to make sure that any information that goes out to others will not identify who you are.

Some of your health information, such as your response to cancer treatment, results of study tests, and medicines you took, will be kept by the study sponsor in a central research database. However, your name and contact information will not be put in the database. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

There are organizations that may look at your study records. Your health information in the research database also may be shared with these organizations. They must keep your information private, unless required by law to give it to another group. Some of these organizations are:

- NRG Oncology
- Other organizations in the National Clinical Trials Network (NCTN): Alliance for Clinical Trials in Oncology (ALLIANCE), ECOG-ACRIN Cancer Research Group (ECOG-ACRIN), and SWOG
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

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.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ *(insert name of study doctor[s])* at _____ *(insert telephone number).*

ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will not be added to your medical records and you or your study doctor will not know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of "yes" or "no" for each of the following studies.

Optional Quality of Life Study *(For patients who have not started chemotherapy before entering the main trial)*

If you choose to take part in this study, you will be asked to fill out two forms with questions about how you are feeling physically and emotionally during your cancer treatment Researchers will use this information to better understand how patients feel during treatments and what effects the medicines are having.

You will be asked to fill out these two forms five times: at start of study, and then at 5-6, 9, 12 and 24 months after your treatment has started. You may fill out the forms during an office visit, by mail, or by telephone. Each form will take about 5 minutes to complete. The forms will ask about things about whether you feel tired, weak and/or are having trouble performing usual activities due to fatigue. You may feel uncomfortable answering some of the questions, and you can skip any you do not want to answer.

Please circle your answer: I choose to take part in the Quality of Life study and will fill out these forms:
YES NO

Optional Sample Collections for Laboratory Studies and/or Biobanking for Possible Future Studies (12-APR 2018)

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part, blood, urine, and a sample of tissue from your previous biopsy will be collected. The researchers ask your permission to store and use your samples and related health information (for example, your response to cancer treatment, results of study tests and medicines you are given) for medical research. The research that may be done is unknown at this time. Storing samples for future studies is called "biobanking". The Biobank is being run by NRG Oncology and supported by the National Cancer Institute.

WHAT IS INVOLVED?

If you agree to take part, here is what will happen next:

1) About 2 tablespoons of blood will be collected from a vein in your arm before you start treatment at the same time that blood is collected as part of your pre-treatment evaluation for the main part of this study. If your cancer gets worse while you are on the study, the researchers would also like to collect about 2 tablespoons of blood.
2) About 2 tablespoons of urine will be collected before you start treatment at the same time that urine is collected as part of your pre-treatment evaluation for the main part of this study.
3) A sample from the tissue that was collected at the time of your surgery before you enrolled on this study will be sent to the Biobank. If your cancer gets worse while you are on the study, and your

doctors decide to perform additional surgery as part of your usual care, the researchers would also like to collect a sample of the tissue that is removed.

4) Your samples and some related health information may be stored in the Biobank, along with samples and information from other people who take part. The samples will be kept until they are used up. Information from your medical record will be updated from time to time.
5) Qualified researchers can submit a request to use the materials stored in the Biobanks. A science committee at the clinical trials organization, and/or the National Cancer Institute, will review each request. There will also be an ethics review to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
6) Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your samples.
7) Some of your genetic and health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

WHAT ARE THE POSSIBLE RISKS?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. *(For non-US participants, please verify existence of such laws before including the following text.)* There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

HOW WILL INFORMATION ABOUT ME BE KEPT PRIVATE?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) When your sample(s) is sent to the researchers, no information identifying you (such as your name) will be sent. Samples will be identified by a unique code only.
2) The list that links the unique code to your name will be kept separate from your sample and health information. Any Biobank and NRG Oncology staff with access to the list must sign an agreement to keep your identity confidential.
3) Researchers to whom NRG Oncology sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4) Information that identifies you will not be given to anyone, unless required by law.
5) If research results are published, your name and other personal information will not be used.

WHAT ARE THE POSSIBLE BENEFITS?

You will not benefit from taking part.

The researchers, using the samples from you and others, might make discoveries that could help people in the future.

ARE THERE ANY COSTS OR PAYMENTS?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

WHAT IF I CHANGE MY MIND?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, *(insert name of study doctor for main trial)* at _____ *(insert telephone number of study doctor for main trial)* who will let the researchers know. Then, any sample that remains in the bank will no longer be used and related health information will no longer be collectd. Samples or related information that have already been given to or used by researchers will not be returned.

WHAT IF I HAVE MORE QUESTIONS?

If you have questions about the use of your samples for research, contact the study doctor, _____, *(insert name of study doctor for main trial)*, at _____ *(insert telephone number of study doctor for main trial)*.

Please circle your answer to show whether or not you would like to take part in each option (*include only applicable questions)*:

SAMPLES FOR FUTURE RESEARCH STUDIES:

My samples and related information may be kept in a Biobank for use in future health research.

YES NO

I agree that my study doctor, or their representative, may contact me or my physician to see if I wish to participate in other research in the future.

YES NO

This is the end of the section about optional studies.

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled ‘yes’.

Participant’s signature_____

Date of signature_____

Signature of person(s) conducting the informed consent discussion_____

Date of signature_____