Approved by the Nemours IRB.	Valid from:	through					
IRB#JAX:		IRB# ORL:		IRB#PNS:		IRB# WIL:	
Abbreviated Study Title:							

NEMOURS
PARENTAL PERMISSION / INFORMED CONSENT FOR PARTICIPATION IN AN ONCOLOGY RESEARCH STUDY

This form may be used as a PARENTAL PERMISSION form for participants less than 18 years of age, or as an INFORMED CONSENT form for participants 18 years of age and older. If you are an adult participant in this research study, please note that any time the term "*your child*" appears in this document, it should be read and understood to mean "you".

You have been asked to permit your child to be in a research study. This form explains the research, your child's rights as a study participant, and any responsibilities that you may have as a result of your child's participation. You should understand the research study before you agree to permit your child to be in it. You will get a copy of this form. Read it carefully. You will be given a copy of the protocol (full study plan) if you ask. You may also talk with your family or friends about it. The research team will answer any questions you have before you make a decision. Your child's oncologist is the study doctor and will explain the research and other options in detail. Do not sign until all your questions are answered.

1. WHAT IS THE TITLE OF THE STUDY?

COG ASCT0631/PBMTC SCT051 "A Phase III Randomized Trial of G-CSF Stimulated Bone Marrow vs. Conventional Bone Marrow as a Stem Cell Source In Matched Sibling Donor Transplantation" **Recipient Informed Consent Form**

2. WHO IS SPONSORING OR PAYING FOR THIS STUDY?

This study is a National Cancer Institute (NCI)-approved study conducted through the Children's Oncology Group (COG). COG develops and coordinates cancer studies conducted in over 200 member institutions throughout the U.S. and Canada, as well as sites in Europe and Australia. As a member institution, Nemours Children's Clinic receives funding from COG to conduct pediatric oncology studies. Funding from COG supports research and educational programs at Nemours.

3. WHO IS IN CHARGE OF THE STUDY AT NEMOURS?

	Nemours – Jacksonville	Nemours - Pensacola	Nemours - Delaware
Principal Investigator	Eric Sandler, MD	Chatchawin Assanasen, MD	Gregory Griffin, MD
Co-Investigators	Paul A. Pitel, MD Michael J. Joyce, MD, PhD Cynthia Gauger, MD Scott Bradfield, MD Manisha Bansal, MD	Jeffrey Schwartz, M.D.	Christopher Frantz MD Andrew Walter MD Robin Miller MD Rita Meek MD Jonathan Powell MD E. Anders Kolb MD
Address	Division of Hematology/Oncology 807 Children's Way Jacksonville, Florida 32207	Division of Hematology/Oncology 5153 North Ninth Avenue Pensacola, Florida 32504	Division of Hematology/Oncology 1600 Rockland Road Wilmington, Delaware
Daytime Phone	[redacted]	[redacted]	[redacted]
After Hours Phone	[redacted]	[redacted]	[redacted]
Long Distance	[redacted]	[redacted]	[redacted]

4. WHO SHOULD RESEARCH PARTICIPANTS CONTACT ABOUT THEIR RIGHTS?

Tim Wysocki, Ph.D., Chairperson, Nemours-Florida Institutional Review Board at [redacted].
Paul Garfinkel, MSH., Director, Nemours Office for Human Subjects Protection, at [redacted].
(Nemours Long Distance Operator) [redacted]
Website: http://www.nemours.org/research/nohsp.html . Email: NOHSP@nemours.org.

5. WHO CAN BE IN THE STUDY?

Your child is being asked to take part in this study to test if G-CSF bone marrow transplantation will keep more patients in remission. Your child has been treated for a cancer of the blood cells called leukemia. He/She has received chemotherapy treatment for his/her cancer and now has no visible signs of leukemia. This is called remission. Your child's doctor has recommended that your child have a stem cell transplant. Stem cell transplant (SCT) is a method of replacing blood-forming cells that were destroyed by cancer treatment. The stem cells are given after treatment to help the bone marrow recover and continue producing healthy blood cells.

We are studying the effect of a growth factor drug given to your child's donor that can help increase the number of stem cells that we collect from your child's donor's bone marrow. This drug is called G-CSF or filgrastim or Neupogen. Throughout the rest of the consent form we will call it G-CSF.

There will be about 425 patients participating in this study at Children's Oncology Group member institutions across the country.

6. WHAT IS THE PURPOSE OF THE STUDY?

Bone marrow transplant is recommended by many physicians for children with leukemia that have a high chance of relapse with chemotherapy alone. Bone marrow transplant is not recommended for all types of leukemia. This is a phase III study of bone marrow transplant using donated bone marrow that has been treated with G-CSF. A phase III study is done to compare the effects, good and/or bad of an experimental treatment against a standard treatment.

G-CSF has been approved by the Food and Drug Administration. It is a white cell growth factor that is often given to people with cancer. When G-CSF is given to a donor, it can help increase the number of stem cells in the donor's bone marrow.This treatment has been previously used in a clinical trial for patients receiving transplants from related donors. The main purpose of this study is to determine if G-CSF will increase the number of stem cells donated by your child's donor for transplant, and if those increased numbers of stem cells might provide a benefit to you in terms of improved survival.

The goals of this study are:

- **To compare the effects, good and/or bad, of an experimental treatment (G-CSF given to the bone marrow donor) against standard treatment (no G-CSF given to the bone marrow donor) for patients during their stem cell transplant (SCT).**
- **To compare the speed of cell recovery in patients receiving the experimental G-CSF bone marrow with those receiving standard treatment bone marrow.**
- **To evaluate and compare the occurrence of GVHD in patients receiving G-CSF bone marrow with those receiving standard bone marrow.**
- **To evaluate how the immune system (body system that helps fight infections) is restored in patients transplanted with G-CSF bone marrow.**

7. HOW LONG WILL PARTICIPATION IN THE STUDY LAST?

Participants in this clinical trial are expected to receive treatment on this study through the day of their transplant (Day 0). After study treatment, participants will have follow-up examinations and will continue to receive standard clinical care for transplant related complications. We will continue to collect some medical information about how your child is doing for up to 10 years after the bone marrow is given.

8. WHAT ARE THE RESEARCH PROCEDURES?

Random Assignment

Your child will go on 1 of the 2 different arms of the treatment plan. The arm your child is assigned to is decided by a process called randomization. Randomization means that the treatment is assigned based on

chance. It is a lot like flipping a coin, except that it is done by computer to make sure that there are about the same number of people on each treatment arm of the study. Some participants will be randomized to receive the Standard Treatment arm. Others will get the Experimental Treatment arm. If you consent to allow your child to take part in the study, randomization will be done before the stem cell transplant. The randomization process is described in your COG Family Handbook for Children with Cancer.

Treatment Plan

Prior to your child's transplant, it is standard to receive chemotherapy or radiation therapy to prepare your child for his/her transplant. The type of preparative treatment your child receives will depend on the type of leukemia he/she has. Your child's doctor determines this treatment and will discuss this with you. Information about the different preparative treatments can be found in Attachment #1. These treatments are different, based on the kind of leukemia your child has. Patients with acute lymphoblastic leukemia (ALL) get one kind of treatment. Patients with acute myeloid leukemia (AML), or related diseases like chronic myelocytic leukemia (CML), juvenile myelomonocytic leukemia (JMML) and myelodysplastic syndrome (MDS) get a different kind of treatment. These treatments are not experimental, but are standard for your child's type of disease. It is also standard to have an extensive evaluation of your child's health and disease status, including a bone marrow test and tests of the function of specific organs such as heart, liver and kidneys.

