Informed Consent to Participate in Research

You are being asked to take part in a large research study. About 800 patients will take part in this study at many centers around the country. Your participation in this study is expected to last approximately 3 and a half years.

This consent form tells you about the study. The Principal Investigator (the person in charge of this research) or a co-worker of the Principal Investigator will also describe this study to you and answer all of your questions. Furthermore, throughout your treatment your care will be discussed with you and questions answered as needed. Before you decide whether or not to take part, read the information below and ask questions about anything you do not understand. Taking part in this study is entirely your choice.

1. Name of the Subject ("Study Subject")

2. Title of Research Study

A Trial of Tandem Autologous Stem Cell Transplants +/- Post Second Autologous Transplant Maintenance Therapy Versus Single Autologous Stem Cell Transplant Followed by HLA-Matched Sibling Non-Myeloablative Allogeneic Stem Cell Transplant for Patients with Multiple Myeloma

3a. Principal Investigator Contact Information

Insert name, affiliation and contact information.

3b. Contact information for emergencies after hours or on weekends or holidays

Call (###) ###-####, the in-patient Bone Marrow Transplant Unit. Ask to speak to the Charge Nurse.

4. Sponsor and Source of Funding or Other Material Support

The sponsor of this study, The National Institutes of Health (NIH), is providing financial support for the coordination of this study through the Blood and Marrow Transplantation Clinical Trials Network (BMT CTN).

5. What is the purpose of this study?

You are being asked to take part in this research study because you have multiple myeloma (MM), a cancer of the bone marrow. The study described in this consent form is designed to test different treatment strategies for patients with multiple myeloma. Multiple myeloma is considered incurable with chemotherapy (drugs that kill cancer) given at usual doses. This standard chemotherapy sometimes produces remission (absence of disease) in some individuals, but the disease recurs in all patients. Past studies have shown that high-dose chemotherapy can improve the survival of myeloma patients. However, this intensive therapy damages the special cells in the bone marrow called blood stem cells. Blood stem cells are cells found in the bone marrow and blood stream that produce all of the body's blood cells. Without healthy blood stem cells, a person cannot produce white blood cells (which fight infection), red blood cells (which transport oxygen to cells) or platelets (which help blood clot). Blood stem cells can be collected before chemotherapy to be returned intravenously (through a vein) after high-dose chemotherapy is given. This procedure is called autologous **stem cell transplantation** (SCT). Autologous transplantation is accepted standard therapy for patients with multiple myeloma. Although high-dose chemotherapy with autologous SCT has significantly improved the survival of myeloma patients, it does not cure them and the potential to further improve treatment remains. One approach has been to kill myeloma cells left after the first autologous SCT with another course of high dose therapy and a second autologous SCT. Studies have shown that receiving two autologous transplants a few months apart (tandem autologous SCT) improves survival for patients with multiple myeloma. Unfortunately, this approach still does not cure myeloma. It is not known if additional drugs given after tandem autologous SCTs will further improve survival of patients with multiple myeloma. This study will test whether additional treatment after two autologous transplants (standard care) will further improve the disease control and survival of patients with multiple myeloma. This will be tested by randomizing patients without a sibling donor to receive additional treatment for one year or no further treatment after their second autologous transplant. Randomizing means assigning to a treatment by chance, like the flip of a coin.

Another type of transplant is an allogeneic stem cell transplant where the patient receives high doses of chemotherapy, with or without radiation, followed by an infusion of blood stem cells donated by a sibling (brother or sister) who has the same tissue type (genetically matched). As with an autologous SCT, the blood stem cells would rescue your bone marrow from the toxic effects of chemotherapy and radiation. However, because the stem cells come from a healthy donor, these blood stem cells also replace your immune system with the donor's immune system. This new immune system also helps fight your myeloma. This effect of an allogeneic SCT is called a graft-versus-tumor effect. Unfortunately, the traditional type of allogeneic SCT that

uses high doses of chemotherapy and radiation can have many serious side effects and a high-risk of treatment-related death, particularly in patients with multiple myeloma.

The inability of many myeloma patients to tolerate a traditional allogeneic SCT may relate to combining the toxic effects of high-dose therapy and the immune effects of the allogeneic SCT in a single procedure. Recent studies have shown that a less toxic type of allogeneic SCT, called a non-myeloablative SCT (also sometimes called a mini transplant or reduced intensity transplant), when done following recovery from an autologous SCT, can more safely be carried out and still control MM. In this study, a patient who has a matched sibling donor will receive an autologous SCT followed by a non-myeloablative transplant once he or she has recovered from the autologous SCT.

The purpose of this study is to look at two different treatment approaches that involve stem cell transplants to improve the outcome of patients with multiple myeloma and to compare them with a common current approach, tandem autologous SCT. The two new approaches being studied are: 1) the use of additional drugs after tandem autologous SCT; and, 2) the use of a non-myeloablative allogeneic SCT after a single autologous SCT. Patients who don't have a matched sibling who can donate blood stem cells will undergo tandem autologous SCT. They will also be randomized (assigned by chance, like the flip of a coin) to receive additional therapy (a combination of two medications given by mouth called dexamethasone and thalidomide) or observation (disease will be watched with no more treatment) after recovery from the second autologous SCT.

Patients with a matched sibling donor who can donate stem cells will undergo a single autologous SCT and upon recovery will receive a non-myeloablative SCT from their sibling after first receiving low dose radiation therapy.

The two main purposes of this study are to determine:

1. For MM patients without a matched sibling donor, whether additional therapy after tandem autologous SCTs improves disease control and survival.
2. For MM patients with a matched sibling donor, whether tandem autologous transplants (with or without additional therapy) or a single autologous transplant followed by a non-myeloablative SCT from their matched sibling improves disease control and survival.

The study may find that patients who have different treatments for MM have similar results.

6. What will be done if you take part in this research study?

If you decide to take part in this study and have signed the informed consent, you and your matched sibling, if you have one, will be evaluated to make sure it is safe for you to participate in the study. Before starting treatment in this study, your doctor will check your general health.

You will have the following tests and evaluations to find out if you can participate:

