10.0 SAMPLE INFORMED CONSENT

NANT 2015-01: Neuroblastoma Precision Trial

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 performed on tumor cells and normal cells in samples that are collected from you. This biology study includes only patients who choose to take part. Participation in this study is completely voluntary. 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 any questions, you may ask your study doctor.

You are invited to take part in this study because your doctors have determined that you have neuroblastoma that has either grown back (relapsed) or has never gone away (refractory tumor) after standard treatment. This research study will test for genetic and immunologic changes (called biomarkers) in tissues of your body where relapsed or refractory neuroblastoma tumors are present.

If you agree to participate in this research study, tumor tissue obtained after relapse along with a sample of your blood will be used to identify specific genetic and immunologic changes that may be present in your tumor. Reports of the changes found in your tumor will be provided to you and your doctor. In some cases, this information may help you plan a cancer treatment that may potentially be more effective for your tumor. It is not the intent of this study to tell you what drugs you should take based on the reported findings but to provide information about the clinical trials available that may match certain genetic and immunologic changes in your tumor. The final decision whether to use this information in treatment planning is for you and your doctor to make.

The main purpose of this study is to gather information about the genetic and immunologic make-up of relapsed or refractory neuroblastoma tumors and to understand the best ways to obtain tumor tissue for such evaluations. While the study attempts to provide this information back to you, we may not always be successful if the tissue samples do not have enough tumor cells or don’t meet the quality requirements established for successful testing.

WHY IS THIS STUDY BEING DONE?

The purposes of this study are:

- To perform genetic mutation and immunologic marker analyses on neuroblastoma tumor cells from tumor tissue, or bone, or bone marrow and blood and count how many times these analyses can be performed successfully.

- To determine how often these tests can identify genetic and immunological changes in tumors of patients with relapsed or refractory neuroblastoma that fall into 4 sub-groups of known changes seen in neuroblastoma tumors.

- To determine how often this testing identifies genetic and immunological changes where a drug is available in the clinic that can act on that change (known as an actionable target).

- To evaluate if the researchers can obtain genetic testing results from very small amounts of tumor found in the bone marrow aspirate (liquid part of marrow) after isolating tumor cells; a process called enrichment.

- To evaluate how the relapsed tumor cells are different from tumor that was obtained at diagnosis or prior to relapse and, if applicable, to evaluate for differences in genetic changes of relapsed/refractory tumors obtained from different body sites (soft tissue, bone or bone marrow).

- To evaluate if the small amount of tumor genetic material floating in the blood can identify the same genetic changes that we identify in your tumor tissue sent for analysis.

- To document any treatments you receive for one year after the NANT Precision report is created and given to you and your doctor.

This research is being done because:

Researchers want to find better ways to treat neuroblastoma and prevent the tumor from growing back. To do this, they need to study the biologic and genetic properties of tumor cells taken from body sites where relapsed or refractory neuroblastoma tumor is present. This could be a tumor mass (soft tissue tumor), a tumor in the bone or in the bone marrow.

Research done with tumor tissue, in addition to blood, and bone marrow that you provide will look for genetic causes of your relapsed neuroblastoma and genetic reasons why your previous therapies may not have worked. Tumor tissue will also be used to look for immunological changes to find out how tumors use immune cells to resist therapies. The results of these studies may or may not directly affect decisions made regarding therapy for you. This research may lead to a better understanding of the genetic or immunologic changes that control the tumor coming back or lack of response to treatment seen in relapsed or refractory neuroblastoma.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

We expect approximately 90 subjects will take part in this study.

WHAT WILL HAPPEN TO ME IF I TAKE PART IN THIS STUDY?

To participate in this study you must agree to let doctors send biopsy material where relapsed or refractory neuroblastoma tumor cells may be present along with a blood sample for genetic testing. Your doctor has determined that performing genetic testing on a tumor sample would be in your best interest. Tumor tissue or tumor cells could come from soft tissues either at your primary tumor site or another site of relapse, from a bone site or from bone marrow. Your doctor will decide where to biopsy based on where your tumor is found and where it would be easiest and safest to obtain a tumor sample. You will likely get general anesthesia for this procedure. This biopsy will be done as part of your clinical care to obtain a clinically certified report of the genetics of your tumor.