The donor bone marrow will be given to your child, through his/her central venous line (CVL). This is considered "Day 0" or "transplant day". These cells will be given to restore normal bone marrow function. The bone marrow will be given in a small transfusion bag through your CVL, much like a blood transfusion.

The two treatment arms are called A and B as follows:

- Arm A: Experimental Treatment Arm (G-CSF bone marrow from your child's donor will be transplanted)
- Arm B: Standard Treatment Arm (standard bone marrow from your child's donor will be transplanted)

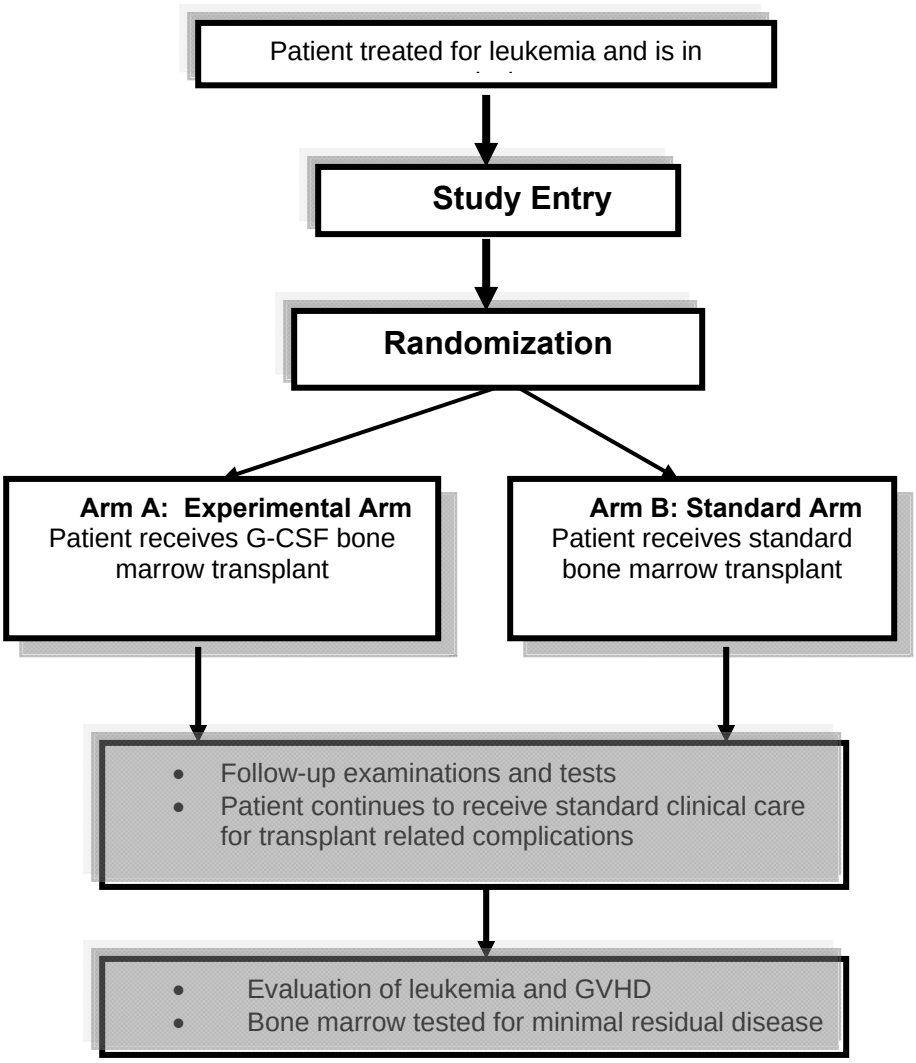
Standard procedure for bone marrow donation/transplantation -The procedure to collect the donated stem cells is called the harvest. Prior to the harvest, a medical evaluation is done and blood is drawn to test for diseases such as hepatitis and AIDS. If your child is a female who is able to become pregnant, a pregnancy test will be required from her. If your child's medical examination and the lab tests show any abnormalities, you will be informed.

If your child's medical evaluation and blood tests are normal, he/she will have the harvest in the operating room. Donated stem cells in children are usually collected from the bone marrow, but they can be collected from the blood as well (peripheral blood stem cells).

The largest amount of bone marrow that contains stem cells is found in the hip bone. The stem cells are collected from the hip bone by insertion of needles and aspiration (*removing by suction of a syringe*) of the marrow. The bone marrow cells are collected over a time period of one to two hours. This is almost always done in the operating room. The donor is given medicine so that they are asleep and don't feel the procedure. Hospitalization may be required on the day of the marrow harvest and your child can expect to be discharged from the hospital one to two days later.

Diagram of treatment

A diagram of treatment can be seen below.



Treatment Plan Tables

The following tables show the difference in how treatment will be given to participants on Arm A and Arm B of this study. Day 0 means the day when the pre-transplant treatment (Attachment #1) is complete and the marrow is infused.

Arm A: Experimental Arm (G-CSF Bone Marrow Transplant)

Drug	How the marrow will be given	Days
G-CSF Bone Marrow Transplant	Given by CVL over about 3-4 hours	Day 0

Arm B: Standard Arm (Standard Bone Marrow Transplant)

Drug	How the marrow will be given	Days
Standard Bone Marrow Transplant	Given by CVL over about 3-4 hours	Day 0

If your child is on Arm A, he/she will receive a standard transplant preparative treatment and will be transplanted with donated G-CSF bone marrow.

If your child is on Arm B, he/she will receive a standard transplant preparative treatment and will be transplanted with standard donated bone marrow.

Optional Research Study Tests and Procedures

We would like to collect an additional amount of blood for optional research tests. These research tests will not affect the treatment your child receives on this study and therefore the results of these tests will not become part of your child's health records, and will not be available to your child or your child's doctor.

If you give permission to use your child's samples and later decide that you no longer want your child's samples used for these studies, you can let your child's doctor know and the specimens will be destroyed.

Please see the signature section at the end of this consent form for details about how the COG will use your child's blood for research purposes. You can decide if your child would like to participate in these optional studies at the end of this consent form. Please read the information sheet at the end of this consent form called "How is Tissue Used for Research?" to learn more about using specimens for research.

You can choose to allow your child to take part in this clinical trial without taking part in the following tests. The results may help to improve treatments for leukemia in the future. No matter what you decide, your child's care will not be affected. A check box for your decision about taking part in this test is provided at the end of this consent form.

Immune Reconstitution Studies

During your child's treatment we will collect blood to monitor your response to treatment at certain time points. Immune reconstitution is how the immune system (body system that helps fight infections) is restored**.** If you agree to allow your child to take part in the Immune Reconstitution Studies, we would like to take about 2 teaspoons of extra blood at 3 time points (month 3, 8, and 12 after bone marrow transplant).

Follow-up

After study treatment, subjects will have follow-up examinations and will continue to receive standard clinical care for transplant related complications. We will continue to collect some medical information about how you are doing for up to 10 years after the bone marrow is given.

9. WHAT ARE POSSIBLE RISKS OF BEING IN THIS STUDY?

Any research has some risks (things that could make your child sick, make your child feel uncomfortable, or hurt your child). The risks with the most chance of happening to someone in this study are listed below. There is a chance of other risks that almost never happen. Other presently unknown side effects may occur. Your child will be watched closely and the drug doses will be decreased or discontinued if serious side effects develop.