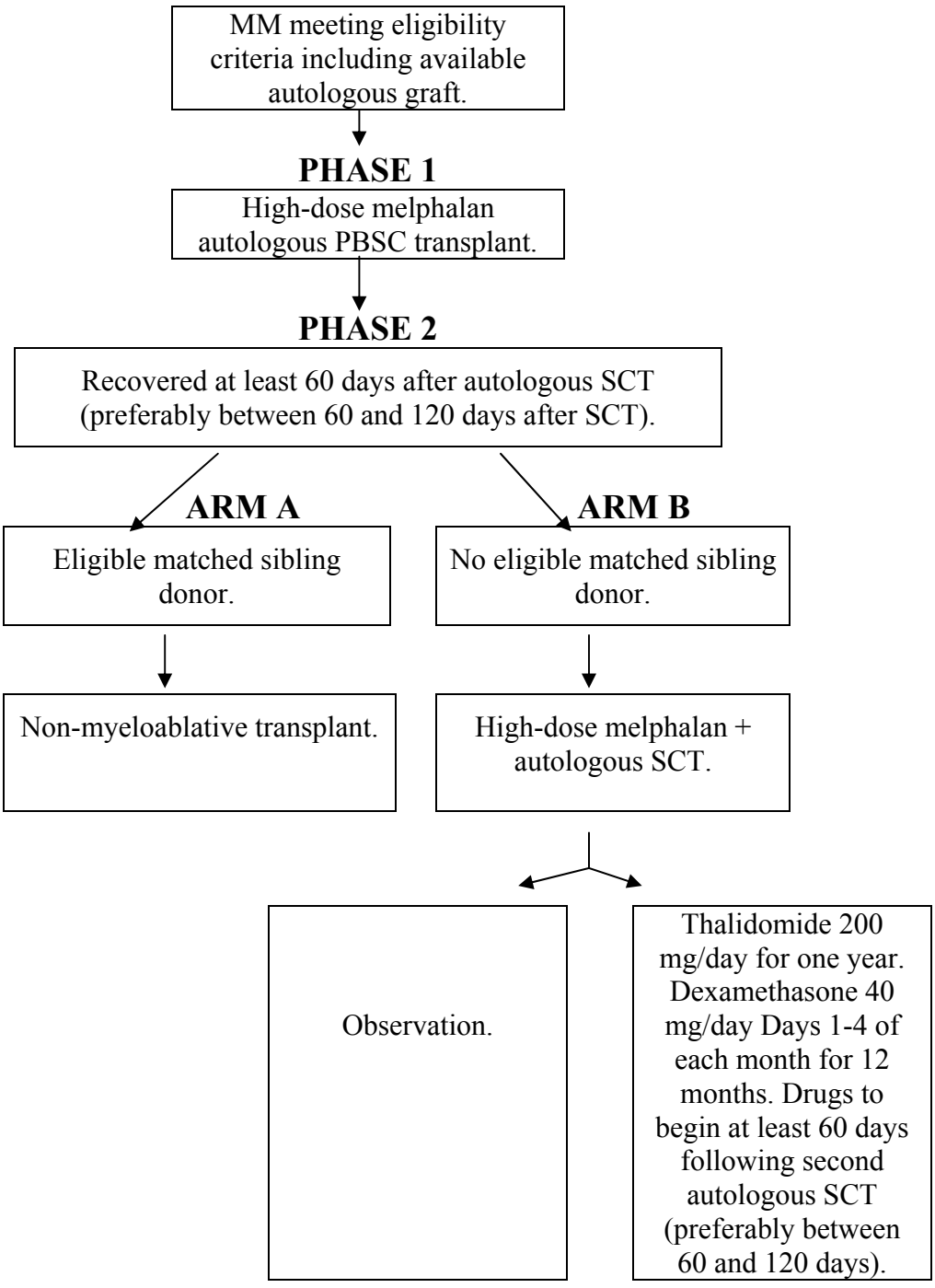
- Medical history and physical examination, including height and weight.
- Blood tests (approximately 4 – 5 tablespoons)
- Urine tests
- Electrocardiogram (ECG or EKG), a picture of the electrical action of the heart)
- Echocardiogram (a picture of the heart in motion made using ultrasound or sound waves) or MUGA scan (a picture of your heart after a small amount of radioactive material is injected into the bloodstream through a vein) to evaluate your heart function
- Pulmonary Function Test (PFT), which is a breathing test that tells how your lungs are working, measures the amount of air taken into your lungs and exhaled as you breath)
- Bone marrow biopsies and aspirates. A bone marrow aspiration is a procedure in which an area of the hipbone is numbed, and a small sample of bone marrow is withdrawn. A bone marrow biopsy is similar to a bone marrow aspiration, except a sample of bone is removed through the needle.
- If you are a woman able to have children, a serum pregnancy test will also be performed. If you are pregnant, you will not be able to take part in this study.

Some additional x-rays will be done to evaluate your disease. These tests will help your doctor determine the amount of disease you have at the start of treatment and to follow the status of your disease throughout your treatment.

This study is divided into two phases and is explained in detail below. All patients will undergo the Phase I treatment portion of this study, using high-dose melphalan followed by an autologous SCT. Under the Phase II treatment portion of this study, if you have a matched sibling donor, you will receive a non-myeloablative allogeneic SCT using your sibling's stem cells (referred to as Treatment Arm A). If you do not have a matched sibling who can serve as your donor, you will receive a second autologous SCT (referred to as Treatment Arm B) using the same high-dose melphalan chemotherapy as described in this consent under Phase I. Patients in Treatment Arm B will be randomized (like the tossing of a coin) to receive or not receive two additional medications (dexamethasone and thalidomide) given by mouth following their second autologous SCT. Your doctor will tell you which Treatment Arm you will be treated on and, if treated on Arm B, whether or not you are to receive the additional drug therapy.

One of the objectives of this study is to evaluate how the treatment affects the quality of the patient's life and whether there is a difference between the two treatment arms. Therefore, all English and Spanish speaking patients will be asked to complete questionnaires asking about their quality of life before the first and second transplant, and at 6 months, 1, 2 and 3 years after the second transplant. It will take you approximately half an hour to complete the questionnaires.

Outline of Treatment Plan



Phase I Treatment (All Study Participants)

Central Venous Catheter: You will need to have central venous catheter (CVC) placed to participate in the study. A central venous catheter is a flexible sterile tube that will be placed into a large vein that runs under your collarbone so that blood can be withdrawn and medications given to you more easily and with less discomfort. This tube is usually placed under local anesthesia. There is a lot of experience with the use of these catheters. Complications include blood clots and infection. Clotting may require removal of the catheter or treatment of the clot by instilling a medicine that dissolves blood clots into the line. If you develop an infection you will require treatment with antibiotics and your catheter may need to be replaced. Other uncommon side effects may include swelling of the face and arm and/or lung collapse. If the lung collapses, it may be necessary to place a tube between the ribs to allow the lung to re-expand.

Mobilization and Leukapheresis: You will receive chemotherapy to release your blood stem cells from your bone marrow into your circulating blood (mobilization) so that they can be collected. Your doctor will explain the side effects, benefits and type of the chemotherapy you will receive to mobilize your blood stem cells. Following chemotherapy for stem cell mobilization, you will receive a bone marrow stimulating medication called granulocyte-colony stimulating factor (G-CSF) by injection under your skin daily for approximately 10 days. G-CSF will help to move your stem cells out of the bone marrow into the bloodstream. You or someone who agrees to be responsible may be taught how to give you the G-CSF, so you can receive it at home. Once the number of stem cells in your blood stream is high enough, they will be collected over 2-5 days, while you are still receiving the G-CSF injections. A procedure called Leukapheresis will be done to collect your stem cells. During this procedure, your blood will be collected either through your central venous catheter or from a vein in one arm, processed through a machine to remove the white blood cells (stem cells), and then the rest of the blood will be returned to you through your catheter or a vein in the other arm. The leukapheresis procedure will last approximately several hours each time. **You will be asked to sign a separate consent form for the leukapheresis procedure.** Enough stem cells will be collected from you for two autologous SCTs in case you do not have a matched sibling donor to donate stem cells. Your stem cells will be frozen (cryopreserved) until the time when they will be given back to you.

Autologous Stem Cell Transplant: A couple of weeks after your stem cells have been collected, you will undergo an autologous SCT using high-dose chemotherapy with a drug called melphalan given over 15 to 20 minutes through your central venous line. Since this high-dose treatment destroys the normal bone marrow in addition to the myeloma cells, your blood stem cells (blood cells able to repopulate the bone marrow) must be given back to you. Your previously collected stem cells will be unfrozen and given back to you through your central venous catheter, similar to a blood transfusion, two days after you received the melphalan. Starting on the fifth day after you received your stem cells, you will be given the drug G-CSF, subcutaneously (under the skin). The G-CSF helps to stimulate the bone marrow to produce cells and will continue until your white blood count returns to normal.

Table -- High-Dose Melphalan / Autologous SCT

Day	-2	-1	0	+5 to Engraftment
Melphalan (200 mg/m^2 /IV)	X			
Stem cell infusion			X	
G-CSF (5 µg/kg/day) SQ or IV until white cells recover				X

After your stem cells have been reinfused, it will take about two weeks before adequate numbers of blood cells are made. During this time you may not be making any blood cells and therefore may require several red blood cell and platelet transfusions. Because your immune system is very weak, you may develop serious infections. You will be watched closely and receive antibiotics at the earliest sign of infection. During the time that your blood counts will be low, you may have mouth sores and feel very tired. You will receive medications to lessen these symptoms as much as possible. You will probably have a poor appetite during this time and may need to be given feedings through the central venous catheter. You may also receive pain medications as needed to minimize and control discomfort and pain. Once you begin to make new blood cells, the risk of serious infections will gradually be reduced. You should gradually come to the point where you will no longer require red cell and platelet transfusions. You should gradually regain your appetite. Although it is possible that the entire process may be done in the outpatient setting, it is also possible that a hospital stay of approximately 3 to 4 weeks will be necessary.

