CHILDREN'S ONCOLOGY GROUP
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Operations and Informatics Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
Executive Plaza North Room 730
Bethesda, MD 20892

Dear Ms. Kruhm,

Enclosed please find Amendment #6 to protocol APEC1621SC, *NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol*.

The primary purpose of Amendment #6 was to remove the aims that are duplicative in the individual treatment subprotocols. Sections of the protocol and consent were updated to reflect this change.

Administrative changes have been made; specific changes are detailed in the Summary of Changes table below. Minor administrative updates (such as the correction of typographical errors, spelling, or updates to the numbers of referenced sections) are tracked in the protocol but not specified.

Please let me know if you have any questions or need additional information.

Sincerely,

[redacted]

SUMMARY OF CHANGES: INFORMED CONSENT

In accordance with the above discussion, the following specific revisions have been made to the consent. Additions are in **boldfaced** font and deletions in ~~strikethrough~~ font.

#	Section	Page(s)	Change
1.	General	All	Updated version date of consent to match the current version of the protocol.
2.	Where can I get more information?	8	The link to the NCI clinical trials information page was updated.

This model informed consent form has been reviewed by the DCTD/NCI and is the official consent document for this study. Local IRB changes to this document are allowed. (Institutions should attempt to use sections of this document which are in bold type in their entirety.) Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to the risks or alternatives sections, they must be justified in writing by the investigator and approved by the IRB.

SAMPLE INFORMED CONSENT / PARENTAL PERMISSION FOR PARTICIPATION IN RESEARCH

APEC1621SC: NCI-COG Pediatric MATCH (Molecular Analysis for Therapy Choice) Screening Protocol

Study Title for Study Participants: Pediatric MATCH screening protocol

NOTE TO SITES: THIS CONSENT FORM ONLY APPLIES TO PATIENTS ENROLLED AFTER AMENDMENT #4A.

If you are a parent or legal guardian of a child who may take part in this study, permission from you is required. The assent (agreement) of your child may also be required. When we say "you" in this consent form, we mean you or your child; "we" means the doctors and other staff.

This study is a clinical trial (a protocol, or research study involving patients). Clinical trials only include patients who choose to take part. Your participation in this study is entirely voluntary. Please read the consent form carefully. You will be given a copy of it to keep if you decide to participate in this study. You may discuss your decision with your friends and family if you would like.

This study is being carried out by the Children's Oncology Group (COG). COG is an international research group that consists of more than 200 hospitals that treat children with cancer in the United States, Canada, Australia, New Zealand and Switzerland.

What is the usual approach to my cancer?

You are being invited to take part in the National Cancer Institute (NCI) – COG Pediatric MATCH study because you have cancer that has become worse following treatment, or because no standard therapy exists for your type of cancer. People like you who are not participating in a study might be treated with chemotherapy, radiation, or surgery. Sometimes, combinations of these could be used. For people who receive the usual approach for this cancer, symptoms may be reduced and the tumor may stop growing for several months or more.

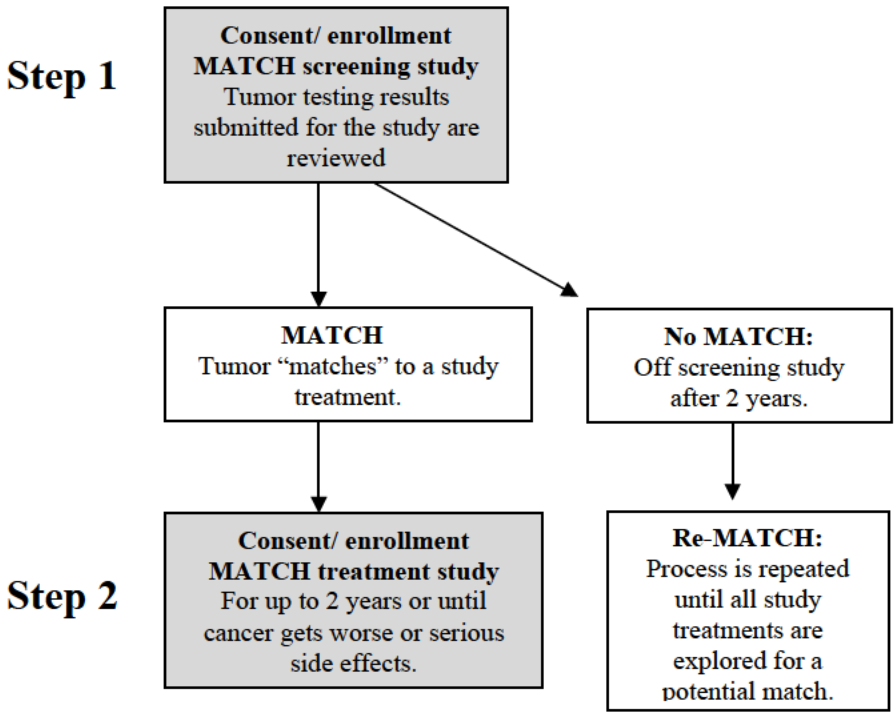
Some patients might also choose not to receive any specific treatment directed at the cancer. Instead, such patients might choose to receive care focused on improving symptoms from the cancer.