Treatment Risks

Patients who receive stem cell transplants are at risk of having significant side effects. Some of the common side effects include infection and graft-versus-host disease (GVHD). More serious side effects can include problems with organ function or possibly death. The risks of transplants are listed in Attachment #3.

There is a risk that the treatment plan will not get rid of the cancer or that the cancer can go away after the treatment and then come back at a later date.

Risks of Study

It is possible that this study treatment may be less effective than other therapy options. It is also possible that the study treatment may cause more side effects than other therapies. Since receiving G-CSF bone marrow might result in receiving a higher stem cell dose, there is the possibility of an increased risk of GVHD.

GVHD is a risk of any bone marrow or stem cell transplant where the cells come from another person (the donor). GVHD occurs when the donor's white blood cells recognize the patient's body as "foreign". In acute graft-versus-host disease, which occurs within 3 months of transplant, the skin, liver, or intestine may be affected. This may result in a rash, yellowness of the skin (jaundice) or very watery diarrhea. Medications will be given to help prevent GVHD. However, mild to severe GVHD may still occur due to the transplant. If GVHD should develop, it will be treated with steroids, which are successful in eliminating or controlling symptoms in many patients. We are often successful in controlling acute graft-versus-host disease with medicines, but not always, and fatal complications may arise.

Chronic graft-versus-host disease occurs most commonly in patients who have had acute graft-versus-host disease, but may occur in patients who did not have any acute symptoms. Patients can have problems with skin, liver, intestine, joints, mucous membranes, eyes, or other organs. Chronic scarring may result. Medicines can help, but may not completely eliminate all the symptoms. Chronic GVHD may have lingering symptoms for years, or may go away completely. Infection is a major risk in patients with chronic GVHD, as the immune system takes a very long time to recover and some cases might not be completely normal again.

We do not know for certain whether the use of G-CSF bone marrow might increase the risk of either acute or chronic GVHD, although other studies have not shown any such risk.

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

10. WHAT ARE POSSIBLE BENEFITS OF BEING IN THIS STUDY?

We hope that your child will get personal medical benefit from participation in this clinical trial, but we cannot be certain. The potential benefit could include a quicker recovery from the low blood counts after transplant or a better chance of a getting rid of cancer for a long time.

We expect that the information learned from this study will benefit other patients in the future.

11. WHAT HAPPENS IF A PROBLEM OR INJURY RESULTS FROM THE RESEARCH PROCEDURES?

If you think that your child has been injured while in this study or has a problem related to the study, you should tell one of the study doctors. The study doctor or research staff will tell you what you should do. The investigators' names and phone numbers are on the first page of this form. If your child needs treatment for a problem related to the study, you might be asked to bring him/her to the clinic or you may be told to take your child to the closest emergency room. Nemours will assure that your child receives treatment, if needed, for study related injuries. However, there are no funds set aside by Nemours the study doctors, or COG, to pay for medical care provided to treat problems or injuries resulting from participating in this study. If your child has health insurance, it may, or may not pay for the cost of treatment resulting from a study-related injury. If insurance does not pay, you understand that you will be responsible for paying for the cost of treatment.

If you have a question or problem related to the study, you can call the staff anytime. The study staff is available Monday-Friday from 8:00am to 5:00pm. During these hours, call the daytime number for your clinic (one page 1 of this form) for medical advice.

During evenings, weekends, and holidays, call the after hours number for your clinic (on page 1 of this form). You will reach the Nemours operator. Ask to page the Oncologist on call.

12. IS BEING IN THE STUDY VOLUNTARY?

Being in this study is totally voluntary. Anyone who takes part in the study can stop being in it at any time. There will be no change to your child's usual medical care if your child decides not to be in the study or decides to stop being in the study. No one will be angry with your child, or treat your child any differently than before your child was asked to be in the study.

If you withdraw your child from this study, your child may continue treatment at Nemours, or you may seek treatment for your child from another doctor of your choice. If you withdraw your child from the study treatment, the study doctor will ask your permission to continue study follow-up. All health information related to the study may continue to be collected from your child's medical records.

13. WHAT OPTIONS ARE AVAILABLE OTHER THAN BEING IN THIS STUDY?

You can refuse to permit your child to participate in this study. There may be other research or treatment choices that could be considered for your child. Your child can still be treated at Nemours according to standard medical care, even if he or she does not take part in this study. Instead of being in this study your child has these options:

- **Receiving a standard stem cell transplant. The therapy is described on page 3. It is Arm B of this study.**
- **Receiving a transplant where your doctor decides to use G-CSF bone marrow. This is not a standard stem cell transplant, and is Arm A of the study.**
- **You may choose a chemotherapy approach and not undergo transplantation.**
- **You may take part in another study.**
- **You may decide not to receive treatment at this time.**

The study doctors will provide detailed information about the benefits and risks of the various treatment options available to your child. Please discuss these options with your regular doctor as well as other trusted personal and family advisors.

14. CAN THE RESEARCHERS REMOVE SOMEONE FROM THE STUDY?

The study doctors may take your child off study treatment if they feel it is in your child's best interest, or if new information becomes available that might affect your child's participation. If the disease becomes worse, if side effects become very severe, or if the study doctor feels that study treatment is no longer the best treatment for your child, the treatment would be stopped and other treatment options would be discussed. If study treatment is stopped, your child will continue in the follow-up phase of this study. There is no reason that we know of for your child to be removed from the study altogether.

15. WHAT ARE THE COSTS OF BEING IN THIS STUDY?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your child's cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

There is no charge for procedures that are done for research purposes only, like the samples that are sent to the COG research laboratories.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site. You can also call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

16. WILL PEOPLE BE PAID FOR BEING IN THIS STUDY?

No arrangement exists that would allow participants to share in any profit generated from this study or future research, or any new products that may be developed from research on biologic specimens.

17. WILL I BE TOLD OF ANY NEW INFORMATION THAT MIGHT AFFECT MY WILLINGNESS TO PERMIT MY CHILD TO STAY IN THE STUDY?

Any new information that may change your mind about allowing your child to be in this study will be given to you. A committee called the Institutional Review Board (IRB) will review this study at least once per year. If the IRB finds that there is new information that you should know about while your child is taking part in this study, it will ask the study doctor to tell you about it. You may be asked to sign a new version of this form after discussing the new information with a member of the research team.

For more information, you may call the National Cancer Institute's (NCI) Cancer Information Service at:

[redacted]

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

The **COG Family Handbook for Children with Cancer** has information about specific cancers, tests, treatment side effects and their management, adjusting to cancer, and resources. Your doctor can get you this Handbook, or you can get it at www.curesearch.org/ <<http://www.curesearch.org/ .

18. WHAT INFORMATION ABOUT MY CHILD WILL BE USED OR DISCLOSED?

Your child's health information will be used and/or disclosed to conduct this study. It will also be used for follow up of possible adverse events, monitoring and audit purposes. By signing this parental permission form, you give permission for the use and/or disclosure of your child's health information for the study described in this form. This authorization to use or disclose your child's protected health information does not have an expiration date.