After completion of the transplant process, you will be followed in the outpatient clinic facility at least weekly, or as clinically indicated, until you are ready for your second SCT.

Phase II Treatment

Approximately 60 to 120 days after your autologous SCT, you will receive one of two therapies. If one of your siblings is a match and is able and willing to serve as your stem cell donor, you will receive a non-myeloablative SCT using your sibling's stem cells (referred to as Treatment Arm A). If you do not have a matched sibling who can donate stem cells, you will receive a second autologous SCT using the same high-dose melphalan chemotherapy (referred to as Treatment Arm B).

Treatment Arm A (allogeneic NMSCT)

Table – Allogeneic Non-myeloablative Stem Cell Transplant Schedule

	Day -3	**Day 0**	**Day +1**	**Day +27**	**Day +84**	**Day +114**	**Day +180**
TBI 200 cGy		X					
Cyclosporine twice a day	Start				Initiate taper	Off if not in PR* or CR* and no GVHD on Day +84	Off if CR or PR and no GVHD on Day +84
Mycophenolate Mofetil (MMF) twice a day		First dose 20:00hrs		Last dose			
Stem cell infusion		X	X				

* CR complete remission: PR partial remission.

If you have a matched sibling donor who is able and willing to donate stem cells for your transplant, he or she will have stem cells collected from his/her bloodstream by leukapheresis after treatment for several days with G-CSF. In most cases, the leukapheresis of the donor is done using the veins in the arms. Occasionally, if the donor's veins are not large enough, a central vein catheter may be required.

Your treatment will start three days before you are to receive your sibling's stem cells. You will begin taking an anti-rejection drug called cyclosporine, by mouth, twice daily for three days. On the fourth day you will receive a low dose of total body irradiation (TBI). The purpose of TBI is to allow your body to accept the donor cells without rejecting them. After the TBI is completed, your sibling's stem cells will be given to you through your central venous catheter. This is called a non-myeloablative allogeneic transplant (mini-transplant or reduced intensity transplant).

After the allogeneic non-myeloablative SCT you will continue to receive cyclosporine (CSA) and will start taking another medication, mycophenolate mofetil (MMF). The evening of your transplant, you will receive one dose of mycophenolate mofetil (MMF) by mouth. Starting the day after your transplant, you will be given MMF twice a day for a total of 27 days. MMF and CSA are given to prevent your body from rejecting your sibling's stem cells and to help decrease the risk of developing a complication called graft-versus-host-disease (GVHD). GVHD is a condition where your donor's immune cells attack your skin, liver, intestines and potentially other organs. Most patients transplanted with stem cells from a matched donor develop only a mild or moderate case of GVHD. However, some patients develop very severe GVHD, which can be fatal.

Because the chance of developing GVHD can persist many months after an allogeneic NMSCT, you will continue to receive cyclosporine for 84 days after your transplant. After 84 days, the cyclosporine dose will be gradually reduced based on how your disease has responded to the allogeneic NMSCT and whether you have developed GVHD. If there is no evidence that your multiple myeloma is worse and you do not have active GVHD, CSA will be stopped approximately 6 months after your non-myeloablative transplant. Patients with active GVHD may require CSA or other drugs that control GVHD for a longer period of time, as long as they have active GVHD. While you are taking CSA, blood tests to monitor the amount of CSA in your blood will be done at least weekly for the first several months and your dose of CSA will be adjusted if necessary to maintain the proper level in your blood.

Blood tests will be performed frequently to evaluate your response to treatment and possible side effects of treatment. If necessary, platelet and red cell transfusions will be given to maintain adequate levels and antibiotics will be given to treat or prevent infection. You may also require intravenous nutritional support and pain medications during or after transplantation. You will be monitored closely for any signs and symptoms of GVHD.

The medications cyclosporine and mycophenolate mofetil, although approved for sale by the Food and Drug Administration (FDA) and used commonly in stem cell transplantation, are not specifically approved by the FDA for use in stem cell transplantation. However, studies have shown that CSA and MMF have been successful in preventing and controlling GVHD.

Discharge and Follow up

After completion of your allogeneic non-myeloablative SCT, you will visit the outpatient clinic facility at least weekly for the first 2 to 3 months and then at least monthly until 6 months after your allogeneic non-myeloablative SCT. If you were referred from another doctor in order to undergo this procedure, you may return to the care of the referring doctor approximately six months after your allogeneic non-myeloablative SCT. You will need to return to the _____(medical facility performing transplant) at least every 6 months until 3 years after your allogeneic non-myeloablative SCT for evaluations. Most patients regain their strength and are able to return to their previous level of activity approximately 6 months after their allogeneic non-myeloablative SCT. However, each patient is different and your recovery may take longer or may even be a shorter period of time. Your ability to fight off infections may be weakened for at least one year or longer after the transplant and it may take you longer to recover from an infection or cold. Therefore, you will need to be careful and call your doctor if you have any symptoms of an infection or cold (e.g. fever, chills, cough, shortness of breath, sore throat or just not feeling well) during the first several months after transplant. If you are not sure, you may contact your doctor anytime and let him/her know how you are feeling and they will advise you on what to do. You should also call your doctor if you experience a skin rash, diarrhea, nausea, vomiting, jaundice (yellow skin), dry mouth, dry eyes, weight loss or difficulty breathing. These symptoms could be due to GVHD and require further evaluation.

Treatment Arm B (Second Autologous SCT)

If you do not have a matched sibling that can donate stem cells, you will have a second autologous SCT using the same procedure that is described under Phase I. You also will be randomized (like the tossing of a coin) between observation and receiving maintenance therapy (two anti-myeloma medications - dexamethasone and thalidomide) to begin once you recover from your second autologous transplant. The reason for this randomization is to determine whether or not receiving additional therapy will improve the outcome after tandem autologous SCT. Results from two recent studies show that thalidomide may slow the rate of relapse after autologous transplantation. These studies show that time to worsening disease may be longer in patients who get thalidomide. In these studies, thalidomide did not prolong survival, and did increase the number of side effects. The dose and timing of of thalidomide was different in these reported studies than in this study. We do not know if it is better to wait until a relapse occurs to use this drug. We also do not know whether thalidomide will significantly affect quality of life.

If you were randomized to receive maintenance therapy with dexamethasone and thalidomide, you will receive these two drugs beginning at least 60 days after your second autologous SCT. You will receive 40 mg of the drug dexamethasone for four days a month (once a day by mouth), for a total of 12 months. The drug thalidomide will be given every day for 12 months. You will start thalidomide 50 mg a day by mouth and the dose will be increased each week if you are tolerating it, until you reach a maximum dose of 200 mg per day.

Table -- Dexamethasone and Thalidomide Treatment Schedule

	Months 1-12
Thalidomide 200 mg/day PO	Start 50 mg/day and increase 50 mg/day each week as tolerated to target dose of 200 mg/day
Dexamethasone 40 mg/day PO	Days 1-4 of each month

You will be seen in the clinic at least weekly, or as clinically indicated, for the first several months, regardless of whether you were randomized to observation or maintenance therapy with dexamethasone and thalidomide. After three months you will be seen at least every month until 6 months after transplant and then you will be seen at least every 6 months until three years. If necessary, you may require more frequent follow-up.

Additional assessments: If you are a female patient that has any chance of becoming pregnant, you must have a serum pregnancy test performed. The test will be performed within 24 hours of starting thalidomide, weekly for the first four weeks of taking thalidomide, and then every four weeks if your periods are regular or every two weeks if they are not, until you have finished taking thalidomide (12 months).

7. Will You Provide Blood Samples for Research?

Research Blood Samples
Genetic material is any sample of tissue, blood, fluid, etc. obtained from you during the study. With your permission, 20 samples of your blood (2 teaspoons for each sample) will be collected during the course of the study and stored to be used solely for research purposes. The samples will be stored for future studies that will look at responses to treatment based on factors not yet known. These factors may relate to characteristics of your MM or to how your body tolerated the study treatments. Usually these blood samples can be drawn from you at the time of routine blood collections. Your confidentiality will be maintained because no identifying markers (name, etc.) will remain with the sample.

