SAMPLE INFORMED CONSENT

NANT 2004-05: Neuroblastoma Biology Studies
New Approaches to Neuroblastoma Therapy (NANT) biology studies.

The word "you" used throughout this document refers to you or your child.

WHAT IS THIS STUDY ABOUT?

This is a biology research study where research is done on normal cells and/or tumor cells in the samples collected from you. This biology study includes only subjects who choose to take part. Please take your time to make your decision about participating. You may discuss your decision with your friends, family, and health care team. If you have questions, you may ask your doctor.

You are being asked to take part in this study because your doctors have determined that you have neuroblastoma, a type of solid cancer that usually affects children. Learning more about patients with neuroblastoma, by studying their tumor and normal cells in the laboratory may help doctors to develop better therapies for neuroblastoma. This protocol will create a storage place or "bank" where samples of blood, bone marrow, and tumor will be kept to provide a number of samples large enough to allow researchers to do studies on neuroblastoma tumor cells and other normal cells that interact with the tumor. This study will also use a highly accurate new test to identify and measure tumor cells that may be in your bone marrow or blood to see if this new method improves evaluating the effect of treatment. All research studies done using the banked samples will first be reviewed by a committee of NANT scientists for approval.

WHY IS THIS STUDY BEING DONE?

The purposes of this study are:

- To establish a storage place or "bank" of samples of blood, bone marrow, and/or tumor, and molecular components isolated from these samples from children with neuroblastoma. The stored specimens will be shared with laboratory researchers studying high risk neuroblastoma.

- To evaluate a new test of blood and bone marrow specimens to find tumor cells. The results of this new test, called 5-gene TaqMan® Low Density Array or TLDA, will be compared between blood and bone marrow and imaging (radiology) studies. Radiology studies (CT scans, MRI scans, and MIBG scans) and the TLDA test will be compared for their ability to measure the amount of tumor present and how this changes with therapy.

- To collect clinical data (such as treatments received, date of diagnosis, tumor stage, etc) and radiology scans to provide this information as needed for the laboratory studies to be done on the specimens.

- To obtain neuroblastoma tumor cells from tumor tissue, bone marrow, and/or blood to use to start "cell lines", or tumor cells that will keep growing in the laboratory. These cell lines will be shared with laboratory researchers studying high risk neuroblastoma.

This research is being done because:
Medical scientists want to find better ways to treat neuroblastoma and to find ways to prevent the tumor from growing back. To do this, they need more information about the characteristics of neuroblastoma cells. Therefore, they want to study samples of neuroblastoma tissues and neuroblastoma and normal cells in the

blood and bone marrow that may be related to the growth of neuroblastoma cells. Doctors and other medical scientists also want to find better ways to detect and measure neuroblastoma to improve the ability to follow the response of tumor cells to therapy.

Some research looks at diseases that are passed on in families (called genetic research). Research done with your tumor tissue, blood, and/or bone marrow may look for genetic causes and signs of disease. If your tissue is used for this kind of research, the results will not be put in your health record. The results of these studies will not directly affect decisions made regarding therapy for you, but may lead to a better understanding of the genes that control neuroblastoma growth.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There is no limit to how many patients can participate in this study. We expect that over 500 subjects will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

A bone marrow test may also be done to determine the extent of disease at the time of recurrence of your tumor, or prior to starting a new therapy. If you are also participating in a NANT or other treatment study, then bone marrow samples are usually obtained at the beginning and the end of the therapy, as well as during the therapy to follow the tumor's response. For this study, we are asking you to allow the researchers to take 1-2 teaspoons of additional bone marrow when a bone marrow evaluation is being done as part of the requirements of your therapy or your medical status. We ask for bone marrow specimens from a minimum of two serial timepoints. Ideally these timepoints would be prior to the start of the treatment you are now receiving, and then at the next time point when you tumor response is checked. However, any two serial timepoints are acceptable. Patients will also be asked to give two teaspoonfuls of blood for special research studies at the same timepoints that bone marrow is obtained, as explained above, for at least two different serial timepoints. Characteristics in the samples of blood may be compared with those in the bone marrow.

Radiologic scans (CT, MRI and MIBG scans) are also done to evaluate your tumor status and its response. Scans are done at timepoints required by the therapy you are receiving and will be submitted and stored in an electronic storage system. Results of the scans will be compared with results from the bone marrow and blood samples taken at the same timepoints. No extra scans are required to be done just for this study.