Nemours study doctors and staff will use information from your medical record as well as information gathered during your child's treatment on this study. The following protected health information will be collected during your child's involvement with this study:

- Personal medical history
- Current and past medications, therapies, surgeries, procedures
- Current and past hospitalizations
- Information from current and past physical examinations
- Results of tests noted in the "Procedure" section of the informed consent

Your child's identifiable health information will be disclosed to organizations other than Nemours to conduct the study. It is possible that information identifying your child may not be removed from these documents, but the agencies reviewing this information will be required to maintain confidentiality. The health information listed above may be used by and/or disclosed to:

- Children's Oncology Group
- Representatives of the National Cancer Institute (NCI), Food and Drug Administration (FDA), and other U.S. and international governmental regulatory agencies involved in keeping research safe for people
- The Nemours Institutional Review Board (IRB) (The IRB is a group of people that reviews research activities. The IRB is responsible for the safety and rights of study participants.); and
- Nemours internal audit staff
- The Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute

Research information about your child will be kept in your child's medical record at Nemours and the Hospital. This will give the doctors and nurses more information about the study so they can take better care of your child. The same information might also be seen by anyone who can look at your child's medical records, such as your insurance company.

Nemours will protect your child's health information by allowing only authorized Nemours, Hospital and Study staff to have access to paper and electronic copies. Study records are kept in secure offices and in password protected computer files. The research results may be presented at meetings or in print. Participants' identities will not be disclosed in those presentations.

To be sure information about your child is kept private, the COG will assign your child a unique identification (ID) number. This unique ID number will be used instead of your child's name or other identifying information. Test results, physical examination reports and therapy summaries will be sent to the COG with your child's unique ID number. COG will take careful steps to prevent misuse of records, and agencies reviewing this information will be required to maintain confidentiality.

Specimens, including blood, bone marrow, and stem cells will be labeled with your child's name, the date, institution and type of specimen. Once the laboratory receives these samples, the information will be recorded and stored in a password-protected database. This database may only be accessed by the COG laboratory staff with proper authority. Once the information has been transferred to the database, the samples will be stored with a random lab number, which can only be identified in the password-protected database. It is crucial that the samples are originally shipped to these laboratories with your child's name in order to avoid errors.

Your child's identity will be protected as much as the law permits. The Children's Oncology Group has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research participants. A copy of the certificate is in Attachment #4 of this consent. The Certificate protects against the involuntary release of information about participants collected during the course of our covered studies. The study doctors involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, you may choose to

voluntarily disclose the protected information. For example, if you request the release of information in writing, the Certificate does not prevent that voluntary disclosure. Information about the certificate is attached at end of this consent.

It is very unlikely that the research testing might uncover important information about your child or your child's current or future health. If this unlikely event occurs, the study doctors at other COG centers may contact your child's Nemours doctor through Children's Oncology Group about what the test results might mean. Only your child's doctor will be notified and the information will remain confidential. Your child's doctor may discuss this unexpected finding with you, and may recommend consultation with a genetic counselor and/or repeat testing in a clinical (not research) laboratory if necessary.

Only health care organizations have to follow laws and rules about protecting the privacy of your child's health information. Other kinds of organizations such as drug companies, private foundations or data management firms can disclose your child's health information without your permission once they have received it.

It may be necessary to contact you at a future date regarding new information about the treatment your child has received. For this reason, we ask that you notify Nemours Children's Clinic of any changes in address. If you move, please provide your child's new address to your local tumor registrar. The contact information for Nemours is provided in the table below.

Nemours – Jacksonville	Nemours - Pensacola	Nemours - Wilmington
Cancer Registrar Nemours Children's Clinic 807 Children's Way Jacksonville, FL 32207 [redacted]	Cancer Registrar Nemours Children's Clinic 5153 North Ninth Avenue Pensacola, Florida 32504 [redacted]	Cancer Registrar AI duPont Hospital for Children1600 Rockland Road Wilmington, Delaware [redacted]

The remainder of this page is intentionally left blank

19. SIGNATURES:

I am making a decision whether or not to permit my child to participate in this research study. I understand that my child may also have to agree to participate in the study before he/she will be allowed to be in this study. I have read, or had read to me in a language that I understand, all of the above. I have been given enough time to make this decision. I have asked questions and received answers about things I did not understand. I willingly give permission for my child to participate in this study. By signing this form, I am not giving up any rights to which I am entitled under law.

I understand that:

- I must sign this permission form in order for my child to be in this study
- I can withdraw this permission by writing to the person in charge of the study listed on the first page of this form. The use and/or disclosure of my child's protected health information will stop after Nemours receives the withdrawal notice. Information that is used or disclosed before the withdrawal may still be used.
- My child's protected health information may be disclosed again by the person or entity (other than Nemours) that receives it. If this happens, Federal or state law may not protect the information.
- I have the right to refuse to sign this form.
- I have the right to ask Nemours to tell me who has received my child's protected health information.
- I have the right to revoke my authorization for the use and disclosure of my child's health information at any time, which would end my child's participation in this study.
- I will receive a signed and dated copy of this completed document in its entirety.

My signature indicates that:

- I give the study doctors and Nemours permission to use and/or disclose my child's individually identifiable health information, for this study, as described in Section 18.
- As his or her parent or legal representative, I give my permission for the minor child named below to participate in the study described in this Parental Permission Form.

Name of Participant (Print)	Participant Date of Birth:	
Signature of Parent/Legal Representative	Printed Name of Parent Legal/Representative	Date

Relation to Participant: ❑ Parent ❑ Legal Guardian

I the undersigned, certify that to the best of my knowledge the parent/legal representative signing this permission had the study fully and carefully explained and that he/she understands the nature, risks and benefits of participation in this study.

Name of Person Obtaining permission (Investigator or Designee)	Signature of Person Obtaining permission	Date

[ ] Copy provided to Parent/Legal Representative and participant on _____.Date

OPTIONAL RESEARCH QUESTIONS

Please read each sentence below and think about your choice. After reading each sentence, check "Yes" or "No" then add your initials and date after your answer.

1. My child's blood may be collected and sent to a COG laboratory to be kept for testing in the Immune Reconstitution Studies.

   #1: Yes_____ No_____ _____ / _____
   Initials Date

2. My child's blood may be kept for use in future research to learn about, treat or prevent cancer or other serious diseases.

   #2: Yes_____ No_____ _____ / _____
   Initials Date

3. Someone from the Children's Oncology Group may contact me in the future to ask me to allow my child to take part in more research.

   #3: Yes_____ No_____ _____ / _____
   Initials Date

How is Tissue Used for Research?

Where does tissue come from?
Whenever a biopsy (or surgery) is performed, the tissue that is removed is examined under the microscope by a trained doctor to determine the nature of the disease and assist with the diagnosis. Your child's tissue will always be used first to help make healthcare decisions. After all tests have been done, there is usually some left over tissue. Sometimes, this tissue is not kept because it is not needed for the patient's care. Instead, a patient can choose to have the tissue kept for future research. People who are trained to handle tissue and protect the donor's rights make sure that the highest standards are followed by the Children's Oncology Group (COG). Your child's doctor does not work for COG, but has agreed to help collect tissue from many patients. Many doctors across the country are helping in the same way. If you agree, only left over tissue will be saved for research. Your child's doctor will only take the tissue needed for his or her care during surgery.

Why do people do research with tissue?
Research with tissue can help to find out more about what causes cancer, how to prevent it, and how to treat it. Research using tissue can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.

What type of research will be done with my tissue?
Many different kinds of studies use tissue. Some study doctors at other COG centers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In the future, some of the research may help to develop new products, such as tests and drugs.

Some research looks at diseases that are passed on in families (called genetic research). Research done with your child's tissue may look for genetic causes and signs of disease.

How do study doctors get the tissue?

Scientists from universities, hospitals, and other health organizations conduct research using tissue. They contact COG and request samples for their studies. COG reviews the way that these studies will be done, and decides if any of the samples can be used. COG gets the tissue and information about your child from your child's study doctor, and sends the tissue samples and some information about your child to the researcher. COG will not send your child's name, address, phone number, social security number, or any other identifying information to the researcher.