All BMT CTN research samples will be paired with the respective donor or recipient sample and given unique bar code designations that cannot be linked back to the donor or the recipient. All research samples will become property of the NHLBI after conclusion of the BMT CTN Protocol #0102 study. An NHLBI Biologic Specimen Repository Utilization Committee will advise NHLBI on requests for samples to perform research with these anonymous samples. If an Investigator request for these samples is approved by the committee, the NHLBI may provide a panel of the specimens requested using unique code numbers. Laboratory test results, clinical information, etc., associated with the coded samples are provided to the Investigator only after completion of the main protocol. Samples sent to researchers cannot be linked with any remaining sample at the repository.

If you agree to allow your blood to be kept for research, you are free to change your mind at any time. We ask that you contact [Principal Investigator] in writing and let him/her know you are withdrawing your permission for your blood to be used for research. His/her mailing address is on the first page of this form.

You are free <u>not</u> to take part in this additional future research. There will be absolutely no change in your care as a result of your refusal to give these additional samples. Please indicate your choice below:

- ❑ I agree to provide blood for future research.
- ❑ I do not agree to provide blood for future research.

_____ _____
Signature Date

8. What are the possible discomforts and risks?

The treatment used in this study may cause all, some, or none of the side effects listed below. Also, there is always the chance of unexpected new side effects.

ALL PATIENTS

Central Venous Catheter: There has been considerable experience with the use of central venous catheters. The most common complications are clotting and local infection which sometimes lead to a generalized infection in the blood. Clotting may require the removal of the catheter or treatment of the clot by a fibrinolytic agent (medicines that dissolve blood clots). Infections will be treated with antibiotics, and sometimes, removal of the catheter may be required. Occasionally, there has been skin redness at the catheter exit site, which may require treatment with an antibiotic. There is also a small risk of puncturing the lung at the time of the catheter insertion. If this occurs, placement of a temporary chest tube to reinflate the lung may be required and there are no long-term effects once it has resolved.

G-CSF: G-CSF may cause local pain and burning at the injection site and some patients experience pain in their bone when treated with this drug. The bone pain is generally mild to moderate in severity and controllable in most patients with oral medication. The growth factor may cause your white count to become very high, which could affect your blood flow. Your white blood cell count will be measured, and if it becomes too high, the dose of the growth factor will be reduced or stopped. Less common possible side effects include headaches, body aches, upset stomach, skin rash, fatigue and trouble sleeping. Local inflammation and rarely an infection at the G-CSF injection site may also occur.

Leukapheresis: If you have a central venous catheter, this procedure will be done through the catheter and not through a vein. If done through a vein, the needle insertion used for the Leukapheresis procedure may cause local bruising and infection in the vein or on the skin around the vein. The bruising resolves on it own and has no additional risks. The infection in the vein or of the skin around the vein would be treated with antibiotics.

Your blood will be thinned with citrate during the Leukapheresis procedure. Citrate decreases the calcium in the blood sometimes causing temporary numbness or tingling of the fingertips or around the mouth. Should you experience any numbness, you must tell the nurse operating the machine. You will be given a dose of calcium to reverse this side effect, before the problem becomes severe. Other possible side effects of the collection procedure include lightheadedness, nausea or more rarely, fainting due to temporary lowering of the blood pressure. Stopping the procedure and giving additional intravenous fluids can correct this. Occasionally, the filtering process also removes platelets (the cells that help the blood to clot). If your platelet count falls low enough to place you in danger of bleeding, any further collection will be postponed until a replacement transfusion is given.

AUTOLOGOUS STEM CELL TRANSPLANT

Melphalan: The most common side effect in patients who have received melphalan has been nausea and vomiting (mild to moderate), loss of appetite (mild), diarrhea and skin rash. Your doctor will prescribe drugs to prevent and lessen these side effects should they occur. Melphalan will irritate your skin if it leaks outside of the vein while being given. Let your doctor or nurse know if you feel any burning, stinging or pain while you are receiving this drug. Notify your doctor right away if the area around the injection becomes red or swollen after you receive the drug. Side effects that occur several days or a week later include low blood count, mouth sores, temporary hair loss, fatigue and poor appetite. You may need blood and platelet transfusions while your counts are low and/or antibiotics to fight infections. Mouth sores which sometimes extend into the throat or esophagus can be painful, and some patients may require 7 to 10 days of morphine or a similar medication to control the discomfort. Mouth sores can also make eating difficult. If this occurs, patients will receive their nutrition intravenously until the problem resolves. In rare instances, melphalan can cause lung damage or a secondary cancer (a cancer caused by prior cancer treatment). Secondary cancers are often very difficult to treat and can be fatal.

Infusion of Autologous Stem Cells: The stem cell infusion is given similar to a blood transfusion. It is given through your central venous catheter. You will be given pre-medications just prior to the infusion to decrease the risk of a reaction. There is a very slight risk of infection due to contamination of the stem cell products during their storage or drawing. Some patients react to the preservative called DMSO, which is used in the freezing process of your stem cells. You may notice a garlic taste or smell from the DMSO. Common, less serious reactions for patients receiving an autologous SCT include mild wheezing, mild shortness of breath, back or chest pain or lightheadedness. In rare instances, a severe allergic reaction called anaphylaxis can occur leading to a drop in blood pressure or extreme difficulty in breathing. You will be monitored very closely during the infusion and afterwards to look for these reactions and given medications and/or intravenous fluids to correct these side effects. These complications are reversible with treatment.

Risk of Infection and Other Complications of Low Blood Counts: After any of the therapies in this study, but before the stem cells have begun to make new blood cells, your ability to fight infections will be very low. During that time you will be very susceptible to serious infections and will need to take extra precautions to limit your exposure to infectious agents. Bacteria, fungi and viruses that can easily be destroyed by a healthy person's immune system can cause a serious, and sometimes fatal infection in patients with low white blood cell counts. You will be given medications to prevent infections and to treat them if you develop one as determined by your doctor.

After transplantation you may not be able to make red blood cells or platelets for approximately two to three weeks until the stem cells start growing in your bone marrow. If your red blood cell count is very low, you may have severe fatigue or shortness of breath. If your platelet count is low, there is a small chance of serious bleeding. Therefore, you may need red blood cell and platelet transfusions.

The risk of dying from the complications of an autologous transplant is less than 5%. This means that for every hundred patients who have an autologous transplant for multiple myeloma, up to 5 of them may die from complications of the treatment. It is not possible to know before your transplant if you will die from complications of treatment.

NON-MYELOABLATIVE ALLOGENEIC STEM CELL TRANSPLANT (Allogeneic NMSCT)

Total Body Irradiation (TBI): The immediate effects of irradiation may include nausea, vomiting, diarrhea, loss of appetite, painful swelling of the salivary gland under the jaw for a few days, and temporary hair loss. TBI may lower your blood counts. The dose of TBI used in this protocol is approximately one-sixth of that used in conventional transplant protocols, and severe side effects are not expected and have not been seen in other patients receiving this dose of TBI. TBI has been associated with causing sterility; however, it is expected that the risk of infertility will be lower than the risk after transplants that use higher doses of TBI. Although TBI can theoretically cause abnormalities in children born to transplant survivors, the incidence of genetic abnormalities has not been reported to be greater than the general population. However, this is a potential risk and birth control should be used for at least one year after transplant to minimize risks of conceiving. In addition, there may be a small increased risk of you developing other cancers in the future as a consequence of having received chemotherapy and TBI. Cancers that are caused by treatment with chemotherapy or radiation are often fatal.

Infusion of Allogeneic Stem Cells: The infusion of your donor's stem cells into you is generally well tolerated. There is a very slight risk of infection due to contamination of the stem cell products. There is a slight risk that the stem cells will not grow after they are infused. If this occurs, you would be expected to recover your blood counts with your own blood cells, if they were relatively normal prior to this treatment. There is a very small chance that if your donor's cells do not grow, your blood counts would not recover. If this were to happen, you could die from this problem.

