Model Informed Consent Document

(Consent Version Date: June 10, 2011)

Systolic Blood Pressure Intervention Trial (SPRINT)

Principal Investigator(s) _____

Institutional Affiliation

INTRODUCTION

You are invited to be part of a research study called Systolic Blood Pressure Intervention Trial (SPRINT). The study is sponsored by the National Heart, Lung and Blood Institute, the National Institute on Aging, the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institute of Neurological Disorders and Stroke (all part of the National Institutes of Health). The investigators listed above are in charge of the study at (clinical site name). Other people may help them or act for them.

Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to participate in SPRINT because you are age 50 or older, have high blood pressure, and a history of heart disease or risk factors that increase your risk for heart disease. Most participants will be in the SPRINT study between 4 to 8 years.

Your participation is voluntary. Please take your time in deciding whether or not you wish to participate. Ask your study doctor or the study staff to explain anything in this informed consent document that you do not understand. You may also discuss the study with your friends, family, and doctor.

WHY IS THIS STUDY BEING DONE?

About two-thirds of those over age 60 have high blood pressure. There is some evidence that lowering blood pressure further than current practice might help prevent heart disease, stroke, and kidney disease. There is also some evidence that high blood pressure can cause changes in memory and thinking as people get older.

SPRINT will answer several research questions. The most important questions are whether treating systolic blood pressure aggressively will reduce the rate of heart disease and stroke, memory decline or worsening of kidney disease in adults over the age of 50 who already have high blood pressure.

SPRINT will have about 10,000 from around 100 sites throughout the United States. The study will involve around ___ participants at (clinical site name).

WHAT IS INVOLVED IN THE STUDY?

Your first study visit is called a "screening" visit. After signing this form, we will perform some tests and ask questions to determine if you qualify for the study. The screening visit will take 2 to 3 hours. Your medical history, blood pressure, smoking status, height, weight, and kidney disease status will be reviewed to determine whether you qualify for the study. If you do, you will have a short physical exam and one tube (about 2 teaspoonfuls) of blood will be drawn from a vein in your arm. The blood will be used to check your fasting glucose, lipids and chemistry profiles. The lipid profile will check your total cholesterol, triglycerides, HDL and LDL. The chemistry profile will check your sodium, potassium, and kidney function, among other things. You may also be asked for a urine sample to check how your kidneys are working.

If you qualify for SPRINT you will be randomized into one of two study groups (either the Intensive or Standard group). Randomization means that you are put into a group by chance – like flipping a coin to decide. You will have an equal chance of being placed in either group. The "Intensive" goal is to have a systolic blood pressure level less than 120 mm Hg. The "Standard" goal is to have a systolic blood pressure level less than 140 mm Hg.

The study doctor will treat your blood pressure according to the SPRINT study protocol. The study doctor will choose the drugs he/she feels will meet the goal of your study group (Intensive or Standard). Therefore, your current blood pressure medication (if any) could be continued as is, changed, or added to. If you do not reach your blood pressure goal, your study doctor will change your treatment until you do. You and your personal physician are responsible for all of your other medical care, including general preventive measures.

Regardless of which group you are in, you will be asked to visit the clinic every month for the first 3 months, and then every three months thereafter until the end of the study.

More monthly visits may be added until you reach your blood pressure goal, if a new drug is added to your treatment plan, or to manage specific side effects if they occur.

At each clinic visit, your health will be reviewed, and any symptoms will be discussed with the study doctor, nurse, or other study staff. Your blood pressure and heart rate will be measured, and your study medications will be reviewed to make sure you are taking them correctly. If you cannot come to the clinic, we may contact you to try to make other arrangements for visits.

You will have blood samples drawn about every three months to measure lipids, glucose, chemistries, and kidney function. Urine samples will be collected about every year. Some of your blood and urine specimens will be stored for future studies. More blood samples may be taken occasionally to monitor your treatments for safety. The total amount of blood drawn at any visit will not exceed five tablespoons.