Will I find out the results of the research using my child's tissue?
No, you will not receive the results of research done with your child's tissue. This is because research can take a long time and must use tissue samples from many people before results are known. Results from research using your child's tissue may not be ready for many years and will not affect your child's care right now, but they may be helpful to other people in the future.

Though research involves the test results of many different people, your child's biopsy result involves only your child. Your child's doctor will give you the results of the biopsy when results are known. These test results are ready in a short time and will be used to make decisions about your child's care.

Will I benefit from the research using my child's tissue?
There will be no direct benefit to your child because your child's tissue may not be used for some time after it is donated and because research can take a long time. However, it is hoped that the results of research on your child's tissue and tissues from other patients will provide information that will help other patients in the future. Your child's tissue will be helpful whether your child has cancer or not.

Why do you need information from my child's health records?
In order to do research with your child's tissue, the study doctors at other COG centers may need to know some things about your child. (For example: Is your child male or female? What is your child's race or ethnic group? How old is your child? Has your child ever smoked?) This helps them answer questions about diseases. The information that will be given to the researcher includes your child's age, sex, race, diagnosis, treatments, and possibly some family history. This information is collected by your child's Nemours study doctor from your child's health record and sent to COG without a name or other identifying information. If more information is needed, COG may send it to the researcher.

Will my child's name be attached to the records that are given to the researcher?
No. Your child's name, address, phone number and anything else that could identify him or her will be removed before they go to the researcher.

How could the records be used in ways that might be harmful to my child?
Sometimes, health records have been used against patients and their families. For example, insurance companies may deny a patient insurance or employers may not hire someone with a certain illness (such as AIDS or cancer). The results of genetic research may not apply only to your child, but to family members. For diseases caused by gene changes, the information in one person's health record could be used against family members.

How is my child protected?
COG is in charge of making sure that information about your child is kept private. COG will take careful steps to prevent misuse of records. Your child's name, address, phone number and other identifying information will be taken off anything associated with the tissue before it is given to the researcher. This would make it very difficult for any research results to be linked to your child or your family. Also, people outside the research process will not have access to results about any one person, which will help to protect your child's privacy.

Attachment #1
Preparative Treatments, Procedures, and Treatments to Prevent GVHD

Central Line (CVL)

For drugs to be given by vein, your child's doctor will likely recommend that your child has a CVL placed. A description of the types of central lines is in your Oncology Family Notebook.

Methods for Giving Drugs

Various methods will be used to give drugs to patients.

- PO - Drug is given by tablet or liquid swallowed through the mouth (PO).
- IV - Drug is given using the CVL. It can be given by IV push over several minute or by infusion over minutes or hours.

Transplant Preparative Treatment:

Your child has received chemotherapy for his/her leukemia and is in remission. Treatment with chemotherapy or radiation as part of the transplant step is needed to restore your child's bone marrow. The type of preparative treatment your child receives will depend on the type of leukemia he/she has. Below is a list of the possible preparative treatments that may be given. The type of therapy your child receives will be determined by your child's doctor and will be indicated on the study form.

Radiation, (only for ALL patients), if your child will be receiving radiation, the form of radiation used is called total body irradiation, or TBI. It is given to the entire body either before or after chemotherapy and prior to your child's transplant. The radiation treatment destroys the tumor cells and controls the function of the stem cells in preparation for the transplant. TBI helps your child's body begin producing new blood cells (engraft). If your child's disease involves the brain or testes, he/she will also have radiation therapy in these organs prior to having TBI.

The following tables show the possible therapy that your child may receive. The type of therapy your child receives will be determined by your child's doctor. The days listed are all related to the day of the marrow transplant, which occurs on Day 0. Therefore, Day -7 is a week before the day of the transplant.

The type of treatment your child's doctor has chosen for your child is: Treatment #_____

Possible Preparative Therapy #1:

Treatment	How the drug will be given	Days
TBI	Radiation given two times a day	Days -8, -7, and -6 or Day -9, -8 -7, and -6
Cyclophosphamide	Given by IV	Days -3 and -2
Thiotepa	Given by IV	Days -5, and -4

Possible Preparative Therapy #2:

Treatment	How the drug will be given	Days
TBI	Radiation given two times a day	Days -7, -6, -5 and -4
Cyclophosphamide	Given by IV	Days -3 and -2

Possible Preparative Therapy #3:

Treatment	How the drug will be given	Days
TBI	Radiation given two times a day	Days -7, -6, and -5 or Day -8, -7 -6, and -5

Etoposide	Given by IV	Day -4
Cyclophosphamide	Given by IV	Days -3 and -2

Possible Preparative Therapy #4:

Treatment	How the drug will be given	Days
Busulfan	Given by IV	Days -9, -8, -7, -6
Cyclophosphamide	Given by IV	Days -5, -4, -3 & -2

In addition, the anti-seizure medicine pheytoin (Dilantin) is given during the period when the busulfan is given.

Standard tests and procedures

The following tests and procedures are part of regular cancer care and may be done even if your child does not join the study.

- To help reduce the risk of GVHD, your child will receive either cyclosporine A or tacrolimus. These will be given by IV initially and then PO later for at least several months.
- Physical exams
- Frequent labs to monitor blood counts and blood chemistries
- Urine tests to measure how the kidneys are functioning
- Pregnancy test for females of childbearing age before treatment begins
- X-rays and scans to monitor the patient's response to treatment.
- Tests to monitor heart and lung functioning
- Bone Marrow Aspirations to see if the leukemia is responding to treatment. The bone marrow procedure is described in your Family Handbook for Children with Cancer.
- Spinal Taps to check for leukemia cells in the spinal fluid and to give chemotherapy into the spinal fluid prior to transplant. This is described in your Family Handbook for Children with Cancer.

Attachment #2
About Using Tissue for Research (Banking)

During your child's diagnosis and treatment your child's doctor will remove some body tissue (blood and bone marrow) to do some tests. We would like to take extra blood or bone marrow samples for future research. If you agree, this tissue will be kept and may be used in research to learn more about cancer and other diseases. Please read the information sheet called "How is Tissue Used for Research?" to learn more about tissue research.
[Note to Local Investigator: This information sheet is available on the COG web site at: https://members.childrensoncologygroup.org/prot/reference_materials.asp *under* **CONSENTS AND IRB FORMS***]*

The research that may be done with your child's tissue is not designed only to help your child. It might help people who have cancer and other diseases in the future.

Reports about research done with your child's tissue will not be given to you or your child's doctor. These reports will not be put in your child's health record. The research will not have an effect on your child's care.

Things to Think About
The choice to let us keep the leftover tissue for future research is up to you. No matter what you decide to do, it will not affect your child's care.

If you decide now that your child's tissue can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your child's tissue. Then any tissue that remains will no longer be used for research.

In the future, people who do research may need to know more about your child's health. While this institution may give them reports about your child's health, it will not give them your child's name, address, phone number, or any other information that will let the researchers know who your child is.

Sometimes tissue is used for genetic research (about diseases that are passed on in families). Even if your child's tissue is used for this kind of research, the results will not be put in your child's health records.

Your child's tissue will be used only for research and will not be sold. The research done with your child's tissue may help to develop new products in the future.

Benefits
The benefits of research using tissue include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them. Participants will not profit from any new product developed from research done on their specimens.