Risk of Infection and Other Complications of Low Blood Counts: It is possible but not likely that you will develop low blood counts after your allogeneic stem cell transplant. However, even if your blood counts are normal your ability to fight infections is decreased after allogeneic transplant. Therefore, you will be very susceptible to serious infections for a period of time after your transplant and will need to take extra precautions to limit your exposure to infectious agents. You will be given medications to prevent infections and to treat them if one develops.

After transplantation you may not be able to make red blood cells or platelets for a few weeks and may need red blood cell and platelet transfusions.

The risk of dying from the complications of an allogeneic transplant as described in this consent are estimated to be less than 20%. This means that for every hundred patients who undergo a non-myeloablative allogeneic transplant for multiple myeloma, up to 20 of them may die from

complications of the treatment. It is not possible to know before your transplant whether you will die from complications of treatment.

Mycophenolate Mofetil (MMF): MMF is a recently approved drug used for suppressing the immune system and has not been extensively used in stem cell transplantation. Preliminary studies indicate that this drug is reasonably well tolerated in the transplant setting. There are a small number of patients who have received transplants and had reversible decreases in their red cell or white cell count while receiving MMF. Your blood counts will be monitored closely and if significant decrease is noted, lowering your dose or stopping your MMF may be indicated. Other uncommon side effects include nausea, vomiting, diarrhea, and abdominal discomfort. Occasional cases of gastrointestinal bleeding have also been reported in transplant patients. Your MMF dose may also be decreased if you have severe gastrointestinal (gut) side effects.

Cyclosporine: The immediate effects of this drug may include nausea or vomiting when given orally. Other possible side effects include developing high blood pressure (hypertension), shaking of the hands (tremor), increased facial hair growth, headache, and an effect on mental function. These effects are generally reversible upon decreasing the dose of the drug. An occasional patient has had a seizure but it is unclear whether cyclosporine, other drugs, or a combination of drugs was responsible. Some patients given intravenous cyclosporine for the treatment of GVHD have experienced a painful sensation in the hands or feet or both. The pain went away after the GVHD improved or when the cyclosporine was switched from the intravenous to the oral form.

The dose of cyclosporine may need to be reduced or possibly withheld if routine blood tests show a change in kidney function. This effect on the kidneys seems to increase when other drugs, which might cause kidney problems, are given at the same time, especially certain antibiotics. Occasionally, the kidney damage is severe enough to require the use of an artificial kidney machine (hemodialysis). During treatment, cyclosporine blood levels will be monitored periodically to determine if there are increased risks of side effects that warrant adjusting the dose.

Graft-Versus-Host-Disease: Graft-versus-host-disease (GVHD) is a known complication of allogeneic stem cell transplantation. This is a process where the donor's stem cells cause inflammation of your skin, liver, gastrointestinal system and/or other organs. About 50% of patients who have undergone a non-myeloablative allogeneic stem cell transplant have developed GVHD. Your risk of developing GVHD is thought to be about the same. Cyclosporine and mycophenolate mofetil will be given to you in this study to minimize the risk of developing GVHD.

GVHD is called acute GVHD when it starts during the first one hundred days after your transplant. It can cause a skin rash, inflammation of the liver and nausea, vomiting and/or diarrhea. Graft-versus-host-disease starting later on, more than 100 days after your transplant, is called chronic GVHD. It may cause mouth sores, diarrhea, inflammation of the liver, weight loss, joint pain, dry eyes, dry mouth, skin thickness and joint problems, and, rarely, lung damage. You may develop acute, chronic or both. If you develop GVHD, several medications to control the severity of GVHD are available and are usually successful in getting rid of or controlling the symptoms. Your doctor will discuss with you the different types of treatment available to treat

GVHD. Both acute GVHD and chronic GVHD are usually mild to moderate in severity. However, severe GVHD or complications of its treatment can be fatal.

LOW RISK PATIENTS

Multiple myeloma does not behave the same in all patients. There are lab tests that can, in general, identify patients who have a better survival after autologous transplantation than other MM patients. These lab tests include a blood test called beta-2 microglobulin and a standard bone marrow test called cytogenetics or chromosome study. As a group, patients with normal cytogenetics in the bone marrow and a low beta 2 microglobulin level in their blood have a better outcome than other MM patients after autologous SCT. On average this low risk group of patients have a survival of greater than 7 years following either single or tandem autologous SCT. These patients, however, are not cured of their MM and eventually they will succumb to their disease. It is possible that for this low risk group of patients, there is a greater risk of complications and dying from the allogeneic non-myeloablative SCT in the first few years after the transplant than if they had tandem autologous SCT. It is possible though that in the long-term, the benefit of a graft versus myeloma effect may result in a better outcome for the patients who received allogeneic non-myeloablative SCT. For low risk patients, this short term risk must be considered when considering participating in the study.

MAINTENANCE THERAPY (ARM B OF PHASE II)

Dexamethasone: This medication may temporarily increase blood pressure and blood sugar levels. Some patients require medication to control their blood sugar. Steroid medications have also been known to cause insomnia (difficulty sleeping), personality changes and depression. Dexamethasone may also cause nausea, vomiting, increased appetite, stretch marks, weight gain, fluid retention, gas and heartburn. These symptoms usually go away once the medication is stopped. Gas and heartburn can be treated with medications. Call your doctor if you experience these symptoms. Dexamethasone can also cause thinning and weakening of the bones.

Thalidomide: Thalidomide may very likely cause sleepiness, decreased alertness, constipation, increased appetite, weight gain, loss of sex drive, nausea, skin rash, dry skin, numbness and tingling of the hands and/or feet, dry mouth and temporary hair loss. Less likely side effects of thalidomide include slowing of the heart, depression, swelling of the face, hands, or feet, irregular menstrual periods, and milky like fluid leaking from the nipples. Your thalidomide dose will be adjusted to try and minimize these symptoms.

Reproductive Risks: Thalidomide causes severe birth defects in unborn babies if females who are pregnant take the drug. The risk of thalidomide causing damage to the embryo is up to 50% for females taking thalidomide during the "sensitive period" which is estimated to range from 35-50 days after the last menstrual period. It is not known whether thalidomide may cause birth defects in unborn babies if it is taken after the "sensitive" period. **A single dose of thalidomide, however, may cause birth defects.**

Birth defects observed in babies exposed to thalidomide during pregnancy include absent or abnormal legs and arms; spinal cord defects; cleft lip or palate; absent or abnormal external ear; heart, kidney and genital abnormalities; and, abnormal formation of the digestive system, including blockage of necessary openings. An association between thalidomide and autism has also been proposed.

Because of the severity of these abnormalities, it is extremely important that pregnancies do not occur while you are taking thalidomide.

You should discuss with your doctor what the best methods of birth control are for you. Remember, however, than no method of birth control besides complete abstinence provides 100% protection from pregnancy.

If you are a female patient taking thalidomide, you must either abstain from all reproductive sexual intercourse or use two methods of birth control or at least one highly active method (e.g., intrauterine device [IUD], hormonal [birth control pills, injections or implants], tubal ligation, or partner's vasectomy) and one additional effective method (e.g., latex condom, diaphragm, or cervical cap), for at least four weeks before starting thalidomide therapy, during therapy, and for at least four weeks after discontinuing thalidomide therapy even when there has been a history of infertility, unless due to hysterectomy or because you have been post-menopausal or have had no menses (that is no menstrual period) for at least 24 continuous months.

If you are a female patient and have any chance of becoming pregnant, you must have a serum pregnancy test performed. The test will be performed within 24 hours of beginning thalidomide, weekly for the first four weeks of treatment, and then every four weeks if the patient's periods are regular or every two weeks if they are not, until you have finished taking thalidomide (12 months).

If you are a male patient, you will be counseled that thalidomide may be present in your semen. You must use a latex condom every time you have sexual intercourse with a woman during therapy and for four weeks after discontinuing thalidomide, even if you have had a successful vasectomy. You should request that female partners use a second method of birth control in addition to using a male condom.

You must be willing and able to participate in the FDA mandated System for Thalidomide Educational Prescribing and Safety (S.T.E.P.S.™) if you are to receive thalidomide. Hence, you will be asked to sign a separate mandatory consent form (as part of the S.T.E.P.S.™ system). Also, all doctors and pharmacists will be registered to prescribe or dispense thalidomide.