Why is this screening study being done?

The main purpose of this study is to learn how well tumors that have specific genetic changes (mutations) respond to drugs that "target" those changes. This combination of a tumor with a mutation and a drug that aims at that mutation is called a "match." There are two steps for participants in this study:

1. The first step is called screening. The purpose of screening is to review tests that have been done on your tumor tissue to see if there is a mutation that makes you eligible for one of the MATCH treatment trials. Please know that your eligibility for this trial may have been determined in part on the basis of a laboratory-developed test that has not been reviewed or approved by the FDA. The consent form you are reading now is for the screening step of the Pediatric MATCH study.

2. If it is confirmed that a mutation in your test report makes you eligible for a MATCH treatment trial, you will have the opportunity to participate in the second step, which is the investigational treatment part of the study. Your study doctor will tell you about the drug and explain the specifics of getting that drug. He or she will explain the potential side effects and benefits of the drug. In some cases, the side effects of these drugs in children might not be known. If you consent and are eligible, you will then receive the drug and we will look to see what its effects are on your tumor.



What will happen if I take part in this research study?

Before you begin the screening study…

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- A medical history
- Physical exam
- Vital signs (blood pressure, pulse, temperature)
- Blood tests

We will also perform the necessary X-rays, MRI scans, or CT scans, or other tests that are needed to check your tumor.

During the screening study…

For Step 1:

By deciding to participate in this screening study, you will give permission to have the results of a tumor mutation test already performed by your care team submitted for review by researchers at the Children's Oncology Group. The results of this test show which of your tumor's mutations might be targeted by study drugs. This review will determine whether you will be offered the option of participating in Step 2 of this study.

For Step 2:

Step 2 is the treatment part of the study. If your tumor has a mutation targeted by one or more of the investigational drugs used in this study, you will be assigned to the study treatment that uses that drug. You will sign a separate consent form if you want to be assigned to the study treatment using that drug. You and your doctor cannot choose which drug you will get. However, if you do not want the assigned drug, you may withdraw from the study.

You will need to have a physical exam, blood and urine tests, and scans or other tumor tests to see if you can receive the study drug under its study treatment. There will be specific eligibility requirements for each study treatment's drug that may differ in part depending upon what is known about the possible side effects of each drug. Your doctor will discuss all of this with you, as well as the risks and benefits of the study treatment's drug and give you a different consent form for step 2.

You should not become pregnant while on this study. Females must not be pregnant while undergoing X-rays, MRI scans, or CT scans, or other tests that might be harmful to the unborn baby.

If you participate in the treatment part of the study and your cancer becomes worse while receiving a study drug, or if you have too many side effects, it is possible that another MATCH study drug might become available. If this is the case your doctor will talk to you about it.

What extra tests and procedures will I have if I take part in this screening study?

You will need to have the following exams, tests and procedures to find out if you can be in the study. Your doctor might do some of them even if you were not in the study:

- **During Step 1:**

  Additional tumor and blood samples are required to be submitted for testing or biobanking as described in the "Additional Research Studies (Required, if Available)" section if available from other procedures done as part of standard of care. Genetic testing may be performed for research purposes on the tumor tissue and blood samples. This genetic testing might not routinely be done as part of your medical care if this study was not being considered. The results of these tests will not be given to you or your doctor.

