BLOOD AND MARROW TRANSPLANTATION
STANDARD CONSENT FORM RISK STATEMENT

Format

The risks associated with the research should be divided into the following sections: (1) chemotherapy agents, including high dose chemotherapy, (2) radiation therapy, (3) other test articles (for example, investigational devices, biotherapy), and (4) procedures (for example, bone marrow aspirates, lumbar puncture, central line). As appropriate, sections on chemotherapy agents, high dose chemotherapy and radiation therapy must have a brief description of the general risks associated with use of this therapy. For protocols involving high dose therapy and transplantation, a section addressing the risks of high dose therapy, and graft-vs-host disease in particular, must be added.

In complicated protocols, especially those involving several phase consisting of different modalities, it may be appropriate to describe the risks associated with these interventions within sub-sections corresponding temporally to each of the phases. When a particular intervention occurs in several phases, the risks do not need to be repeated in each subsection. As appropriate, the consent should refer back to the previous occurrence of this risk.

Risks of specific chemotherapy agents

Descriptions of side effects of each chemotherapy agent will be divided into two parts. The first part will list the Common or Significant Side Effects, that is, those toxicities which are expected, or whose effect is significant. The second part (Other) may contain a more comprehensive listing of less likely, or rare toxicities.

In addition, this second part may contain the standard risk descriptions mandated by the cooperative groups or the NCI. Alternately, mandated Cooperative Group or NCI Statements may be included as an addendum to the consent form. In this case, the consent form will contain a clear reference to the presence of the addendum. The addendum will be initialed by the subject at the time that the consent document is signed. The addendum will have the same IRB number as the full consent, and will be retained by the investigator in the same manner as the full consent. A copy of the addendum will be given to the subject to keep.

The purpose of this division is to present to the subject, in a clear and understandable fashion, what effects he/she is likely to experience, or which would be of relevance to him/her.

revision: 10/28/97
Standard Statements

Standard statements, including risks of specific chemotherapy drugs, will be made available to all investigators, in various word processor formats, for use in preparing consent documents. We believe that this requirement will ease the burden on investigators and the IRB alike, as well as facilitating the process of informed consent with the subject.
STANDARD RISKS AND DISCOMFORTS STATEMENT
HEMATOPOIETIC STEM CELL TRANSPLANTATION PROTOCOLS

The following statements must be included in the consent form in the appropriate sections. Additional text should be added as necessary and appropriate.

ADULT CONSENT FORM
POTENTIAL RISKS AND DISCOMFORTS

This consent form covers the use of [PREP REGIMEN DRUGS] as preparation for [ALLO VS AUTO] [BM VS. PBSC] transplantation. You may also get a consent form for the collection and storage of your bone marrow or blood stem cells. The risks and possible side effects of the collection and storage of these cells are discussed in detail in those consent forms.

Autologous Stem Cell Transplantation

If you are being transplanted with your own blood or bone marrow cells (called an autologous transplant) these are the risks you may experience:

   Stem Cell Mobilization: If you are going to have an autologous blood stem cell transplant, you will be treated with chemotherapy, or medicines called growth factors, or both, in order to increase the number of stem cells in the blood. If you get chemotherapy as part of the mobilization, you may have side effects from the chemotherapy as described below. Also, the chemotherapy will damage your bone marrow and lead to a decrease in your blood cells (white blood cells, or red blood cells or platelets). This will put you at high risk for infection and bleeding, which may be life threatening. You may require blood transfusions.

   [specific drugs for mobilization]

   If you are treated with growth factors (like G-CSF or GM-CSF) you may have side effects as described below. Also, there is a chance that medicines like G-CSF which stimulate normal bone marrow cells may also stimulate some cancer cells. However, this has never been shown to happen in people.

   [specific growth factors for mobilization]
Stem Cell Collection (Leukapheresis): Collection of your stem cells can lead to low blood pressure and you may feel lightheaded. During the procedure, the medicine used to prevent clotting of the blood can cause bleeding, muscle spasms, and tingling in your legs, nose, fingers and toes. You may get low blood counts (which may increase the chance of bleeding) and you may need red blood cell or platelet transfusions. You may also find the repeated, long (4 hours) collections boring. It is also possible that we will not be able to collect enough stem cells from you, because the cells do not mobilize, or because you are getting too many side effects from the G-CSF or the leukapheresis. If we cannot get enough stem cells, you will not be able to get a peripheral blood stem cell transplant.

Bone Marrow Harvest: If you are getting an autologous bone marrow transplant, you will have your bone marrow collected in the operating room, while you are asleep. The risks of this procedure are bleeding (which may require blood transfusion), infection or pain. In addition, there are risks associated with general anesthesia which will be discussed with you in detail by the anesthesia doctor.