You will have an electrocardiogram (a recording of the electrical activity of the heart, also called an ECG) at your first visit, and every two years until study exit (or your 60 month visit). Your weight will be measured every year. You will also be asked to fill out questionnaires about your medical history,

smoking and alcohol use, medications, hospitalizations, and quality of life. You will undergo testing to evaluate your memory. If you are age 75 or older, you will be asked to walk about 4 yards. We will obtain medical records from any hospitalizations, emergency room visits and other medical procedures. A member of your clinic or the national SPRINT study team may call you or a person you designate between your clinic visits to ask how you are feeling and to see if your blood pressure levels are under control.

If you agree, we will send copies of your test results to your personal doctor. We are also requesting permission to record your voice for some portions of your memory testing to check the work of the study staff. No identifying information will be on the tape recordings. The tapes will be destroyed at the end of the study.

You will be asked for your contact information, as well as the contact information of a family member or friend who can provide information and answer questions for you if you are unable to answer for yourself or can provide more information about your health if needed.

GENETIC STUDIES

DNA (deoxyribonucleic acid) from your blood sample will be stored for future genetic studies. DNA stores and transmits inherited traits, such as eye color and blood type. As part of SPRINT, your DNA will be studied to see if there are genes that contribute to blood pressure, kidney disease, heart and blood vessel diseases, changes in memory, other major diseases, health conditions, or risk factors. Your DNA sample may also be shared with other researchers studying the genetics of these conditions. These scientists would be given the DNA without any information to identify you. That is, they will not know your name, date of birth, social security number, etc. At the end of the study, your samples may be provided to other investigators under certain conditions, without any personal identifying information.

A sample of your DNA may be used for a Genome Wide Association Study (GWAS). These tests create a very detailed picture of your DNA for researchers. In this case, your genetic and clinical information will be sent to the National Institutes of Health's GWAS data bank, where it will be shared with other investigators for research purposes. The GWAS studies may help to improve ways of selecting treatments for certain diseases. Before your information is used for GWAS analyses, we will remove any identifying information such as your name, date of birth, or address. Researchers using your DNA and clinical data cannot link this information back to you.

You will not be informed of results of genetic studies unless the result indicates a greatly increase risk of a clinically significantly disease or disorder for which a treatment to prevent or lessen the condition is known. When the study ends, the link between you and your genetic test results will be destroyed, so that it will not be possible to provide you any results after that time. If we do provide you with results of genetic studies, we will also provide information about what the result means and what treatment options are available.

STORAGE OF BLOOD AND URINE

Some of your blood and urine may be used in future research to learn more about high blood pressure and other diseases. Your specimens will be stored at a facility in Minnesota and will be given only to researchers approved by the SPRINT investigators**.** After the study ends, samples of your blood, urine, and DNA will be transferred to a National Institutes of Health specimen bank for storage. The specimen bank is a secure facility that collects, stores, and distributes samples from people with many kinds of conditions, from affected family members, and from healthy people. Sending samples to the specimen bank may give scientists valuable research material that can help them develop new diagnostic tests, new treatments, and new ways to prevent diseases. Your specimens may be used by future investigators not associated with the SPRINT study. We will remove any identifying information such as your name, date of birth, or address from these specimens. Your specimens will be stored for as long as they are useful to researchers.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 4 to 8 years. You can stop participating at any time. If you decide to stop, we ask you to talk to the investigators or study staff first to learn about any possible health or safety consequences.

You can also agree to allow the study to review your medical records and information through national databases at the Social Security Administration, Medicare and Medicaid, the National Center for Health Statistics, the United States Renal Data System, and the Veterans Administration after SPRINT ends. This would include your hospitalizations for heart disease, kidney disease, falls and brain disorders. If you have moved to an assisted living facility or a nursing home, the study will collect this information too. All of these records will be kept confidential. When we are using national data bases to collect information, no one from SPRINT will contact you or your family for any further information. The data base searches would begin after your final close-out visit at site _____, and may last until 2030.

WHAT ARE THE RISKS OF THE STUDY?

The risk of harm or discomfort from SPRINT is not expected to be more than in daily life or from routine physical or psychological examinations or tests. You should discuss the risk of being in this study with the study staff. Those risks include the following:

- You may have some discomfort, bruising and/or bleeding where the needle is inserted for blood draws. 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.