- **During Step 2:**
  - Blood tests to check the function of your organs, such as liver and kidney.
  - X-rays, MRI scans, CT scans or other tests to measure the size and location of your tumor.
  - Pregnancy test if you are capable of becoming pregnant.
  - Additional exams or procedures may be required for specific treatment studies in step 2. This information will be discussed in the treatment study consent form.

- **During Steps 1 and/or 2:**
  - Your doctor may request to submit a second tumor mutation test result for review if such a test was performed as part of your routine cancer care.
  - If your cancer becomes worse during treatment with the study drug, you may be invited to take part in another MATCH study treatment. There may be additional exams or procedures required for another MATCH study treatment. These will be discussed in a separate consent form.

Another important question that study researchers are trying to answer is how much tumors change over time and in response to chemotherapy and radiation therapy. In order to learn more about this, we will also study a tumor sample that was obtained before you received any treatment for your cancer, if one is available. We will obtain this sample from the hospital where you had the initial biopsy or surgery, perform genetic research tests on it, and compare the results to those of your clinical MATCH study sample. The results from the pre-treatment tumor sample will not be used to select treatments on this study.

Any leftover tissue from any of the tumor samples submitted for the study will be saved in a tissue bank ("biobank"). This is discussed below in "Additional Research Studies (Required, if Available)."

Additional Research Studies (Required, if Available)

This section is about studies that are required, if there are samples available to use.

1. Research testing of blood and tumor biopsy samples

If available, some of your tumor and blood samples that were already collected will be sent to us so that we can use them to do additional research. Please note that these are not being used for clinical testing and there will not be any test results returned to you.

These samples will potentially be used to work on new kinds of tests for gene changes or other changes in your DNA, RNA, or proteins, as well as growing tumor or blood cells in the laboratory to test how the genes work. If research from this project is presented at research conferences or published in professional journals, we will not include any identifying information about you in study presentations or publications. Any results of these research tests would be preliminary. In the unlikely event that we identify a genetic change that we think is clinically important for your care or that of your family, we will share those results with your doctor so that they can discuss them with you. Only your doctor will be notified and the information will not become part of your medical record. It is important to realize that these will be research results and must be confirmed in a clinical laboratory in order to be used for clinical purposes.

2. Biobanking

We will save some of your tumor and blood samples (if available) for future research. This is called "biobanking" or "tissue banking." A tissue bank is a lab where specimens (such as tumor, blood or bone marrow) are kept for use in future research studies. The results of these studies will not affect your treatment. Therefore the results of the tests will not become part of your health records.

Your samples will be stored in the Biopathology Center at Nationwide Children's Hospital, in a locked freezer. The samples will be kept until they are used up, unless you request that they be destroyed. Some information from your medical record will also be kept in secure databases at the Biobank and updated from time to time. The information and samples will be kept under a code, not your name.

How long will I be in the screening study?

From the time the tumor mutation test result is submitted, it will take several days to get the result of the review and see if there is a study drug for your tumor. During this time your doctor will continue to advise you on all available treatment options as well as any potential risks of waiting for results before starting a new treatment. If you are matched to a study drug, that separate consent form will tell you how long the treatment study will last. In general, if you choose to participate in step 2 you will take the study drug until your cancer becomes worse, your treatment has lasted about two years, you have side effects and can no longer tolerate the treatment, or you choose not to continue with the study drug. If one of these things happens, you may be invited to participate in another treatment study if there is another study drug for your tumor. If you do participate in step two, we would like to continue to find out about your health for about 5 years after you start a study drug. You will be removed from the screening protocol after two years if you have not been enrolled on a treatment study.

Can I stop being in the screening study?

Yes. You can decide to stop being part of this research project at any time. If you decide to stop for any reason or withdraw from the study, it is important to let the study doctor know as soon as possible. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study. Information that has already been sent might not be able to be removed from the study database.

Your doctor will talk with you about going off the study if:

- Your health changes and the study is no longer in your best interest
- New information becomes available that may affect your health or your willingness to continue in the study.
- The study is stopped by the study sponsor (NCI), Institutional Review Board (IRB) or the Food and Drug Administration (FDA).

What side effects or risks can I expect from being in the screening study?