ALL PATIENTS

Blood Drawing: The risks of drawing blood from a vein include discomfort at the site of puncture (where the needle is placed in the vein); possible bruising and swelling around the puncture site; rarely, an infection; and uncommonly, faintness from the procedure. If you have a central line or catheter, these risks will not apply to you and the risks of the central line were explained to you at the time you had the line or catheter placed. Occasionally even if you have a central catheter, you may require blood draws from a vein requiring a needle stick.

Bone Marrow Aspiration and Biopsy: A bone marrow aspiration is a procedure in which an area of the hip (buttock area) is numbed with local anesthetic, and a small sample of bone marrow is withdrawn. A bone marrow biopsy is similar to a bone marrow aspiration, except a sample of bone is removed through the needle. When the local anesthesia is given, you may initially feel a burning sensation in your skin and bone surface for several seconds. During the actual procedure itself, you may temporarily feel pressure and/or pain of varying degrees. If necessary, you may ask your physician for additional local anesthesia or a medication to ease your stress. You also may experience bleeding, and/or bruising after the procedure is completed and you may experience soreness in the area for a few days afterwards. Rarely an infection can develop.

Bone marrow aspirates and biopsies will be used to check how your disease is responding to the study treatments.

Unexpected Organ Damage and Other Side Effects: Although your major organs function well, it is possible that unexpected heart, lung, kidney, or liver damage may occur as a result of this therapy, which are rarely life-threatening and usually reversible with treatment. You will be informed if problems arise and the measures being taken to help you. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal despite intensive medical management. Other unpredictable side effects can occur and will be explained to you and treated by your physicians should unforeseeable problems arise.

Late Effects: These may include gland problems resulting in poor growth and sterility. There may be poor function of the thyroid gland, requiring thyroid hormone supplementation. There is also a risk of second cancers as a result of the chemotherapy and/or underlying disease. The risk of developing and dying from a secondary cancer is far less than the risk of dying from your disease without treatment. The long-term effects upon heart, lung, and brain are unknown.

Risk to the Unborn: The treatments in this study have not been proven to be safe at any stage of pregnancy. Therefore, if you are pregnant or nursing, you are not eligible for this study. Women who have the potential of becoming pregnant must use some effective method of birth control. Effective birth control would be defined as the following: 1) refraining from all acts of vaginal intercourse (ABSTINENCE); 2) consistent use of birth control pills; 3) injectable birth control methods (Depo-Provera, Norplant); 4) tubal sterilization or male partner who has undergone a vasectomy; 5) placement of an IUD (intrauterine device); and, 6) use, with every act of intercourse, of a diaphragm with contraceptive jelly and/or condoms with contraceptive foam.

Sterility and Future Childbearing Potential for Men and Women: Chemotherapy and /or irradiation may affect fertility. Male patients may become sterile (unable to produce sperm). Female patients may find that their menstrual cycle becomes irregular or stops permanently. However, this DOES NOT MEAN THAT YOU CANNOT BECOME PREGNANT, and you must use some effective method of birth control. Damage to reproductive tissue may result in birth defects or permanent inability to father a child or become pregnant. You should discuss these risks and options in detail with your doctor before entering this study.

Other Information:

There may be some unknown or unanticipated discomforts or risks associated with this treatment in addition to those specified above, but every precaution will be taken to assure your personal safety and to minimize discomforts.

Throughout the study, the researchers will tell you of new information that might affect your decision to remain in the study.

If you wish to discuss the information above or any other discomforts you may experience, you may ask questions now or call your doctor _____, the Principal Investigator or contact person listed on the front page of this form.

9a. What are the possible benefits to you for taking part in this study?

Although this study cannot be guaranteed to be of benefit to you, it is hoped that your taking part may lead to the improvement or disappearance of your myeloma and prolongation of your life. However, no benefit is guaranteed.

9b. What are the possible benefits to others?

A possible advantage of this study is that benefit to others may result from the knowledge gained from your participation in this research study.

10. If you choose to take part in this study, will it cost you anything?

You are responsible for the costs of treatment for your disease on this protocol. Your insurance provider may not cover all or part of these costs. You are not required to pay for tests or research samples that are being performed or collected only for research purposes. You or your family will have to pay installments based on your verified ability to pay. If you have concerns or questions regarding coverage or potential charges, you should contact (contact person's name) at (###) ###-####, or the Principal Investigator of the study, to review the situation.

11. Will you receive payment for taking part in this research study?

No.

12. What if you are injured because of the study?

You agreed to take the risks listed above. If you experience an injury that is directly caused by this study, only the professional medical care you receive at the [participating clinical facility] will be provided without charge. Hospital expenses will be paid by you or your insurance provider. No other compensation is offered. By signing this form you have not waived any of your legal rights. If you have any questions about injuries, you may call [insert name] at (###) ###-####.

13. What other options or treatments are available if you do not want to be in this study?

Participation in this study is entirely voluntary. You are free to refuse to be in the study, and your refusal will not affect current or future health care you receive at this institution. You and your doctor will discuss any other treatment options available to you.

Current therapies for multiple myeloma include:

- Chemotherapy using single or combinations of drugs
- Single autologoustransplants with or without additional drugs to prevent relapse after transplantation
- Double autologous transplants with or without additional drugs to prevent relapse after transplantation
- Allogeneic transplantation using a related or unrelated donor

You may also be eligible to receive other investigational treatment or you may decide not to receive any treatment. Your doctor will discuss these and other possible treatment approaches with you.

14a. How can you withdraw from this research study?

If you agree to be in this study, you are free to change your mind. At any time you may withdraw your consent to be in this study and for us to use your data. If you withdraw from the study, you will continue to have access to health care at [participating clinical facility]. If you decide to withdraw, we ask that you tell the [Principal Investigator] in writing; his/her mailing address is on the first page of this form. If you do withdraw your consent, there will be no penalty and you will not lose any benefits to which you are otherwise entitled.

Due to the nature of your illness and the study treatments, it is important to continue to receive medical follow-up even if you withdraw from the research study. If you have any questions about your rights as a study subject, you may call the Institutional Review Board (IRB) office at (###) ###-####.

14b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study, we ask that you agree that we can continue using all information about you that has already been collected as part of the study prior to your withdrawal, and to continue to allow your doctor to tell us about your progress until 12 months after your transplant. You may, of course, say no.

14c. Can the Principal Investigator withdraw you from this research study?

You can be taken off the study (with or without your consent) for any of the following reasons:

- You do not qualify to be in the study because you do not meet the study requirements.
- You need a medical treatment not allowed in this study.
- The investigator decides that continuing in the study would be harmful to you.
- The study treatments have a bad effect on you.
- You become pregnant as the study treatment could be harmful to the fetus.
- You are unable to keep appointments or take study drugs as directed.
- Other study-specific reasons; for example, if the study treatment you are taking has been found to be unsafe.
- The study is cancelled by the Food and Drug Administration (FDA) or the National Institutes of Health (NIH).
- Your myeloma returns.

15. How will your privacy and the confidentiality of your research records be protected?

Study records that have your name will be kept private as required by law. You will not be identified by name in the central study records. Your records will be given a unique code number. The key to the code will be kept in a locked file in the offices of the Coordinating Center for the study. Authorized persons from the [participating clinical facility], the hospital or clinic (if any) involved in this research, and the Institutional Review Board have the legal right to review your research records and will protect their confidentiality to the extent permitted by law. This research study is sponsored by and conducted with funds from the National Institutes of Health; therefore, the sponsor, the sponsor's agent, the Blood and Marrow Transplant Clinical Trials Network (BMT CTN), the investigators conducting this study, Southwest Oncology Group, and the FDA also have the legal right to review your research records. Otherwise, your research records will not be shown to anyone without your consent unless required by law or a court order.

If the results of this research are published or presented at scientific meetings, your name will not be disclosed.