If you previously had a tumor tissue biopsy after relapse of your neuroblastoma that has been stored properly and you and your doctor are interested in submitting that sample for genetic analysis instead, you will not have to have another procedure done to obtain more tissue. In this case, we will ask your doctor to send us the tumor tissue that was already removed and stored along with a new blood sample.

What will happen to my tumor after it is taken from me and how will I find out about the results?

Your local pathologist will keep part of your tumor specimen obtained from the biopsy for clinical testing at your institution. The remaining tumor will be sent to the central laboratory for this study, located at Children's Hospital Los Angeles (CHLA). The central laboratory will examine the tissue submitted for numbers of tumor cells. If there are enough tumor cells present, your tumor sample and blood sample will be sent to the genetic testing laboratory.

If the CHLA central laboratory determines there are not enough tumor cells identified in your tumor sample, your doctor will be informed of this finding. If there are any left over specimens at your institution your doctor may elect to send another sample for analysis. It is possible that despite the biopsy, no specimen will be found to have enough tumor cells for genetic testing. In this case, you and your doctor will have to decide whether to have another biopsy procedure done. In order to limit the number of times you would have to have a procedure done, it is recommended that when either a soft tissue or bone biopsy is being performed, a bone marrow biopsy also be performed when possible and if determined to be in your best interest.

Once the CHLA central laboratory determines the tumor is adequate for genetic testing, it will be sent together with your blood to the genetic testing laboratory. The analysis will look for any changes in the genetic make-up of the tumor that are different from those changes found in your normal genetic material obtained from your blood sample. A report that describes these changes will be created by the genetic testing laboratory

and sent to the CHLA central laboratory. This report will be given to you and your doctor.

In addition, if soft tissue tumor was submitted, CHLA central laboratory will use special stains to look for proteins that might be in your tumor cells and determine if your tumor has a special immune cell associated with it. The information from these analyses will help us in classifying your tumor into one or more groups.

The NANT Precision Study Committee will review the genetic report issued by the gene testing laboratory as well any results from tests done by the CHLA central laboratory and create a comprehensive study report (called NANT Precision Report) that will be returned to you through your doctor.

This NANT Precision Report will include the genetic report prepared by the genetic testing laboratory that details specific genetic changes found in your tumor and whether or not there are potential drugs that may target those changes. In addition, the NANT Precision Report will also show if your tumor belongs to any of the four neuroblastoma specific classification groups the researchers associated with NANT Precision are studying. For patients who submit a soft tissue sample, the report will also include the results from the special stains performed on your tumor.

The NANT Precision Report will include a link to a regularly updated webpage on the NANT Consortium website that will provide a list of open pediatric clinical trials in the NANT Consortium, Children's Oncology Group, and non-NANT clinical trials being conducted in NANT participating institutions. These trials are selected based on current available data matching the clinical trial's drug/s to genetic or immunologic alterations seen in one of the 4 groups. Your decision to enroll in any one of the clinical trials presented on the NANT website or other therapy recommended by your doctor should be made in discussion with your doctor. The NANT Precision Committee will collect data on what treatments you receive for one year after getting the NANT Precision Report.

Companion NANT Biology Study (required)

You will also be expected to consent to a companion NANT Biology Study that provides a place (called NANT biorepository) where left-over samples of tumor tissue, bone, bone marrow and blood collected for this study would be transferred and stored. While you must consent to the Biology study, the decision to store/bank your leftover tissue samples is optional and will not affect your ability to participate in this study. You will be asked whether you wish to provide consent for banking these leftover samples for future research purposes on this study (found at the end of this consent form). Your doctor will talk with you in detail about the NANT Biology study and have you sign a separate consent form for that study. Your doctor will talk with you in detail about the NANT Biology Study and have you sign a separate consent form for that study. Your doctor will discuss with you whether additional blood and bone marrow samples should be drawn as part of the NANT Biology Study if you are participating in the Precision Biology

Study.