Stem Cell Infusion: Side effects of getting back your stored stem cells include chills, fever, abdominal cramping, diarrhea, nausea, vomiting, aching all over, chest tightness, shortness of breath, red colored urine, headache, rapid heart beat, scratchy throat and rash. Occasionally there can be damage to the kidneys caused by the broken down red blood cells mixed in with your stem cells. There is a small risk that the stem cells will not work after they are injected back into you. This is called "graft rejection or graft failure". If this happened, your blood cells would remain very low and you would be at risk for infection and bleeding. This could be permanent, and it would eventually lead to your death.

There is also a chance that stem cells collected from your blood or bone marrow may be contaminated by live cancer cells. Therefore, these cancer cells may be given back to you after the high dose chemotherapy, and may cause the cancer to come back after transplantation.
Allogeneic Stem Cell Transplantation

If you are being transplanted with blood or bone marrow cells from someone else (called an allogeneic transplant) these are the risks you may experience:

**Graft-vs-Host Disease** - You may get graft-vs-host disease (GVHD), which happens when the grafted marrow reacts against you. This can lead to damage to your liver (yellow jaundice and decreased function), damage to your intestine (diarrhea, pain, or bleeding) and damage to your skin (rash, peeling or shedding). This can be severe or even fatal. Even if treated, GVHD may cause skin thickening, joint pain and stiffening, dry mouth and eyes, diarrhea, intestine, lung or liver damage. GVHD also causes damage to the immune system, which could mean you get severe or fatal infections.

Some GVHD happens in most allogeneic bone marrow transplant patients, but it is severe in less than 20% of patients, and in many of those it is treatable. **[FOR UNRELATED BMT: Some GVHD happens in most unrelated bone marrow transplant patients, and it is severe in up to 40% of them. However, it is treatable in many of those patients.]**

Depending on how close you are matched to the donor, and the type of cancer you have, different medicines may be used to prevent graft-vs-host disease. These medicines may have side effects:

- **Cyclosporine** - damage to the immune system leading to severe infections, damage to the kidneys, high blood pressure, liver damage.
- **Methotrexate** - damage to the immune system leading to severe infections, liver damage, worsening of mouth sores, damage to the bone marrow which could lead to a longer time until the donor marrow starts to work.
- **Prednisone / Methylprednisolone** - damage to the immune system leading to severe infections, weight gain, high blood pressure, increased appetite, mood changes, softening of the bones (which could cause them to break), rarely high blood sugar (diabetes), or clouding of the lens of the eye (cataracts).
- **Antithymocyte Globulin** - damage to the immune system leading to severe infections, fever, muscle or joint pain, rash. Allergic reactions, such as rash, hives, or difficulty breathing, can happen. These allergic reactions can be severe or even fatal.
T-cell Depletion - taking T-cells out of the donated bone marrow may increase the chance that the bone marrow will not work after it is injected back into you (graft rejection or failed engraftment). In addition, taking out T-cells may increase the chance that the cancer will come back after the transplant, and may increase the chance that you will get another cancer.

Unrelated Donor Transplantation: Unrelated bone marrow is obtained from committed, well-informed, volunteer donors, using reliable registries. However, it is possible that the donor may change his/her mind and decide not to donate, after you have started the high-dose chemotherapy. If this happens, the chemotherapy would certainly cause prolonged or permanent bone marrow aplasia. Donors are informed prior to signing "Intent to Donate" that changing their decision after the chemotherapy has begun would be harmful or fatal to the person receiving the marrow transplant.

Stem Cell Infusion: Side effects of getting someone else's stem cells are the same as those for blood transfusion from another person. Transfusion may cause allergic reactions, such as fever, difficulty breathing, or in rare cases death. Transfusions can also lead to virus infections such as hepatitis or AIDS, but these risks are extremely small.

There is a small risk that the stem cells will not work after they are injected back into you. This is called "graft rejection or graft failure". If this happened, your blood cells would remain very low and you would be at risk for infection and bleeding. This could be permanent, and it would eventually lead to your death if not treated.

General Risks of High Dose Therapy - High dose chemotherapy kills your bone marrow cells. This is called "aplasia". Bone marrow aplasia leads to decreases in number of white blood cells, red blood cells and platelets. This will put you at high risk for infection and bleeding, which could be fatal.

You will probably need blood transfusions after high dose therapy. These transfusions may cause allergic reactions, such as fever, difficulty breathing, or in rare cases death. Transfusions can also lead to virus infections such as hepatitis or AIDS, but these risks are extremely small.