16. Expiration date for retention of records

The study results will stay in your research record at [insert Institution] for at least six years or until after the study is completed, whichever is longer. At that time either the research information not already in your medical record will be destroyed or your name and other identifying information will be removed from such study results. Research information in your medical record will be kept indefinitely.

17. How will the researcher(s) benefit from your being in this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator may benefit if the results of this study are presented at scientific meetings or in scientific journals. In addition, the sponsor is providing funds to the Principal Investigator to facilitate the conduct of this study.

18. HIPAA[1] authorization to use and disclose individual health information for research purposes

a. Purpose: As a research participant, I authorize the Principal Investigator and the researcher's staff to use and disclose my individual health information for the purpose of conducting the research study entitled *A Trial of Tandem Autologous Stem Cell Transplants +/- Post Second Autologous Transplant Maintenance Therapy Versus Single Autologous Stem Cell Transplant Followed by Matched Sibling Non-myeloablative Allogeneic Stem Cell Transplant for Patients with Multiple Myeloma.*

b. Individual Health Information to be Used or Disclosed: My individual health information that may be used or disclosed to conduct this research includes: demographic information (e.g., age, date of birth, sex, weight), medical history (e.g., diagnosis, complications with prior treatment), physical examination findings, and laboratory test results obtained at the time of work-up and after transplantation (e.g., bone marrow tests, blood tests, biopsy results).

c. Parties Who May Disclose My Individual Health Information: The researcher and the researcher's staff may obtain my individual health information from (*list hospitals, clinics or providers from which health care information can be requested*).

_____

_____

_____

d. Parties Who May Receive or Use My Individual Health Information: The individual health information disclosed by parties listed in item "c." above and information

1 HIPAA is the Health Insurance Portability and Accountability Act of 1996, a federal law related to privacy of health information.

disclosed by me during the course of the research may be received and used by the following parties:

- Principal Investigator and the researcher's staff
- Dr. David Maloney, Study Chairperson and staff/laboratories at Fred Hutchinson Cancer Research Center
- Dr. Amrita Krishnan, Study Chairperson and staff/laboratories at City of Hope National Medical Center
- National Heart, Lung and Blood Institute (NHLBI) and National Cancer Institute (NCI), both of the National Institutes of Health (NIH), study sponsors
- Blood and Marrow Transplant Clinical Trials Network (BMT CTN), data coordinating center
- Southwest Oncology Group (SWOG), clinical trials cooperative group
- U.S. government agencies that are responsible for overseeing research such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP)
- U.S. government agencies that are responsible for overseeing public health concerns such as the Centers for Disease Control (CDC) and federal, state and local health departments
- Celgene (the manufacturer of thalidomide) and the S.T.E.P.S.™ Survey Coordinating Center (Slone Epidemiology Unit of Boston University School of Public Health)

e. Right to Refuse to sign this Authorization: I do not have the sign this Authorization. If I decide not to sign the Authorization, I will not be allowed to participate in this study or receive any research-related treatment that is provided through the study. However, my decision not to sign this authorization will not affect any other treatment, payment, or enrollment in health plans or eligibility for benefits.

f. Right to Revoke: I can change my mind and withdraw this authorization at any time by sending a written notice to the Principal Investigator to inform the researcher of my decision. If I withdraw this authorization, the researcher may only use and disclose the protected health information already collected for this research study. No further health information about me will be collected by or disclosed to the researcher for this study.

g. Potential for Re-disclosure: My individual health information disclosed under this authorization may be subject to re-disclosure outside the research study and no longer protected. Examples include potential disclosures for law enforcement purposes, mandated reporting or abuse or neglect, judicial proceedings, health oversight activities and public health measures.

h. This authorization does not have an expiration date.

19. Further Information

If you have further questions concerning this project at any time, you are free to ask them of Dr. _____, who will be available to answer them. His/her telephone number is located on the first page of the consent.

20. Consent Instructions

To voluntarily become a participant in this research study I must confirm the following and sign below.

* I have read all of the information in the Informed Consent and I have had time to think about it.
* All of my questions have been answered to my satisfaction. If I did not understand any of the words or parts of this study, I asked the study doctor or the research staff to explain what I did not understand.
* I voluntarily agree to be part of this research study and to follow the study procedures as directed. I agree to keep the research staff informed of my current contact information.
* I have been informed that I may discontinue my participation in this study at any time.
* Signing this consent form is not a waiver of my legal rights.
* I have received a signed copy of this Informed Consent to keep for my reference.

_____
Subject Name (please print)

_____ _____
Subject Signature or Legal Representative (relationship) Date & Time

_____
Name of Individual Conducting Informed Consent Discussion
(please print)

_____ _____
Signature of Individual Conducting Informed Consent Discussion Date

_____ _____
Signature of Witness (where Applicable) Date

I have fully explained the research study to the subject and answered all of the subjects questions.

_____
Name of Principal Investigator or Authorized Representative
(please print)

_____ _____
Signature of Principal Investigator or Authorized Representative Date

THALOMID™ (thalidomide) Informed Consent Forms

Important Information and Warnings for ADULT MALES

WARNING: SEVERE, LIFE THREATENING HUMAN BIRTH DEFECTS.

IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50, 100 OR 200 MG)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.

CONSENT FOR MEN:

INIT: _____ 1. I understand that severe birth defects can occur with the use of THALOMID® (thalidomide). I have been warned by my doctor that any unborn baby will almost certainly have severe birth defects or can even die if a woman is pregnant or becomes pregnant while taking THALOMID® (thalidomide).

INIT: _____ 2. 1 have been told by my doctor that I must NEVER have unprotected sexual contact with a woman who can become pregnant. Because THALOMID® (thalidomide) is present in semen, my doctor has explained that I must either completely abstain from sexual contact with women who are pregnant or able to become pregnant, or I must use a latex condom EVERY TIME I engage in any sexual contact with women who are pregnant or may become pregnant while taking THALOMID® (thalidomide) -- and for 4 weeks after I stop taking the drug, even if I have had a successful vasectomy.

INIT: _____ 3. I know that I must inform my doctor if I have had unprotected sexual contact with a woman who can become pregnant; or if I think, FOR ANY REASON, that my sexual partner may be pregnant. If my doctor is not available, I can call Celgene Drug Safety at 1-888-423-5436 or 1-888-668-2528 for information on emergency contraception.

INIT: _____ 4. I understand that THALOMID® (thalidomide) will be prescribed ONLY for me. I must not share it with ANYONE, even someone who has similar symptoms to mine. It must be kept out of the reach of children and should NEVER be given to women who are able to have children.

INIT: _____ 5. I agree any unused drug will be returned to Celgene by calling 1-888-423-5436. Shipping costs will be paid by Celgene.

INIT: _____ 6. I have read the THALOMID® (thalidomide) patient brochure and/or viewed the videotape, "Important Information for Men and Women Taking THALOMID® (thalidomide)." I understand the contents, including other possible side effects from THALOMID® (thalidomide). I know that I cannot donate blood or semen while taking THALOMID™ (thalidomide).

INIT: _____ 7. I understand that I must participate in a telephone survey and patient registry while I am on THALOMID® (thalidomide).

INIT: _____ 8. My doctor has answered any questions I have asked.

INIT: _____ 9. I understand that I might be asked to participate in an additional voluntary survey by mail or telephone to evaluate this S.T.E.P.S® program. My agreement or disagreement will not interfere with my ability to receive THALOMID® (thalidomide).

INIT: _____ 10. I acknowledge I may be contacted by a Celgene representative in regards to following the rules of the S.T.E.P.S. ® program.

AUTHORIZATION:

This information has been read aloud to me in the language of my choice. I understand that if I do not follow all of my doctor's instructions, I will not be able to receive THALOMID® (thalidomide). I now authorize my doctor to begin my treatment with THALOMID® (thalidomide).

Patient Name (please print)	Social Security No. (only last six digits required)	Date of birth (mm/dd/yyyy)	Patient, Parent/Guardian Signature	Date (mm/dd/yyyy)

I have fully explained to the patient the nature, purpose, and risks of the treatment described above, especially the risks to women of childbearing potential. I have asked the patient if he has any questions regarding his treatment with THALOMID® (thalidomide) and have answered those questions to the best of my ability. I will comply with all of my obligations and responsibilities as a prescriber registered under the *S.T.E.P.S.* restricted distribution program.