Additional research procedures (optional)

As part of this study researchers will be looking at other less invasive ways to obtain tumor cells for genetic testing that does not require doing biopsies of tumor sites. You will be asked if you want to participate in several optional research tests. You can decide not to let the doctors do these tests and still participate in this study. There is a place at the end of this consent form to mark whether you are willing to participate in these voluntary studies.

These tests are OPTIONAL

- **Using extra bone marrow aspirate to enrich for tumor cells:**

Many patients have tumor cells present in their bone marrow aspiration samples but not in high enough numbers to be able to identify any genetic changes in the tumor cells themselves**.** For this study we are asking that approximately 1 ½ extra teaspoons (8 mL) of bone marrow aspirate above what is needed for clinical care be taken for research purposes when a bone marrow biopsy procedure is being performed to collect samples to be sent for genetic testing**.** Aspirates received on this study will be "enriched" to concentrate the tumor cells so genetic changes can be detected more easily. Study researchers want to see if this method can be used to perform genetic testing instead of using the bone marrow biopsy material. The results of this research test will not be shared with you as this is still considered investigational and cannot generate a clinical certified report.

- **Using extra blood to look for genetic changes seen in tumor cells:**

Dying tumor cells often release small pieces of their DNA into the blood stream where it can be detected by sensitive tests. For this study, researchers would like to take 2 additional teaspoons of blood (10mL) to see if the same genetic changes found in your tumor cells obtained from a tumor biopsy specimen can be seen in your blood without needing a biopsy to be done. The results of this test will not be shared with you as this is still considered investigational and cannot generate a clinical certified report.

- **Comparing the genetic changes between tumor leftover from an earlier surgery (diagnosis or second look) to relapsed tumor tissue leftover from samples collected for genetic testing on this study:**

You may consent to participate in this optional research test if you had a soft tissue, bone or bone marrow biopsy done for genetic testing on this study and your doctor has confirmed that there is enough leftover tumor tissue available from an earlier surgery done at diagnosis or after upfront treatment (second look surgery) to send to the CHLA Research Laboratory. The genetic and immunologic make-up of your tumor changes over time. If you consent, doctors will compare the tumor taken at an earlier time before relapse to the tumor taken at relapse to see how different they are from each other. The results of this research test will not be shared with you or your doctor as this is

being done for research purposes to learn more about relapsed/refractory neuroblastoma.

- **Comparing genetic changes between relapsed tumor samples taken from different body sites.**

You may consent to participate in this optional research test if you had tumor samples taken from more than one body site (soft tissue, bone and/or bone marrow). As the genetic make-up of your tumor changes over time, researchers want to evaluate if there are any differences in the genetic changes between tumors found in different body sites. If you consent, researchers will compare the genetic changes found in these tumor samples to see how different they are from each other. The results of this research test will not be shared with you or your doctor as this is being done for research purposes to learn more about relapsed/refractory neuroblastoma.

- **Storing genetic information obtained about your tumor and normal cells (called germline) for re-interpretation of results in the future.**

The genetic testing laboratory generates a lot of genetic data about your tumor of which a small amount is used to create the genetic report that is given to you and your doctor. If you consent, researchers would like to store all the genetic information (tumor and germline) generated by the genetic testing laboratory so it is available for re-analysis in the future as new information about cancer causing genes and/or technologies for testing/detecting these genes becomes available. Stored genetic information will be de-identified after the genetic report for clinical use is generated and sent to you. As such, future re-analysis of stored genetic and germline information will not be returned to you and will be used strictly for research purposes.

- **Storing left-over blood, tumor tissue, bone and bone marrow samples collected for genetic testing on this study in a biorepository under the NANT Biology Study for use in future research:**

There may be left-over blood, tumor tissue, bone and bone marrow samples once all the requirements for the genetic testing laboratory have been met or it has been determined that the tissue samples did not have enough tumor cells or did not meet the quality requirements established for successful genetic testing. With your consent, we will store these left-over specimens in a biorepository established under the NANT Biology Study so they are available for use in future research as yet to be determined.