If you choose to take part in this study, there are some medical risks:

- Because the study requires additional tests, you may lose time at home or school and spend more time in the hospital or doctor's office than if you don't join the study

- If you participate in the required research testing or biobanking (if samples are available) you will have your blood drawn. The risk of drawing blood includes a small risk of bleeding or infection at the site, and some pain or discomfort with the needle stick. There may also be some bruising at the site of the needle stick after the blood draw. If a central line is in place, we will draw blood samples from this line.

- If you participate in the required research testing or biobanking (if samples are available) a sample of your tumor that was already collected will be submitted to the study. If there is only a small amount of your tumor sample left, this might all be used for the research and you might not have any left for other testing in the future.

- The review of your tumor genetic testing might show that there is NOT a mutation for which there is a matched targeted drug. We expect that some people in the study will NOT have a matched drug identified and will therefore not be eligible for treatment.

- Even if a matched drug is identified, it might not be effective against your tumor.

Are there benefits to taking part in the screening study?

- The main benefit to you of being in this screening study is that the review might identify a mutation in your tumor that helps us choose a study drug for you. If so, you might benefit from treatment with a drug that targets mutations found in your tumor.

- It is important to realize, however, that the review team may not agree that your tumor has a mutation that can be targeted by a study drug. In addition, we do not know if using targeted drugs works better than choosing drugs without doing genetic testing. Whether targeting drugs is helpful to patients is part of what we are trying to learn in this study. You might not benefit personally from being in the study at all.

- An important benefit of this study is that it will help researchers learn things that will help improve treatment for children and adolescents with cancer in the future.

What other choices do I have if I do not take part in this screening study?

If you decide not to take part in this study, you have other choices. For example:

- You may choose to have chemotherapy, radiation, and/or surgery your doctor recommends that is not related to a study.
- You may choose to take part in a different study, if one is available.
- You may choose not to receive treatment directed at your cancer, but rather to receive comfort care to relieve symptoms.

Talk to your doctor about your choices before you decide if you will take part in this study.

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. 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 test results will be identified in study databases by a unique code. The list that links the code to your name will be kept separate from your sample and health information. Your privacy is very important to us, and we will make every effort to protect it. However, we cannot guarantee total privacy.

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 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.

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

- The 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 overseeing research
- The Institutional Review Board (IRB) of this hospital
- 'The Pediatric Central Institutional Review Board (CIRB) of the National Cancer Institute
- The study sponsor (NCI) and the drug companies supporting the study

In addition, your clinical and genetic information may be shared by releasing it into scientific databases, including those maintained by the Children's Oncology Group and some maintained by the National Institutes of Health. These databases are restricted and can only be accessed by approved researchers. Sharing this information will help advance medicine and medical research by allowing other researchers to use this information to help solve questions of what causes cancers and other diseases. Your individual genomic data and health information may be put in a controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your genomic data and health information will not be labeled with your name or other information that could be used to identify you. Researchers approved to access information in the database will agree not to attempt to identify you.

What are the costs of taking part in the screening part of this screening study?

You and/or your health insurance company will need to cover the cost of the biopsy, tests, procedures, or medicines to manage any side effects of your biopsy. There are no costs to you for the genetic testing that will be done as part of the study. Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for. If a financial counselor is available at your hospital you may wish to talk to him or her.
If screening shows you are eligible to get study drug(s), any costs of being in the study will be discussed along with details of your treatment.

You will not be paid for taking part in any part of this study, including screening.

What happens if I am injured because I took part in this screening 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. There are no plans for the study to pay for medical treatment for injuries. In the case of injury resulting from this study, you do not lose any of your legal rights to seek compensation by signing this form

What are my rights if I take part in this screening study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave 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. Leaving the study will not affect your medical care. You can still get your regular medical care from our institution.

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. Whether you participate or not, you will continue to get the best medical care this hospital can provide.

Who can answer my questions about the screening 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). [Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]*

Where can I get more information?

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 https://www.childrensoncologygroup.org/index.php/cog-family-handbook

If you are in the United States, you may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

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

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

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

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

Signature

I have been given a copy of all _____ pages of this form.
I have read it or it has been read to me.

I have reviewed the information and have had my questions answered. I agree to take part in this study.

Participant:_____ Date:_____

Participant / Parent (or Guardian): Date:_____
_____

Participant / Parent (or Guardian): Date:_____
_____

Physician or Responsible Investigator: Date:_____
_____