- Sometimes, people who take blood pressure medications may experience blood pressure that is too low. If you are in the intensive blood pressure group, your risk of this will be higher. Symptoms of low blood pressure may be mild, such as feeling a little lightheaded. Occasionally they may be more severe, such as dizziness, tiredness, or fainting. Sitting or lying down often

relieves these symptoms. You should notify your clinic doctor or nurse if you have these symptoms. Clinic staff will follow you closely to make it less likely that your blood pressure becomes too low.

- Being in this research study may involve providing details that you consider confidential or private. We will code research records, keep them secure and allow only specific people to have access to them to keep your information safe.

- Some people worry that genetic information could be used to discriminate against them. To prevent misuse, SPRINT will take special precautions to protect your information that is stored in data banks and used for research. The data will be sent with only your code number attached. Your name or other identifying information will never be given to the data banks. In addition, a law was passed in 2008 by the Federal Government that prohibits many forms of discrimination based on genetic information.

A Data Safety and Monitoring Committee, an independent group of experts, will review the data on the safety of this research throughout the study.

WHAT ARE THE SIDE EFFECTS OF THE MEDICINES USED IN THE STUDY?

The Food and Drug Administration (FDA) has approved all drugs that will be used in SPRINT. Most have been used to treat high blood pressure for many years. However, all drugs have a potential risk of an allergic reaction, which if not treated quickly, could become life threatening. You may have side effects from the specific medications chosen as treatments. In addition, because you are likely to need more than one medication to control your blood pressure, side effects due to combinations of medications may occur. These include electrolyte abnormalities (such as low sodium or low potassium), slow or irregular heartbeats, dizziness, fainting, and changes in your kidney function. Your doctors will monitor you for side effects and can treat these effects and possible interactions with other drugs. Drugs that may be used in SPRINT are listed below, along with some of the possible side effects.

- **Thiazide type diuretics** (**chlorthalidone, hydrochlorothiazide, also known as "water pills"):** Frequent urination, muscle weakness, dizziness, cramps, thirst, stomach pain, upset stomach, vomiting, diarrhea, loss of appetite, headache, hair loss
- **Loop diuretic (furosemide):** Muscle cramps, weakness, dizziness, confusion, thirst, upset stomach, vomiting, blurred vision, headache, rash, restlessness, and constipation
- **Potassium sparing diuretics (spironolactone, amiloride):** Vomiting, diarrhea, stomach pain or cramps, dry mouth, thirst, dizziness, unsteadiness, headache, enlarged or painful breasts in men or women, irregular menstrual periods, vaginal

bleeding in post-menopausal women (who no longer have monthly menstrual periods) , difficulty maintaining or achieving an erection, deepening of voice, increased hair growth on parts of the body, drowsiness, tiredness, restlessness

- **Calcium channel blockers (diltiazem, amlodipine):**

  Dizziness or lightheadedness, flushing (feeling of warmth), headache, weakness, slow heartbeat, vomiting, diarrhea, constipation, nasal congestion, cough, swelling of the feet or legs

- **Beta blockers (atenolol):**
  Dizziness, lightheadedness, tiredness, drowsiness, depression, nausea, diarrhea, slow heart beat
- **Vasodilators (hydralazine, minoxidil):**
  Flushing (feeling warm), headache, upset stomach, vomiting, loss of appetite, diarrhea, constipation, eye tearing, stuffy nose, rash

- **Adrenergic inhibitors (reserpine):**
  Dizziness, loss of appetite, diarrhea, upset stomach, vomiting, stuffy nose, headache, dry mouth, and decreased sexual ability

- **Alpha 2 blockers (guanfacine, clonidine):**

  Dry mouth, tiredness, weakness, headache, irritability, decreased sexual ability, decreased appetite, stomach pain, nausea, vomiting, and constipation

- **Alpha 1 blockers (doxazosin):**

  Headache, tiredness, swelling of the hands, feet, ankles, or lower legs, shortness of breath, weight gain, muscle or joint pain or weakness, abnormal vision, runny nose, decreased sexual ability

- **Angiotensin converting enzyme inhibitors or ACE-I (lisinopril):**
  Cough, dizziness, headache, excessive tiredness, nausea, diarrhea, weakness, sneezing, runny nose, and decrease in sexual ability

- **Angiotensin receptor blockers or ARBs (valsartan, losartan, olmesartan):**
  Dizziness, lightheadedness, congestion, cough, diarrhea, trouble sleeping, headache, muscle aches, fever, runny nose, excessive tiredness, abdominal pain, back pain, and swollen joints

- **Potassium supplement (KCl):**
  Upset stomach, diarrhea, and vomiting.