A table detailing the tests and procedures either done for the research or done for standard of care has been attached to the end of this form.

HOW LONG WILL I BE ON THIS STUDY?

The time it takes to process your tumor samples, complete the genetic and immunologic testing and generate the NANT Precision Report for this study depends on the specific procedures needed to obtain your neuroblastoma tumor tissue. However, we aim to generate the report back to you within 4 – 6 weeks after we receive the specimens from your medical institution. If the CHLA central laboratory determines there are not enough

tumor cells for analysis, it will take additional time to generate a report for you and your doctor if additional tissue needs to be obtained or evaluated and sent for genetic analysis.

CAN I STOP BEING IN THE STUDY?

Yes. Your participation in this research is VOLUNTARY. If you are thinking about stopping your participation in this study, you should talk to your doctor before making a final decision. The study doctor may also stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow study rules, or if the study is stopped.

WHAT ARE THE RISKS OF THE STUDY?

- **Extra Bone Marrow Aspirate Collection:** 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. If you consent, there may be additional bone marrow aspirate taken, however, the total amount taken will be limited to the amount set as safe by the human subjects protection committee.

- **Extra Blood Sample Collection:** Blood drawing may cause pain, bruising, bleeding, or infection at the site of the needle stick. Care will be taken to avoid these complications. This blood would be drawn at a time when blood is being collected for a clinically indicated reason and would not require an additional blood draw procedure to be done. There should be no added risks to you from the blood drawing as a result of participating in this study. There will be extra blood taken, however the total amount taken will be safe..

- **Tumor Genetic Testing:** It is also possible that the genetic testing could show no cancer related abnormalities in your tumor, or the specimen did not have sufficient tumor cells to conduct these studies. Your tumor may also have cancer specific changes that cannot be targeted with a drug or a drug has not been developed yet. Current technologies are not able to find and identify every possible genetic change that might be related to cancer. You may still have genetic changes that are related to your cancer or your cancer risk but the tests we performed may not be able to detect them. Therefore, there is the risk that you go through these study procedures and have no new treatment options. While there may be no current therapy to treat your tumor, your doctor will keep your genetic report and may find a treatment option in the future as new therapies are discovered.

- **Germline Genetic Testing:** The genetic testing laboratory uses the blood sent with your tumor for determining the genetic make-up of your normal cells (known as germline testing) that is used as a baseline to compare to the genetic make-up of your tumor. This helps the laboratory in identifying the genetic changes they may see in your tumor tissue. However, the germline testing may show other changes that you and/or your family may learn of that increase your risk of cancer or other diseases/ disorders. This information is not part of the NANT Precision Report and you must tell us specifically if you want to find out this information at the end of this form. If you choose not to find out germline genetic testing information, regardless of the findings, you will not be notified of any alterations discovered in germline testing. This information could upset you. Learning this genetic information may cause anxiety, depression, anger and/or fear of what could happen in the future.

  The testing done on this study is focused primarily on genes associated with cancer and conditions that may lead to cancer. All known disease causing genetic changes are NOT evaluated as a part of this study. Therefore, a negative result does not mean that a change in another disease-causing gene is not present. Further, this study does NOT confirm whether or not a genetic change is inherited and further testing may be indicated depending upon the results. Your doctor or a genetics counselor can discuss these risks with you and recommend follow-up for these results, if necessary, only if you consent to have germline testing results given back to your doctor. The germline genetic testing is for research purposes only. These studies do not provide you with medical information or diagnoses. Because of this, it is recommended that any genetic changes that are found in your blood (known as germline) be confirmed by commercial testing in a laboratory that can produce a clinically certified report. There may be additional costs associated with this confirmatory testing.

- **Confidentiality:** The greatest risk to you is the release of information from your health records. The NANT Precision Report that contains genetic information may be placed in your medical record and your child's other doctors and health care team will have access to it. Health insurance companies may also have access to your medical records. Sometimes, health records have been used against patients and their families. Laws exist to prevent this, but you may have to submit the medical records when applying for life or disability insurance.