If you have tumor tissue removed for medical reasons, then the extra tissue not needed for routine medical purposes can also be submitted to be stored in the storage bank for future research. If you submit tumor tissue alone without any other sample or radiologic scans, you are still eligible to be part of this study. No surgical procedures to remove tumor tissue will be done just for this biology study.

Clinical information (for example the stage of your tumor, what treatments you have received in the past) will also be obtained and used in the evaluation of the results of the research tests done on your blood, bone marrow, radiologic studies, and/or tumor tissue.

HOW LONG WILL I BE ON THE STUDY?

The time to complete a set of specimens for this study depends on your specific therapy. The blood and bone marrow specimens are usually taken approximately every two months while you are receiving a treatment therapy, but will be done at the timepoints required by your specific therapy, and not at timepoints set by this biology study. The specimens and information obtained from you can be used indefinitely. Researchers will continue to ask information about you for a lifetime about the regarding the last time you were seen by your doctor. You have the right to remove yourself and have the samples destroyed from this bank at any time (see below under "What other options are there").

CAN I STOP BEING IN THE STUDY?

Yes.

WHAT ARE THE RISKS OF THE STUDY?

Blood drawing and bone marrow sampling may cause pain, bruising, bleeding, or infection at the site of the needle stick. Care will be taken to avoid these complications. These procedures will be done as needed for the treatment you are receiving, and no extra procedures will be done just for this biology study. If you have a central line in place, blood may be drawn for this study at a time when you may not be getting other laboratory tests although every effort would be made to add this test to an already scheduled test. There will be extra blood and bone marrow taken, however the total amount taken will be limited to the amount set by the human subjects protection committee at your institution.

There should be no added risks to you from the blood drawing or bone marrow procedures as a result of participating in this study.

The greatest risk to you is the release of information from your health records. 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 New Approaches to Neuroblastoma Therapy (NANT) Consortium will protect your (child's) health records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There are no direct benefits to you from taking part in this study. We hope the information learned from the research tests will benefit patients in the future.

WHAT OTHER OPTIONS ARE THERE?

As this is not a treatment study, the alternative to participation is to not participate.

WILL MY MEDICAL INFORMATION BE KEPT PRIVATE?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Your research records will be reviewed for quality assurance and data analysis. Participant's names will be known only to the patient's doctors and their research team. As stated earlier, the New Approaches to Neuroblastoma Therapy (NANT) Consortium will protect your medical records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small.

Each patient enrolled will be given a unique patient identifier. The unique number is assigned at enrollment on this study through the NANT Operations Center and will be used on specimens sent to the NANT Specimen Bank. Research scientists will receive samples identified only by a code and with no identifying personal information.

NANT has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. Information about the certificate is included at the beginning of this

consent.

Organizations that may look at and/or copy your research records for quality assurance and data analysis include groups such as:

- NANT Consortium
- Independent auditor evaluating quality assurance for the NANT Consortium.
- The National Cancer Institution (NCI) and other governmental agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury. You or your insurance company will be charged for continuing medical care and/or hospitalization. There is no charge to the participants in this study for the tests done on tumor tissue and blood. There is no charge for the banking of samples or for storing radiologic images. You will not be paid for taking part in this study.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, _____ *[investigator's name(s)],* if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ *[telephone number].*

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is your choice. You may choose not to take part or not take part in the study. If you decide to take part in this study, you may remove yourself from the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

If you decide now that your tissue can be kept for research and change your mind later, contact your doctor and let him or her know that you no longer want your (child's) tissue used for research purposes. Any tissue that remains in the bank will be destroyed.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

You can talk to your study doctor about any questions or concerns you have about this study or have a research-related injury. You may contact your study doctor _____NAME(S) at TELEPHONE NUMBER.

For questions about your (child's) rights as a research participant, contact the NAME OF CENTER Institutional Review Board (which is a group of people who review the research to protect your rights) at TELEPHONE NUMBER.

WHERE CAN I GET MORE INFORMATION?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

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/

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at anytime.

You will get a copy of this form. If you want more information about this study, ask your study doctor.

You are making a decision whether or not you will participate in this research. You should not sign until all your questions with regard to participation have been answered to your satisfaction. Your signature indicates that you have decided that you will participate after you have read (or been read) the information provided above. In no way does your signature reduce any of your legal rights nor release the doctors at this medical center, sponsor, director of tissue bank, or directors of other NANT affiliated research laboratories from their legal and professional responsibilities.