Additional drugs may be used in SPRINT in the future. The staff will tell you about any new medicines that they may give you.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to be part of SPRINT, the treatment may or may not be of personal benefit to you. We hope what we learn will be very important for treating high blood pressure in the future. If you are in the Intensive group, your risk of heart disease may decrease. However, since this study is being done to determine if *intensive treatment* can actually prevent heart disease, we do not yet know if *the intervention* will provide help over and above standard treatment. So, you will help add to medical knowledge about the possible usefulness of *intensive treatment* in preventing heart disease.

Your blood, urine, and DNA 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 of commercial value. However, there are no plans to share with you any potential profits from the research.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this research study to receive treatment. Many treatments are available for high blood pressure. These treatments include drugs, diet, and exercise. If you decide to stop participating in this study, your personal doctor should manage your medical care. You should talk to your doctor about all of these choices. You could be treated with the same drugs used in SPRINT even if you are not in the study.

WHAT IF WE LEARN ABOUT NEW RISKS DURING THE STUDY?

You will be given any new information gained during SPRINT that might affect your health, welfare, or willingness to stay in the study. Results of your laboratory and clinical tests will be given to you and your doctor if you choose.

WHAT ABOUT THE USE, DISCLOSURE AND CONFIDENTIALITY OF HEALTH INFORMATION?

[HIPAA language from WFU – may need to be adjusted by each clinic]

By being in SPRINT, your personal health information and details that directly identify you ("your health information") may be used and disclosed. This information includes, but is not limited to, things like your name, address, telephone number, social security number, and date of birth. Your personal health information includes anything about you which is collected or created during SPRINT for research purposes. It also includes your personal health information related to this study in your medical records at this institution or other places where you may have received medical care. Examples of your personal health information include your health history, how you respond to study activities or procedures, laboratory and other test results, audiotapes and information from study visits, phone calls, and physical examinations.

Your health information may be given to others during SPRINT to help do the study, to make sure the research is being done correctly, and to prepare required reports. Your health information may be given to others after SPRINT is finished to help determine the study results.

Some people, agencies and businesses that may receive and use your health information are the research sponsor (National Institutes of Health) or NIH representatives assisting with the research; investigators at other sites who are part of the research; central laboratories, reading centers or

analysis centers; the Institutional Review Board; representatives of the data center (Wake Forest University School of Medicine); and representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS).

Some of these people, agencies and businesses may further disclose your health information. If so, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

[text required for clinic-based sites:]
Information collected or created as part of SPRINT may be placed in your medical record and discussed with care providers not in the SPRINT study. This will help them to give you appropriate medical care. All or part of your health information may be used or disclosed for treatment, payment, or healthcare operations related to providing your medical care.

When you sign this consent and authorization form, you give permission to use your health information as described in this form. You can take away this permission at any time. You do this by sending a written notice to the investigator in charge of the study at the following address:

Principal Investigator Name
Address
City, State, ZIP

If you withdraw your authorization, you cannot be in this study and no new health information about you will be gathered after that date. Any of your health information already gathered may still be used and disclosed to others. This is done to help determine if the research was correctly done. You will not have access to your health information collected by the SPRINT study until the end of the study.

This authorization is valid for six years (or five years after the completion of the study), whichever is longer.

How will your privacy be protected?
Any information obtained about you during SPRINT will be treated as strictly confidential to the full extent permitted by applicable law. Your name and any other potentially identifying information will not be used on any data or samples you provide. However, your name and Social Security and Medicare numbers will be recorded and stored centrally to help the study keep track of any illnesses you may experience. You will not be identified in any SPRINT report or publication.