  For this study, all research data collected will be physically and electronically secured. The New Approaches to Neuroblastoma Therapy (NANT) Consortium will protect your health records so that your name, address, and phone number will

be kept private. You will be assigned a coded study number when you enroll that will be used in place of your name on all study related activity. The link connecting your identity to this coded number will be stored in a confidential password-protected database, accessible only by research study personnel. Your name will not be used in any published study results. The chance that your personal information will be given to someone else is very small.

- **Unknown Risks:** There may be other unknown risks as part of participating in this research study. While many safeguards are in place, we cannot always anticipate all risks or predict how the data collected will be used in the future. While we believe the risks to your child and your family from participating in this study to be relatively low, we are unable to tell you exactly what all of these risks are.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

This study provides the opportunity to obtain genetic information on your tumor that can be used immediately or in the future to identify clinical trials testing drugs that target the specific genetic changes found in your tumor. The NANT Precision Report that is returned to your doctor can help with deciding your future treatment options, and hopefully lead to enrollment on clinical trials that your tumor has the potential to respond to. We hope the information learned about genetic changes in tumors from patients with relapse/refractory neuroblastoma will benefit patients in the future.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT TAKE PART IN THE STUDY?

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.

Organizations that may look at and/or copy your medical records for research, quality assurance and data analysis include:

- New Approaches to Neuroblastoma Therapy (NANT) Consortium at Children's Hospital Los Angeles in Los Angeles, CA. The NANT Consortium identifies you by a number.
- Independent auditor evaluating quality assurance for the NANT Consortium.

- The National Cancer Institute (NCI) and other governmental agencies, like the Food and Drug Administration (FDA) or Health Canada, involved in keeping research safe for people.

Because this study is related to the treatment of a medical condition, a copy of this consent form will be placed in your medical record. This will allow the doctors that are caring for you to obtain information about what procedures you are receiving in the study and treat you appropriately.

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 from this study that are sent to the NANT Specimen Bank (biorepository). 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 end of this consent.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

Participants and their families are not responsible for any of the costs of the research procedures. Neither you nor your insurance company will be billed for your participation in this research.

The cost of procedures that are also a part of the standard treatment of your disease will be billed to your insurance or other third-party payer. You may be responsible for any co-pays or deductibles.

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.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

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 STUDY PARTICIPANT?

Taking part in this study is your choice. You may choose not to take part in this study. If you decide to take part in this study, you may remove yourself from this 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. If you remove yourself from this study, we will still take care of you. If you decide now that your tumor tissue can be kept for research and change your mind later, you can contact your doctor at any time and let him or her know that you no longer want your tissue used for research purposes. Any tissue that was obtained for this study that remains in the NANT specimen bank will be destroyed. However, any research that was conducted on your samples or data collected up to that point will not be destroyed.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing data from this research throughout the study. We will tell you about new information from this Board or other studies that may affect your health and willingness to stay in the study.

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ [*name(s)*] at _____ [*telephone number*].

For questions about your rights while taking part in this study, call the _____ [*name of center*] Institutional Review Board (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 NCI's **Cancer Information Service** at

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

You may visit the NCI Web sites 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 consent form. If you want more information about this study, ask your study doctor.

CONSENT FOR EXTRA STUDIES FOR RESEARCH

Obtaining Germline Information:

_____ I agree to have germline genetic information results sent to my physician.
(Initial here)

The following tests are optional for all patients in the study. You may still participate in the study even if you do not agree to these tests.

1. Using extra bone marrow aspirate to enrich for tumor cells:

Initial next to YES if you agree to let researchers take1 ½ extra teaspoons (8mL) of bone marrow aspirate to enrich or concentrate the tumor cells present. This would be done at the same time the bone marrow biopsy procedure was being done. The results of this test will be confidential and not made available to your treating physican.

Initial next to NO if you do not want researchers to take extra bone marrow aspirate above what is needed for clinical purposes.