The high dose therapy may effect any of your organs (like lungs, heart, kidneys or liver), and this damage can be made worse by infections or use of other medicines. This damage may be severe or even fatal. Usually the damage gradually improves.
after transplant, however it is possible that some of these changes could be permanent.

**Specific Risks of High Dose Chemotherapy** - The following medicines will be used to prepare you for the transplant. These are the side effects you may get.

[There is another list of side effects attached to this form. Be sure and read that list and discuss it with your doctor.]

Most chemotherapy medicines will cause nausea or vomiting, and hair loss. Many will also cause decrease in blood counts (white blood cells, red blood cells, platelets) which can lead to infection, bleeding or fatigue. Many chemotherapy medicines will cause sterility (inability to father or bear a child). Some chemotherapy medicines can cause second malignant cancers to occur.

[list drugs by generic and trade name]

In addition to these side effects, high dose chemotherapy, especially when combined with radiation therapy, may cause damage to your heart, lungs, liver, kidneys or other organs. This damage may be made worse by infections you may get after transplantation, or because of other medicines (like antibiotics) you have to take to treat other side effects. Usually this organ damage gradually gets better after you recover from the side effects of the high dose chemotherapy, but in other cases it can be permanent or can be fatal.

**Specific Risks of Radiation Therapy** - These are the side effects of the radiation therapy you may get:

**Total Body Irradiation** - during or right after the radiation you may have loss of appetite, nausea and vomiting, mouth sores, hair loss or reddening of the skin, damage to liver, kidneys or intestine. Other side effects of radiation may happen months or years later. These side effects include decreased bone growth (leading to mildly decreased height), inability to father or bear children (sterility), clouding of the lens of the eye (cataracts) and decreased function of some glands like the thyroid (which may require that you take hormone supplements), damage to other organs like lungs, kidneys and heart.

revision: 10/28/97
[Radiation may also slow the growth of the brain of young children. This can cause school or learning problems, which can be severe.]

Radiation may cause you to get a second cancer.

**Testicular Radiation** - most men who get radiation to their testicles will become sterile (unable to father a child).

**Risks Associated with Other Test Articles**

[as appropriate]

**Risks Associated with Other Procedures**

Blood Drawing: You may experience slight pain when the needle is inserted. There may also be a small amount of bleeding or bruising at the site where the needle is inserted, or you could get an infection or clot in the vein when blood is drawn.

X-rays and CT Scans: X-rays and CT scans involve exposure to radiation, but below the levels considered to cause harmful effects. You will have to lie still on a table for a period of time to have these scans performed, and this may be uncomfortable. For some of these tests you will have a medicine called "contrast dye" injected by vein. This medicine can rarely cause allergic reactions such as rash, low blood pressure, difficulty breathing, or in very rare cases, death.

MRI Scans: You will have to lie still on a table for a period of time to have this scan performed, and this may be uncomfortable. You may also be uncomfortable being in an enclosed space. For some of these tests you will have a medicine called "contrast dye" injected by vein. This medicine can rarely cause allergic reactions such as rash, low blood pressure, difficulty breathing, or in very rare cases, death.

Bone Marrow Aspirate or Biopsy: This procedure may be painful. There may also be bruising or bleeding at the site of the biopsy, and there is a small risk of infection.

Venous Access Device (Central Line): In order to undergo this therapy you will
need one or more central lines. These are the risks associated with these central lines:

Placement of Vascular Access Device: The surgeon or radiologist who puts this catheter in will explain the risks in detail to you before he/she performs the procedure. These risks include the risks associated with anesthesia as for any operation, infection and bleeding. There may also be pain at the site where the device is inserted. Although it is rare, occasionally the lung is punctured during placement of a device and a tube must be placed in the chest to reinflate the lung. It is also possible that there may be injury to a major blood vessel, which could lead to severe bleeding.

Use of Venous Access Device: These devices can become infected and these infections may require antibiotics for treatment, or occasionally removal of the device. It is possible for a blood clot to develop at the end of the catheter in the vein. This might prevent the catheter from working or rarely lead to swelling of the arm or neck and face, or to pain. Sometimes the device would need to be removed and replaced.

[other procedures as appropriate]

Other Risks

Hazard to Unborn Child: This therapy may have harmful effects on an unborn child. Patients of child bearing potential must use effective birth control while participating in this study. Pregnant women and nursing mothers may be excluded from this study.

Experimental Therapy: Due to the experimental nature of this study, it is possible for you to have side effects which have not been seen before or are unexpected.
Addendum - Side Effects Associated with Specific Chemotherapy Drugs

**BCNU (Carmustine)**
*Significant/Common* - nausea, vomiting, mouth sores. BCNU can cause scarring of the lungs and difficulty breathing.