At the end of the study, all forms with your name or other identifying information will be kept in a locked room for five years. Only your study doctor or co-workers will have access to these forms.

After five years, the forms will be destroyed.

Also at the end of the study, the SPRINT data center will give the National Heart, Lung, and Blood Institute (NHLBI) all the data from the study, without any personal identifying information. Your blood, urine, tissue samples or other materials given during the study will be considered as your donations to medical research. The data and/or materials may be shared with NHLBI or other scientists who meet NHLBI requirements. They must treat the data or materials as confidential, get approval from their Human Subjects review boards, and agree not to share the data or materials with other parties. Drug companies that have contributed drugs, and in some cases money to SPRINT also will be given study data without any personal identifying information.

U.S. Federal Certificate of Confidentiality

SPRINT has received a Certificate of Confidentiality from the U.S. Federal Government to help protect your privacy. This certificate means that the SPRINT researchers cannot be forced to tell anyone unconnected with SPRINT about your participation. This includes courts and police. The researchers will only release information if you request it.

There are some limits to the researcher's ability to maintain your confidentiality. If we learn that keeping information private would immediately put you in danger, or put someone else we know about in danger, then we must tell the appropriate agencies to protect you or the other person.

WHAT ARE THE COSTS?

There are no costs to you for taking part in SPRINT. Clinic visits, physical exams, laboratory tests, electrocardiograms, and other procedures associated with this research are paid for by the study. In addition, your blood pressure drugs will be provided free of charge. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOU BE PAID FOR PARTICIPATING?

[each site must customize this section]

You will be paid $$ if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be paid $$ for each completed study visit.

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

[each site must use the language provided by their specific institution]

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 North Carolina Baptist Hospitals, Incorporated do 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 (336) 716-3467.

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 PI's Name at telephone number (also include after hours number).

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

You may choose not to take part in SPRINT, 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 ask you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators can stop your participation in SPRINT at any time. This could be because you had an unexpected reaction, did not follow instructions, or because the entire study has been stopped.

You will be given any new information gained during the study that might affect your health, welfare, or willingness to stay in SPRINT. We will give you the results of your laboratory tests and clinical measurements to share with your personal physician.

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, *Name* at *telephone number (also include after hours number)*.

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, you should contact the Chairman of the IRB at _____.

You will be given a copy of this signed consent form.

SIGNATURES

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 given to me. I have had a chance to ask questions about being in SPRINT and have had 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.

PARTICIPANT'S AGREEMENT FOR SPRINT STUDY

I have read the information provided above. I voluntarily consent to participate in the SPRINT study.

_____	_____
Subject Name (Printed)	Date
_____	
Subject Signature	
_____	_____
Person obtaining consent	Date

AGREEMENT FOR REPORTING MEDICAL RESULTS TO PHYSICIAN

I wish for important medical findings from my study tests/exams to be sent to my personal physician.

Yes_____ No_____

If Yes, provide full mailing address of the physician on the Contact Form.

AGREEMENT FOR AUDIO RECORDING

I agree to allow my memory testing to be recorded (voice only).

Yes_____ No_____

AGREEMENT TO PARTICIPATE IN GENETIC STUDIES

I agree to allow my genetic sample (DNA) to be used to study hypertension, heart and vascular disease, kidney disease, memory and brain disorders, and their risk factors.

Yes_____ No_____

AGREEMENT FOR SHARING GENETIC SAMPLE (DNA)

I agree to share my genetic sample (DNA) with other investigators who meet National Institutes of Health (NIH) standards and procedures.

Yes_____ No_____

AGREEMENT FOR SHARING GENETIC INFORMATION WITH National Institutes of Health (NIH) GWAS Data Bank

I agree to allow my genetic information to be transferred to the NIH GWAS Data Bank and to be shared with investigators who may not be associated with the SPRINT study.

Yes_____ No_____

AGREEMENT FOR LONG-TERM FOLLOW-UP

I agree to allow the SPRINT Data Center located at Wake Forest University or its designee to review and collect data on my medical records for specific study information through national data bases until 2030.

Yes_____ No_____