_____ YES _____ NO

2. Using extra blood to look for genetic changes seen in tumor cells:

Initial next to YES if you agree to let researchers take 2 extra teaspoons (10mL) of blood to see if the same genetic changes found in your tumor cells that are sent for genetic analysis can be found in blood. This blood would be drawn at a time when blood was being drawn for clinical purposes. The results of this test will be confidential and not made available to your treating physican.

Initial next to NO if you do not want researchers to take extra blood above what is needed for clinical purposes.

_____ YES _____ NO

3. Using available tumor taken at an earlier surgery (diagnosis or second look) to compare to leftover tumor tissue taken at relapse for this study:

Initial next to YES if you agree (and if there is tumor remaining) to let this tumor be sent to the CHLA Research Laboratory to compare to the relapsed tumor that was leftover from genetic testing where researchers will look for differences between the

two tumor samples. The results of this test will be confidential and not made available to you or your treating doctor.

Initial next to NO if you do not want leftover tumor from an earlier surgery sent to the CHLA Research Laboratory to be compared to leftover tumor tissue taken at relapse for genetic testing on this study.

_____ YES _____ NO

4. Comparing genetic changes between relapsed tumor samples taken from different body sites:

Initial next to YES if you agree to let researchers compare the genetic changes found in tumor samples taken from more than one body site (if available-soft tissue or bone and/or bone marrow) to see how different they are from each other. The results of this test will be confidential and not made available to you or your treating doctor.

Initial next to NO if you do not want researchers to compare genetic changes found in tumor samples collected from more than one body site for this study.

_____ YES _____ NO

5. Storing genetic information obtained about your tumor and normal cells (called germline) for re-interpretation of results in the future

Initial next to YES if you agree to let the CHLA Research Laboratory store all the genetic data created by the genetic testing laboratory that supports the creation of the report sent to you and your doctor. Researchers would like to have the ability to re-analyze these data as new knowledge and technologies become available in the future. The results of any future analysis done on stored genetic data will be confidential and not made available to you or your treating doctor.

Initial next to NO if you do not want the CHLA Research Laboratory to store any of the genetic data created by the genetic testing laboratory for future re-analysis as new knowledge and technologies become available.

_____ YES _____ NO

6. Storing left-over tumor tissue, bone and bone marrow samples collected on this study for genetic testing in a biorepository on this study under the NANT Biology Study for use in future research:

There may be left-over tumor tissue, bone and bone marrow samples once all the requirements for the genetic testing laboratory have been met or it has been determined that the tissue samples did not have enough tumor cells or did not meet the quality requirements established for successful genetic testing. Researchers are asking for your consent to store these left-over specimens in a biorepository established under the NANT Biology Study so they are available to for use in future research as yet to be determined.

Initial next to YES if you agree to let researchers store these left-over specimens in the biorepository of the NANT biology study for use in future research.

Initial next to NO if you would prefer to have any left-over specimens destroyed and not stored in the biorepository of the NANT Biology Study for use in future research.

_____ **YES** _____ **NO**

STATEMENT OF CONSENT

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 Date

_____ _____/_____/_____

Signature of Physician or Responsible Investigator Date

_____ ____/_____/_____

Signature of Witness Date

_____ ____/_____/_____

Signature of Translator Date

Consent Addendum #1: Tests that will be done on this study (including studies done for research and standard clinical care)

Observation	Before Entry	After Study Entry	
Physical exam	X		
CT/MRI scans and/or MIBG/PET scans	X		
REQUIRED Tests for generating a clinically certified report			
Bone marrow biopsy		X	2 extra specimens will be needed for genetic testing*
Bone biopsy		X	2 extra specimens will be needed for genetic testing*
Soft tissue biopsy		X	
Blood sample for genetic analysis		X	
OPTIONAL TESTS for research purposes			
Bone marrow aspirate for tumor cell enrichment		X	
Blood sample for circulating tumor cells		X	
Archive tumor collected from surgery at diagnosis or after upfront treatment (second look) compared to leftover relapsed tumor*		X	*If there is enough tumor tissue available to send for this research test
Comparing genetic differences between relapsed tumor samples collected for this study from different body sites^		X	^ Tumor samples from more than one body site must have been submitted in order to do this research test
De-identifying and storing all genetic information (from tumor and normal cells) generated by the genetic testing laboratory for use in future re-analysis as new information and technologies become available		X	

***Extra samples will be placed in a specific solution that preserves genetic material so it can be sent for genetic testing**

CONSENT ADDENDUM #2

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.