Risks
The greatest risk to your chid is the release of information from your child's health records. We will do our best to make sure that your child's personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice
If you have any questions, please talk to your child's doctor or nurse, or call our research review board at IRB's phone number. No matter what you decide to do, it will not affect your child's care.

Attachment #3
Chemotherapy, Radiation Therapy and Stem Cell Transplant Risks

Radiation Risks

Radiation therapy may produce the following side effects: nausea, vomiting, diarrhea, generalized redness or dryness of the skin, bone marrow failure (absent blood counts resulting in increased risk of infection, weakness and bleeding), loss of hair (which may take 6 months or more for full re-growth), parotitis (swelling of salivary glands) causing jaw pain and swelling, damage to major body organs which may include the brain, eyes, heart, lung, liver and kidneys, and reddening of the skin. There is also the risk of temporary worsening of neurological symptoms such as weakness or loss of sensation. Some children experience a week or two of low grade temperature and extreme sleepiness six to eight weeks after radiation therapy has been completed. Both total body radiation and testicular radiation will cause sterility.

Possible late effects may include: shortened height, back bone change of shape (vertebral deformities), difficulty with vision (cataracts), changes in endocrine function (low hormones), learning disabilities or brain damage, and increased risk of developing another cancer.

Your child's radiation therapy doctor will discuss these issues with you and have you sign a separate consent for that part of the treatment.

Risks of the Preparative Treatments and the SCT

1. Loss of Bone Marrow Function: The preparative treatments are designed to remove all bone marrow cells, including leukemia cells. Loss of bone marrow function means decreased blood counts, including red blood cells, white blood cells and platelets. Until the new bone marrow cells begin to grow, your child is at risk of developing infections or bleeding. Infections can be treated with antibiotics. Bleeding can be corrected, at least in part, by transfusions. The effect of receiving G-CSF stimulated bone marrow on the duration of bone marrow depression is not known.

2. Infection: The immune system will be not be normal for many months, and the white blood cells that fight infection will be very low until the new cells grow. Your child will be taking antibiotics by mouth to help decrease the possibility of infection, and will probably be receiving intravenous gammaglobulin to help decrease the possibility of a serious viral infection. If your child should have a fever, intravenous antibiotics would be started. Usually, we are successful in treating a bacterial infection with antibiotics, but infection can be life-threatening, and some patients may die as a result of an infection. Other types of infections that can occur are from fungi or viruses. Viral infections can, in particular, be dangerous, as there are few antibiotics against most viruses.

3. Graft-versus-host disease (GVHD): GVHD is described above and is a risk of any bone marrow transplant where the cells come from another person.

4. Graft Rejection: This occurs when the patient's body does not accept the transfused bone marrow. If this occurs, it is sometimes possible to infuse additional cells, but the risk of infection or bleeding may be higher due to the delay in engraftment.

5. Bleeding: as the platelets which help blood clot will be low until the new bone marrow grows, bleeding may occur. This can be minor bleeding, such as nosebleeds or bruising, but more serious, life-threatening bleeding in the lungs and brain can occur if the

platelet count remains low. Usually, we are successful in preventing major bleeding problems with transfusions of platelets. However, some patients may not respond well to transfused platelets, and may be at serious risk for bleeding.

6. Veno-Occlusive Disease (VOD): This can occur as a result of chemotherapy, radiation therapy (if given), or both. Symptoms include jaundice (yellowness of the skin and eyes), with liver dysfunction, weight gain, and extra fluid in the abdominal cavity. It may often be managed successfully, and completely resolve. However, complications can arise that can be fatal.

7. Mucositis and diarrhea: The large doses of medicines and radiation cause damage to the lining of the mouth and intestines. This can result in painful mouth sores and diarrhea. Pain medicine like morphine is almost always required, because the mucositis is often severe. Mucositis gets better when the white blood count starts to rise.

8. Capillary leak syndrome: This may occur as a result of chemotherapy and radiation therapy. The blood vessels may become "leaky" and fluid may enter the abdominal cavity and tissues. A patient may gain water weight and the urine output may fall. Capillary leak syndrome can be difficult to manage if extra fluid enters the lungs and causes difficulty breathing. Patients may die if there is continued fluid collections in the lungs.

9. Unexpected organ damage: Although your child's major organs function well, it is possible that unexpected, life-threatening heart, lung, kidney, or liver damage may occur as a result of this therapy. If problems arise, you will be informed of the measures being taken to help your child. Rarely, multi-organ failure (such as lung and kidney failure) may occur, which is often fatal despite intensive care management.

10. Late Effects: The treatments will cause sterility. Other late effects may include gland problems resulting in poor growth. There may be poor function of the thyroid gland, requiring thyroid hormone supplementation. Cataracts may occur as a result of radiation, and may require treatment. In some patients, the kidneys may be affected, causing anemia or high blood pressure. There is also a risk of second cancers as a result of the chemotherapy, radiation and/or underlying disease. This risk is felt to be outweighed by the risk of you dying from the return of the leukemia. The long term effects upon heart, lung, and brain are unknown.

Treatment Risks

For Women:

The treatment on this study can affect an unborn child. Your child should not become pregnant or breast feed a baby while being treated on this study. If your child is sexually active and are at risk of getting pregnant, she must use an effective method to avoid pregnancy or must not have sex. The study doctor will talk to your child about acceptable methods to avoid pregnancy while she is being treated on this study. She will have to use the chosen method to avoid pregnancy or abstain (not have sexual intercourse) the whole time you are being treated on this study. Your child may need to continue this for a while, even after she finish the cancer treatment, so talk to your child's doctors about the length of time she needs to avoid pregnancy or abstain. Natural family planning and the rhythm method will not be permissible means of avoiding pregnancy during study participation. If you have questions about this or want to change your child's method to avoid pregnancy during therapy, please ask your child's doctor. If your child becomes pregnant during the research study, please tell your child's doctor and her regular doctor immediately.

If your child is nursing a baby, the drugs used in this research could pass into the breast milk. She should not nurse a baby for the whole time she is getting the study medicines. Your child may need to continue this for a while, even after she finishes the cancer treatment, so talk to your child's doctors about the length of time she needs to avoid nursing.

For Men:
The treatment on this study can damage sperm. Your child should not father a child while on this study as the treatment may indirectly affect an unborn child. If your child is sexually active and are at risk of causing a pregnancy, he must use a method to avoid pregnancy that works well or must not have sex. Yor child's doctor will talk to your child about the acceptable methods to avoid pregnancy while he is being treated on this study. He will have to use the chosen method to avoid pregnancy or abstain (not have sexual intercourse) the whole time he is being treated on this study. Your child may need to continue this for a while, even after he finishes the cancer treatment, so talk to your child's doctors about the length of time he needs to avoid pregnancy or abstain. Natural family planning and the rhythm method will not be permissible means of avoiding pregnancy during study participation. If you have questions about this or want to change your child's method to avoid pregnancy during therapy, please ask your child's doctor. If your child's partner becomes pregnant during the research study, please tell you child's doctor and his regular doctor immediately.

Listed on the pages below are drugs which are given as part of the transplant and to control GVHD. Your doctor will tell you which of these drugs you will be given. No one will be receiving all of these drugs, only some.