Physician Name (please print)	DEA No.	Physician Signature	Date (mm/dd/yyyy)

THALOMID™ (thalidomide) Informed Consent Forms

Important Information and Warnings for ADULT FEMALES OF CHILDBEARING POTENTIAL

WARNING: SEVERE, LIFE THREATENING HUMAN BIRTH DEFECTS.

IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50, 100 OR 200 MG)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.

CONSENT FOR FEMALES OF CHILDBEARING POTENTIAL:

INIT: _____ 1. I understand that severe birth defects can occur with the use of THALOMID® (thalidomide). I have been warned by my doctor that my unborn baby will almost certainly have severe birth defects or can even die if I am pregnant or become pregnant while taking THALOMID® (thalidomide).

INIT: _____ 2. I understand that I must not take THALOMID® (thalidomide) if I am pregnant, breast-feeding a baby, or able to get pregnant and not using the required two methods of birth control.

INIT: _____ 3. If I am having sexual relations with a man, and I am less that 50 years of age, and/or menses stopped due to treatment of my disease, I understand that it I am able to become pregnant. I must use at least one highly effective method and one additional effective method of birth control (contraception) AT THE SAME TIME:

At least one highly effective method	**AND**	**One additional effective method**
– IUD		– Latex condom
– Hormonal (birth control pills, injections, patch, implants)		– Diaphragm
– Tubal ligation (tubes tied)		– Cervical cap
– Partner's vasectomy		

These birth control methods must be used for at least 4 weeks before starting THALOMID® (thalidomide) therapy, all during THALOMID® (thalidomide) therapy, and for at least 4 weeks after THALOMID® (thalidomide) therapy has stopped. I must use these methods unless I completely abstain from heterosexual sexual contact. If a hormonal (birth control pills, injections, patch or implants) or IUD method is not medically possible for me, I may use another highly effective method or two barrier methods AT THE SAME TIME.

INIT: _____ 4. I know that I must have a pregnancy test done by my doctor within 24 hours prior to starting THALOMID® (thalidomide) therapy, even if I have not had my menses due to treatment of my disease, then every week during the first 4 weeks of THALOMID® (thalidomide) therapy. I will then have a pregnancy test every 4 weeks if I have regular and/or no menstrual cycles, or every 2 weeks if my cycles are irregular while I am taking THALOMID® (thalidomide).

INIT: _____ 5. I know that I must immediately stop taking THALOMID® (thalidomide) and inform my doctor if I become pregnant while taking the drug; if I miss my menstrual period, or experience unusual menstrual bleeding; stop using birth control; or think, FOR ANY REASON, that I may be pregnant. If my doctor is not available, I can call Celgene Drug Safety at 1-888-423-5436 or 1-888-668-2528 for information on emergency contraception.

INIT: _____ 6. I am not now pregnant, nor will I try to become pregnant for at least 4 weeks after I have completely finished taking THALOMID® (thalidomide).

INIT: _____ 7. I understand that THALOMID® (thalidomide) will be prescribed ONLY for me. I must not share it with ANYONE, even someone who has similar symptoms to mine. It must be kept out of the reach of children and should NEVER be given to women who are able to have children.

INIT: _____ 8. I agree any unused drug will be returned to Celgene by calling 1-888-423-5436. Shipping costs will be paid by Celgene.

INIT: _____ 9. I have read the THALOMID® (thalidomide) patient brochure and/or viewed the videotape, "Important Information for Men and Women Taking THALOMID® (thalidomide)." I understand the contents, including other possible side effects from THALOMID® (thalidomide). I know that I cannot donate blood while taking THALOMID™ (thalidomide).

INIT: _____ 10. I understand that I must participate in a telephone survey and patient registry while I am on THALOMID® (thalidomide).

INIT: _____ 11. My doctor has answered any questions I have asked.

INIT: _____ 12. I understand that I might be asked to participate in an additional voluntary survey by mail or telephone to evaluate this S.T.E.P.S® program. My agreement or disagreement will not interfere with my ability to receive THALOMID® (thalidomide).

INIT: _____ 13. I acknowledge I may be contacted by a Celgene representative in regards to following the rules with the S.T.E.P.S® program.

AUTHORIZATION:
This information has been read aloud to me in the language of my choice. I understand that if I do not follow all of my doctor's instructions, I will not be able to receive THALOMID® (thalidomide). I now authorize my doctor to begin my treatment with THALOMID® (thalidomide).

Patient Name (please print)	Social Security No. (only last six digits required)	Date of birth (mm/dd/yyyy)	Patient, Parent/Guardian Signature	Date (mm/dd/yyyy)

I have fully explained to the patient the nature, purpose, and risks of the treatment described above, especially the risks to women of childbearing potential. I have asked the patient if he has any questions regarding his treatment with THALOMID® (thalidomide) and have answered those questions to the best of my ability. I will comply with all of my obligations and responsibilities as a prescriber registered under the *S.T.E.P.S*. restricted distribution program.

Physician Name (please print)	DEA No.	Physician Signature	Date (mm/dd/yyyy)

THALOMID™ (thalidomide) Informed Consent Forms

Important Information and Warnings for ADULT FEMALES NOT OF CHILDBEARING POTENTIAL

WARNING: SEVERE, LIFE THREATENING HUMAN BIRTH DEFECTS.
IF THALIDOMIDE IS TAKEN DURING PREGNANCY, IT CAN CAUSE SEVERE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. THALIDOMIDE SHOULD NEVER BE USED BY WOMEN WHO ARE PREGNANT OR WHO COULD BECOME PREGNANT WHILE TAKING THE DRUG. EVEN A SINGLE DOSE [1 CAPSULE (50, 100 OR 200 MG)] TAKEN BY A PREGNANT WOMAN CAN CAUSE SEVERE BIRTH DEFECTS.

CONSENT FOR FEMALES NOT OF CHILDBEARING POTENTIAL:

INIT: _____ 1. I understand that severe birth defects can occur with the use of THALOMID® (thalidomide). I have been warned by my doctor that my unborn baby will almost certainly have severe birth defects or can even die if a woman is pregnant or becomes pregnant while taking THALOMID® (thalidomide).

INIT: _____ 2. I certify that I am not now pregnant, nor am I of childbearing potential as I have been in a natural menopause for at least 24 months (been through the changes of life); or I had my uterus/womb completely removed (hysterectomy).

INIT: _____ 3. I understand that THALOMID® (thalidomide) will be prescribed ONLY for me. I must not share it with ANYONE, even someone who has similar symptoms to mine. It must be kept out of the reach of children and should NEVER be given to women who are able to have children.

INIT: _____ 4. I agree any unused drug will be returned to Celgene by calling 1-888-423-5436. Shipping costs will be paid by Celgene.

INIT: _____ 5. I have read the THALOMID® (thalidomide) patient brochure and/or viewed the videotape, "Important Information for Men and Women Taking THALOMID® (thalidomide)." I understand the contents, including other possible side effects from THALOMID® (thalidomide). I know that I cannot donate blood while taking THALOMID™ (thalidomide).

INIT: _____ 6. I understand that I must participate in a telephone survey and patient registry while I am on THALOMID® (thalidomide).

INIT: _____ 7. My doctor has answered any questions I have asked.

INIT: _____ 8. I understand that I might be asked to participate in an additional voluntary survey by mail or telephone to evaluate this S.T.E.P.S® program. My agreement or disagreement will not interfere with my ability to receive THALOMID® (thalidomide).

INIT: _____ 9. I acknowledge I may be contacted by a Celgene representative in regards to following the rules with the S.T.E.P.S® program.

AUTHORIZATION:

This information has been read aloud to me in the language of my choice. I understand that if I do not follow all of my doctor's instructions, I will not be able to receive THALOMID® (thalidomide). I now authorize my doctor to begin my treatment with THALOMID® (thalidomide).

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Physician Name (please print)	DEA No.	Physician Signature	Date (mm/dd/yyyy)