*Other* - vision changes, numbness or tingling of any area, damage to kidneys, flushing of skin, watering eyes.

**Busulfan (Myleran):**
*Significant/Common* - nausea and vomiting, rash (including darkening of the skin), inability to father or bear children (sterility). Busulfan can cause scarring of the lungs and difficulty breathing. Busulfan can rarely cause a liver problem called veno-occlusive disease, which can be fatal.

*Other* - dryness of mouth, cracking of lips, blurred vision, rash, dry skin, decreased size of testicles.

**Cytarabine (Cytosine Arabinoside, Ara-C, Cytosar):**
*Common or Significant:* nausea and vomiting, fever, loss of appetite, eye irritation, mouth sores, diarrhea, liver damage. Rarely Ara-C may cause fluid in the lungs (which can lead to difficulty breathing), or irritation of the brain (leading to dizziness and difficulty walking).

*Other* - inflammation of the nerves (pain, numbness, paralysis), ulcer and/or inflammation of the esophagus, abdominal pain, inflammation of the pancreas, urine retention, freckling, itching, skin ulcerations, general body aches, bone pain, chest pain.

**Carboplatinum (Carboplatin, Paraplatin)**
*Common or Significant:* nausea and vomiting, diarrhea, liver damage, damage to nerves (leading to tingling or pain in the arms or legs). Carboplatinum may cause kidney damage and hearing loss. Rarely carboplatinum causes allergic reactions (like rash, wheezing or rarely lowering of blood pressure).

*Other* - seizures, changes in vision (including blindness), loss of taste, low magnesium, calcium, potassium, phosphate in blood, swelling of the face, shortness of breath, increased heart rate, low blood pressure.

revised 11/18/97
**Cisplatinum (Cisplatin, Platinol)**
*Common or Significant:* nausea and vomiting, damage to nerves (leading to tingling or pain in the arms or legs), hearing loss. Cisplatinum can cause kidney damage, which may be severe

*Other:* seizures, loss of taste, low magnesium, calcium, potassium, phosphate in blood, swelling of the face, shortness of breath, increased heart rate, low blood pressure.

**Cyclophosphamide (Cytoxan):**
*Significant/Common:* nausea, vomiting, diarrhea, bleeding and irritation of urinary bladder, inability to father or bear children (sterility). Cyclophosphamide can rarely cause heart problems. Cyclophosphamide may cause second malignant cancers.

*Other:* mouth sores, kidney damage, darkening of skin and fingernails.

**Hydroxyurea (Hydrea):**
*Significant/Common -* nausea, vomiting, headache, dizziness, mouth sores, diarrhea, rash. Hydroxyurea may rarely cause seizures.

*Other:* hallucinations, disorientation, rash, redness of face, constipation, liver damage.

**Ifosfamide (Ifex):**
*Common or Significant:* nausea and vomiting, bleeding and irritation of urinary bladder. Ifosfamide may cause inability to father or bear children (sterility). Ifosfamide may cause second malignant cancers.

*Other:* seizures, hallucinations, coma, confusion, depression, dizziness, diarrhea, mouth sores, kidney damage, darkening of the skin and fingernails.

**Mitoxantrone (Novantrone)**
*Common or Significant:* nausea and vomiting, diarrhea, vomiting, mouth sores. If the drug leaks from the vein, it can cause severe skin and tissue damage. Mitoxantrone can cause damage to the heart and difficulty breathing, chest pain, or heart failure and death.

*Other* - Seizure, chest pain, rapid heart beat, rash.

*revised 11/18/97*
Melphalan (Alkeran): Significant/Common: nausea, vomiting, damage to lungs (including lung scarring), liver damage, loss of menstrual periods. Melphalan may cause inability to father or bear children (sterility). Melphalan may cause second malignant cancers.

Other: mouth sores, swollen joints, skin rash, itching.

Nitrogen Mustard (Mustargen):
Significant/Other: nausea, vomiting, weakness, dizziness. If the drug leaks from the vein, it can cause severe skin and tissue damage. Nitrogen mustard may cause second malignant cancers.

Other: Ringing in ears, hearing loss, diarrhea, liver damage, skin rash.

ThioTEPA
Common or Significant: nausea and vomiting, fever, severe mouth sores, and darkening and shedding of skin (like a severe sunburn). ThioTEPA may cause inability to father or bear children (sterility).

Other: headache, dizziness.

VP-16 (Etoposide, Vepesid)
Common or Significant: nausea and vomiting, fever, chills, mouth sores. VP16 may cause allergic reactions (rash, wheezing, shortness of breath, low blood pressure) which may be serious or fatal. VP-16 may cause leukemia or other cancers.

Other: liver damage, irregularities of the heart beat.