Risks and side effects related to the thiotepa include those which are:

Likely

- **Nausea**
- **Vomiting**
- **Loss of appetite**
- **A feeling of extreme tiredness or weakness**
- **Fewer white blood cells, red blood cells and platelets in the blood.**
  - **A low number of red blood cells can make you feel tired and weak.**
  - **A low number of white blood cells can make it easier to get infections.**
  - **A low number of platelets causes you to bruise and bleed**
- **Absence or decrease in the number of sperm which may be temporary or permanent which may decrease the ability to have children**
- **Absence or decrease in monthly periods and could affect your ability to become pregnant**

With High Doses used before marrow transplants:

- **Inflammation and/or sores in the mouth, throat and/or esophagus (the passage between the throat and stomach)**

Less Likely

- **Pain at the injection site**
- **Dizziness**
- **Headache**
- **Blurred vision**
- **Hives, skin rash**
- **Wheezing**
- **Sudden high fever**
- **Pain in the abdomen**
- **Difficulty emptying the bladder**
- **Feeling the urgency to urinate or pain on urination**
- **Hair loss**
- **Inflammation and reddening of the eye**
- **Inflammation of the skin where the drug comes into contact with the skin**

With High Doses used before marrow transplants:

- **inappropriate behavior**
- **confusion**
- **drowsiness**
- **Elevation in the blood of certain enzymes and/or bilirubin found in the liver**
- **Bronze discoloration or darkening of the skin**

Rare But Serious

- **Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure and a rapid heart rate**
- **Swelling and tightening of the throat which can cause difficulty with breathing**
- **A new cancer or leukemia resulting from this treatment**

Risks and side effects related to <u>methotrexate (when given by vein)</u> include those which are:

Likely	Less Likely	Rare But Serious
• High levels of liver enzymes in the blood which may mean liver irritation or damage	• Nausea • Vomiting • Loss of appetite • Diarrhea • Chills and/or fever • Inflammation and/or sores in the mouth, gums, throat and/or esophagus • Inflammation of the intestines which may cause bleeding • Sensitivity to sunlight and increased risk of sunburn • Fewer white blood cells, red blood cells and platelets in the blood. ○ A low number of red blood cells can make you feel tired and weak. ○ A low number of white blood cells can make it easier to get infections. ○ A low number of platelets causes you to bruise and bleed • Learning disability • Dizziness • Sense of not feeling well or tiredness • Drowsiness • Blurred vision • Rashes with itching and hives • Hair loss, inflammation of the hair follicles • Acne • Tearing and inflammation of the eyes • Darkening of the fingernails	• Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure and a rapid heart rate • The rapid death of large numbers of tumor cells which can cause the potassium and phosphate salts and the uric acid in the blood to rise quickly and this could lead to a life-threatening irregular heart beat or damage to the kidneys. • Severe rashes which can cause loss of skin or damage to mucous membranes or which can cause peeling, redness and pain on the palms of the hands and soles of the feet • Damage, inflammation and/or scarring of lung tissue which may make you short of breath and cough • Seizures • Temporary damage to the brain such that you may experience headaches, drowsiness, difficulty speaking or forming words, blurred vision or temporary blindness, and decreased reflexes • Temporary loss of function or feeling in the lower part of the body (partial paralysis) • Severe damage to brain tissue which over time could lead to difficulty carrying out normal daily tasks or could lead to a coma. • Inflammation and scarring of the liver • Damage to the bone which could lead to arthritis pain and weakness of the bone • Inflammation of the heart • Fluid buildup around the heart • Damage to the kidney

Risks and side effects related to Tacrolimus include those which are:

Likely	Less Likely	Rare But Serious

• Headache
• Nausea and vomiting
• High Blood Pressure
• Loss of desire to eat or appetite
• Reduced ability of the body to fight infection
• Diarrhea or Constipation
• Fever
• Tremor (shakiness usually of the hands)
• Increases in the levels of certain chemicals in the blood because the kidney is not working as well as normal which may require lowering the dose
• Fewer red blood cells in the blood
  o a low number of red blood cells can make you feel tired and weak
• Difficulty sleeping or falling asleep
• A feeling of weakness and/or tiredness
• Pain which may be in the abdomen (belly), back and/or other parts of your body
• High levels of sugar in the blood that may require treatment
• Abnormal levels of magnesium in the body which may require that you take extra magnesium by mouth or vein
• Low (*or High*) levels of certain salts in the body like potassium and phosphate which may require treatment
• Numbness and tingling in the fingers and toes
	• Chest pain
	• Hair loss
	• Dizziness
	• Elevation in the blood of certain enzymes or bilirubin found in the liver which may mean the liver is not working as well
	• Bladder or kidney infection
	• Fluid retention and build-up in the tissues usually of the lower legs leading to an increase in weight
	• Rash that may itch
	• An increase in the levels of lipids (fats) and cholesterol in your blood which if prolonged could lead to heart problems later in life
	• Acid or upset Stomach (heartburn)
	• Difficulty or discomfort on swallowing
	• Inflammation of the stomach or esophagus (the tube that leads from the mouth to the stomach)
	• Too much gas produced in the intestines
	• Shortness of breath and/or a tight feeling in the chest with wheezing and shortness of breath (asthma)
	• Increased cough
	• Flu type symptoms with fever, tiredness, aches and pains
	• Changes in your brain function such that you have difficulty in thinking clearly, are sleepy, depressed, anxious, have strange dreams, are nervous, have changes in your mood which may include severe depression, feelings of suicide, feelings of aggressiveness and violent behavior or see or hear things that are not there
	• Fewer white blood cells and platelets in the blood
	  o a low number of white blood cells can make it easier to get infections
	  o a low number of platelets causes you to bruise and bleed more easily
	• Greater than normal numbers of
		• Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure, rapid heart rate chills and fever (usually only with the IV form)
		• Allergic reactions
		• Fluid build-up in the lungs that can make you feel short of breath
		• Convulsions
		• A fast heartbeat which may cause pain in the chest
		• Chest pain or discomfort that occurs when your heart muscle does not get enough blood
		• Severe damage to the brain which may lead to difficulty carrying our normal daily tasks and to coma
		• Abnormal clotting of the blood which could lead to bleeding in the intestines or elsewhere
		• Inflammation and clotting of blood vessels which can lead to pain and swelling in the area of the clot
		• Infections including those caused by bacteria, virus, and fungus which could be locate in the skin, blood, throat, sinuses, lungs or abdomen (belly)
		• Severe rashes which can result in loss of skin and damage to mucous membranes
		• Erosion (ulceration) of the lining of the intestines which can result in pain and/or bleeding or a hole in the intestines which would cause leakage into the abdomen (belly) with pain and infection
		• Damage to the liver which can lead to inflammation and/or scarring which could lead to a yellow appearing skin, and fluid collection in the abdomen (belly) which makes it look larger
		• Severe kidney damage (which may be permanent)
		• Diabetes mellitus may develop later on - a condition where the sugar in the blood is not appropriately controlled and may require treatment with insulin by injection or drugs taken by mouth
		• Damage to the heart muscle which may make you tired, weak, feel short of breath, and retain fluid

	white or red blood cells in the blood • Aches and Pains in the joints or muscles • Skin changes including pimples, change in color, increased tendency to sun burn and skin sores • Wounds may be slower to heal • Excessive hair growth such as on the face, eyebrows, arms and legs • Bleeding or tender gums, overgrowth of gum tissue • Changes in your vision or a decrease in vision • Ear pain or ringing in the ears • Gallstones	and may require treatment • Excessive growth of white blood cells that may lead to lymphoma a cancer of the white blood cells • Increased chance of skin cancers

Risks and side effects related to <u>cyclosporine A</u> include those which are:

Likely

- **High Blood Pressure**
- **Decreased ability of the body to fight infection**
- **Tremors**
- **A decrease in kidney function which may require lowering the dose**
- **Excessive hair growth such as on the face, eyebrows, arms and legs**