STATEMENT OF CONSENT

Now please read the instructions below then circle the answer that is right for you.

Instruction 1: Circle YES to this instruction if you agree to let someone use your specimens and radiologic images in research to learn about, prevent, or treat neuroblastoma, or other diseases. Circle NO if you do not want your (child's) specimens used for research about neuroblastoma or other diseases.

YES NO

I have already read the information in this informed consent document. I have read all the attachments that were included with this informed consent document. I have asked all of my questions and I have gotten answers. I agree to enroll myself (my child) in this study.

_____
Patient Name

_____ _____/_____/_____
Signature of Parent or Guardian **Date**

_____ _____/_____/_____
Signature of Parent or Guardian **Date**

_____ _____/_____/_____
Signature of Patient (If > 7 years old) **Date**

_____ _____/_____/_____
Signature of Physician or Responsible Investigator Date

_____ ____/_____/_____
Signature of Translator (If applicable) Date

CONSENT ADDENDUM #1

Certificate of Confidentiality Information

NANT has received a Certificate of Confidentiality from the federal government, which will help us protect the privacy of our research subjects. The Certificate protects against the involuntary release of information about subjects collected during the course of our covered studies. The researchers 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.

NANT 04-05
NANT Biology Study

SAMPLE ASSENT TO PARTICIPATE IN A RESEARCH STUDY

Creating a Storage Bank for Neuroblastoma Cells.
A New Approaches to Neuroblastoma Therapy (NANT) treatment protocol

Subject's Name: _____	
_____#: _____	Birth Date: _____

1. _____ is doing a research study.

2. You have a kind of cancer called **Neuroblastoma.** We are asking you to take part in a research study because doctors want to learn more about neuroblastoma tumors by keeping your collected blood, bone marrow, or tumor cells in a special storage bank. They are hoping to have a large amount of cells so that scientists can do studies on neuroblastoma cells and normal cells that interact with the tumor.

3. If you agree to be in this study this is what will happen:
    - Samples from two separate times will be submitted to the specimen bank. These may either be from blood or bone marrow. These will usually be taken at the same time you have to have blood or bone marrow drawn for your clinical care. You will not have any painful extra procedures if you are in this study, but blood can be drawn from your line specifically for this study when it is not drawn with the other blood tests. Scans will be submitted for radiologists to review.

    - If you have your tumor removed for medical reasons, a left over sample of your neuroblastoma tumor that would normally be thrown away will be kept and sent to this storage bank for special research studies. You will not have a special surgery just for this study.

- Some of your medical records, including the treatments you have had in the past will be sent and used for research.

4. Sometimes things happen to children in research studies that may make them feel bad. These are called “risks.” Some of the risks of this study are:
    - Blood drawing and bone marrow sampling may cause pain, bruising, bleeding, or infection at the site of the needle stick. These procedures will be done for the normal care of your neuroblastoma. There will be no extra blood draws or bone marrows done for this study. There are no other risks involved in this study.

5. People also have good things that happen to them when they are in research studies. These are called “benefits.” We hope to learn more neuroblastoma by having this new bank of samples and being able to do special research tests. There is a chance that we could find things out which could help other children with neuroblastoma.

6. Please talk this over with your parents before you decide whether or not to be in this study. We will also ask your parents to give their permission for you to take part in this study. But even if your parents say “yes” you can still decide not to do this.

7. Being in this study is up to you. You do not have to be in this study if you don’t want to. You may stop being in this study at any time, and your samples will no longer be sent to the special bank. The specimens being stored in the bank can also be destroyed at any time you decide to stop being on the study.

8. You can ask any questions that you have about the study. If you have a question later that you didn’t think of now, you can call me at _____ or ask me next time. You may call me at any time to ask questions about your disease or treatment.

9. Signing your name at the bottom means that you agree to be in this study. Your

doctors will still take good care of you whether or not you agree to be in this study. Your parents will be given a copy of this form after you have signed it.

Please check to show if you do or do not agree to allow us to use your specimens for research mentioned earlier.

_____Yes, it is okay to use my specimens and scans for neuroblastoma research.

_____ No, it is not okay to use my specimens and scans for neuroblastoma research.

_____ _____
Signature of Subject Date

_____
Name of Investigator/Person obtaining consent

_____ _____
Signature of Investigator/Person obtaining consent Date