11.0 SAMPLE ASSENT FORM

NEUROBLASTOMA PRECISION TRIAL

A New Approaches to Neuroblastoma Therapy (NANT) Biology Protocol

INVESTIGATOR [Insert Name of Investigator]
[Insert Name of Institution]

[Insert Address (include City, State and Zip Code)]
Insert Telephone/Fax Numbers]
[Insert Email]

1. My name is _____

2. You have a kind of cancer called **Neuroblastoma** that has either come back (relapsed) or never gone away with treatment (refractory).

3. **If you agree to be in this study, this is what will happen:**
    - Allow the doctors to send samples of your tumor and blood to the laboratory for testing.

    - After the testing is done, a report will be sent to your doctor. The report will talk about any genetic changes found in your tumor (how your tumor cells have changed the program or code for how they live and grow), as well as how the immune system may be involved in the fight against your tumor cells. Your doctor can use this information to plan further treatments for you if he/she feels it will be of benefit to you.

    - As part of this study, researchers are looking at other ways of collecting tumor cells from bone marrow and blood that could be used for testing that would not involve having an operation. You will be asked if you want to take part in optional research tests at the end of this form. You do not have to agree to be in ay of the optional tests to take part in this study.

4. **When you are in a research study, sometimes good things and bad things can happen:**

    - Things that happen to children in research studies that make them feel bad are called “risks”. Some of the bad things for this research study could be:
        - Blood drawing and bone marrow sampling may cause pain, bruising, bleeding or infection at the site of the needle stick. These procedures are done for the normal care of your neuroblastoma.

Not all of these things may happen to you. None of them may happen. Or things may happen that the doctors don't know about yet.

5. Things that happen to children in research studies that are good are called "benefits." Some of the good things for this research study could be:
    - We hope to learn more about relapsed neuroblastoma by finding out about the genetic and immunologic changes in the tumor cells. Giving a report of these changes to your doctor may help him/her to plan treatments for you that might be more effective against your tumor now or in the future.

    - There will be a chance we could find things out which could help other children with neuroblastoma.

6. We will do everything possible to keep your information private.

7. 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. Remember, being in this study is up to you.

8. Please talk 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.

9. You can ask any questions that you have about the study. If you have a question later that you didn't think of now, please write it down to help you remember. You can call me or ask me next time you see me.
    - Study doctor's phone number: _____

Special Study Tests:

There is a request for extra optional tests in this study. These are done for research purposes only. You do not have to take part in the optional parts of the study in order to participate in the main study.

#1: About 1 ½ teaspoons of bone marrow aspirate (liquid part of bone marrow); will be taken at the same time a bone marrow collection will be done as part of your normal neuroblastoma care.

- _____ Yes
- _____ No

#2: 2 teaspoons of extra blood are taken at the same time blood will be as part of your normal neuroblastoma care.

- _____ Yes
- _____ No

#3: The doctors will compare old and new tumor samples collected from you as part of your normal neuroblastoma care.

- _____ Yes
- _____ No

#4: The doctors will compare tumor samples collected from different parts of your body as part of your normal neuroblastoma care.

- _____ Yes
- _____ No

#5: The doctors will store your genetic information for future testing that does not exist yet.

- _____ Yes
- _____ No

#6: There may be left-over blood, tumor tissue, bone and bone marrow samples. The doctors will store these samples so that we can use them for future research.

- _____ Yes
- _____No

10. Signing your name at the bottom means that you agree to be in this study. You and your parents will be given a copy of this form after you have signed it.

Name of Subject: _____

Signature of Subject	Date
Signature of Investigator	Date
Signature of Person Conducting Discussion	Date