Less Likely

- **Headache**
- **Nausea and vomiting**
- **Diarrhea**
- **Lower levels of magnesium in the blood**
- **Higher levels of potassium or creatinine in the blood which may mean that your kidneys are not working as well**
- **Bleeding or tender gums, overgrowth of gum tissue**
- **Fever**
- **Reddening of the face with feelings of warmth**
- **Pimples**
- **Changes in your mood such that you feel depressed, confused or anxious**
- **An increase in the levels of lipids (fats) in the blood**
- **Rashes, itching and/or hives**
- **Sleepiness or an inability to sleep**
- **Cataracts**
- **Dizziness**
- **Damage to the ear causing balance problems and ringing in the ears**
- **Gallstones**
- **Enlarged breasts**
- **Fewer red and white blood cells and platelets in the blood**
  - **a low number of red blood cells can make you feel tired and weak**
  - **a low number of white blood cells can make it easier to get infections**
  - **a low number of platelets causes you to bruise and bleed more easily**
- **Increased number of infections**
- **Elevation in the blood of bilirubin and certain enzymes found in the liver which may mean the liver is not working as well**

Rare but serious

- **Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure, rapid heart rate chills and fever usually only with the IV form**
- **Severe allergic reaction which can be life threatening with rapid build-up of fluid under the skin, in the lining of the intestine and possibly in the throat or swelling of the tongue which could make it difficult to breath. Usually only with the IV form.**
- **Irregular heart beat**
- **Chest pain, heart attack**
- **Damage to the heart muscle which may make you tired, weak, feel short of breath, and retain fluid and may require treatment**
- **Convulsions**
- **Damage to the brain that may lead to coma**
- **Clotting in the small blood vessels of the kidney that can lead to kidney failure**
- **Excessive growth of white blood cells that may lead to lymphoma a cancer of the white blood cells**
- **Increased chance of skin cancers**

Risks and side effects related to cyclophosphamide include those which are:

Likely

- Loss of appetite
- Nausea
- Vomiting
- Fewer white blood cells in the blood.
  - A low number of white blood cells may make it easier to get infections.
- Hair loss
- Decreased ability of the body to fight infection
- Absence or decrease in the number of sperm which may be temporary or permanent which may decrease the ability to have children

Less Likely

- Abnormal hormone function which may lower the level of salt in the blood
- Abdominal pain
- Diarrhea
- Fewer red blood cells and platelets in the blood
  - A low number of red blood cells may make you feel tired and weak.
  - A low number of platelets may cause you to bruise and bleed more easily.
- Bleeding and inflammation of the urinary bladder
- Absence or decrease monthly periods which may be temporary or permanent and which may decrease the ability to have children
- Temporary blurred vision
- Nasal stuffiness with IV infusions
- Skin rash
- Darkening of areas of the skin and finger nails
- Slow healing of wounds
- Infections

Rare but serious

- Heart muscle damage which may occur with very high doses and which may be fatal
- Abnormal heart rhythms
- Damage and scarring of lung tissue which may make you short of breath
- A new cancer or leukemia resulting from this treatment.
- Damage or scarring of urinary bladder tissue
- Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure, rapid heart rate chills and fever
- Infertility which is the inability to have children

Risks and side effects related to Etoposide include those which are:

Likely	Less Likely	Rare but serious
• Nausea and vomiting • Hair Loss • A feeling of weakness or tiredness • fewer red and white blood cells and platelets in the blood o a low number of red blood cells can make you feel tired and weak o a low number of white blood cells can make it easier to get infections o a low number of platelets causes you to bruise and bleed more easily	• Loss of appetite • Decreased blood pressure during the infusion which may require treatment • rashes • Diarrhea • Pain in the abdomen • Mouth sores • Tingling sensation or loss of sensation in fingers or toes • A feeling of extreme tiredness or weakness • The finger or toe nails may loosen from their nail beds • Inflammation of the vein through which the medication was given • Chest pain	• Damage to the liver • Severe allergic reaction which can be life threatening with shortness of breath, low blood pressure, rapid heart rate chills and fever • A new cancer or leukemia resulting from this treatment • Severe rashes which can result in loss of skin and damage to mucous membranes • Absence or decrease monthly periods which may be temporary or permanent and which may decrease the ability to have children • Damage to the heart muscle which may make you feel tired, weak, feel short of breath, and retain fluid

Risks and side effects related to intravenous Busulfan include those which are:

Likely	Less Likely	Rare but serious

• Nausea and vomiting
• Fever
• Headache
• Bloody nose
• Fewer red and white blood cells and platelets in the blood
  o a low number of red blood cells can make you feel tired and weak
  o a low number of white blood cells can make it easier to get infections
  o a low number of platelets causes you to bruise and bleed more easily
• Dizziness
• Difficulty sleeping
• Mood changes including depression and anxiety
• Rash with itching and/or hives
• Pain and inflammation in the vein through which the drug is given
• Back pain or pain in the abdomen
• Diarrhea or constipation
• Rectal pain or discomfort
• Loss of Appetite
• A fast heart beat which may cause pain in the chest
• Shortness of breath
• Fluid build-up in the tissues usually of the lower legs
• Inflammation and/or sores in the mouth, throat and/or esophagus
• Absence or decrease in the number of sperm and/or damage to the testis which may be temporary or permanent which may decrease the ability to have children in the future
• Absence of menstrual cycles (periods) and damage to the ovaries that may decrease the ability to have children in the future
• Lower levels of certain salts in the blood such as calcium, magnesium, phosphate, and sodium
• High blood sugar which may require treatment
• Elevation in the blood of bilirubin found in the liver
• A feeling of discomfort or not feeling well and/or tiredness
	• Weight gain
	• Confusion
	• Temporary hair loss or thinning
	• Aches and pains in the muscles and joints
	• Increased levels of creatinine in the blood which could mean kidney damage
	• Darkening of the skin
	• Elevation in the blood of certain enzymes found in the liver
	• Inflammation or damage to the liver which can be severe and life-threatening and which may lead to an enlarged liver and spleen, bleeding from the veins in the esophagus (the passage that leads from the throat to the stomach), a yellow appearing skin, and fluid collection in the abdomen which makes it look larger.
	• Damage to the bladder which can lead to large amounts of blood in the urine, pain and the urge to urinate frequently and also scarring of the bladder
	• Elevation in uric acid in the blood
	• Redness and burning at sites which have received radiation in the past
	• Cataracts later in life
	• Enlargement of the breast
		• Convulsions even though you will be treated with drugs to prevent convulsions
		• Vomiting blood
		• Bleeding into the lungs
		• A new cancer or leukemia resulting from this treatment
		• Abnormal heart rate
		• Damage to the adrenal glands that may affect the hormones that maintain blood pressure and prevent shock in stressful situations
		• Damage to the lungs that can lead to fluid in the lungs and/or scarring of the lung tissue, cough, and affect your ability to breath and the levels of oxygen in your blood.
		• Scarring of the heart muscle which could lead to heart failure
		• Damage to the bone which could lead to arthritis pain and weakness of the bone

Attachment #4
Certificate of Confidentiality

The Children's Oncology Group has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research participants. The Certificate protects against the involuntary release of information about participants collected during the course of our covered studies. The study doctors involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, the subject or the researcher may choose to voluntarily disclose the protected information under certain circumstances. For example, if the subject or his/her guardian requests the release of information in writing, the Certificate does not protect against that voluntary disclosure. Furthermore, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act. The Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others.