Memorial Sloan-Kettering Cancer Center
IRB Protocol#: 12-235A(11)

INFORMED CONSENT FOR CLINICAL RESEARCH

Clinical and Histopathologic Characteristics of *BAP1* Mutations

Enrollment (Informed Consent 1)

You have been asked to participate in a research study. In order to decide whether or not you should agree to be part of this research study, you should know enough about its risks and benefits in order to make a sound judgment. This process is known as informed consent.

A member of the study staff will explain the research study to you. Research studies include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your family and friends.

This consent form gives you detailed information about the research study. Once you understand the study, its risks, and its benefits, you will be asked to sign the form if you wish to take part. You will be given a copy to keep.

The study is funded by the United States Department of Defense (DOD).

Why is this study being done?

The purpose of this study is to learn more about *BAP1* and other genes in mesothelioma, uveal melanoma, and choroidal nevi. We hope that the information from this study can be used to assess a person's risk of developing mesothelioma and uveal melanoma and to develop good cancer screening recommendations for people at high risk of developing these cancers. This study has 3 parts and this consent deals with part 1 of the study. This part of the study will determine how common *BAP1* mutations are among people being treated for mesothelioma, uveal melanoma, and choroidal nevi.

Mesothelioma is a cancer of the lining around the lung or abdomen. Uveal melanoma is a tumor that begins in the eye. These are uncommon cancers. Choroidal nevi are darkened spots in the eye which are common but do not usually become uveal melanoma. Most people with mesothelioma, uveal melanoma, or choroidal nevi do not have anyone else in the family with the same problem. However, some families show a pattern of either mesothelioma, uveal melanoma, or other cancers. We do not know much about these familial forms of mesothelioma and uveal melanoma. There may be a link to changes in a gene called *BAP1*. Inherited changes (mutations) in *BAP1* may lead to an increased risk of mesothelioma or uveal melanoma, or increase the chance that a choroidal nevus becomes a melanoma. We do not know how high these risks are, or whether changes in *BAP1* may lead to increased risks of other cancers.

Is there a potential conflict of interest for this study?

There are no known investigator and/or institutional conflicts of interest for this study.

How was I selected to be in this study?

You are being asked to take part in this study because you have mesothelioma, a choroidal nevus, or uveal melanoma.

How many people will take part in the study?

About 460 people will take part in this study at MSKCC.

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

This study has 3 parts. This consent deals with the first part of the study. All patients who decide to participate will be in the first part of the study. In addition to testing your blood or saliva, if a sample of your tumor is available, that tumor will be tested for mutations in the *BAP1* gene. You will not receive the results of this part of the study. Only patients who are thought to have a high risk for a mutation (by family or personal history) or patients with tumor tissue that has a mutation will be asked to participate in part 2 of the study. If your tumor tissue does not have a mutation or if you are considered "low risk" you will not be asked to participate further and you will not receive the results of the genetic testing. You will continue with medical care as advised by your physician.

During the 2nd and 3rd parts of the study, patients are given the results of the genetic testing. Part 2 of the study tests you for *BAP1* mutation. If the test is positive, you will be asked to contact family members to take part in part 3 of the study. We will not contact any of your relatives unless they have first contacted us. All parts of the study are voluntary.

Before you begin the study …

Carefully read this consent form and discuss this study with your doctor. Make sure all of your questions are answered.

During the study…

If you choose to take part, then you will be asked to do the following:

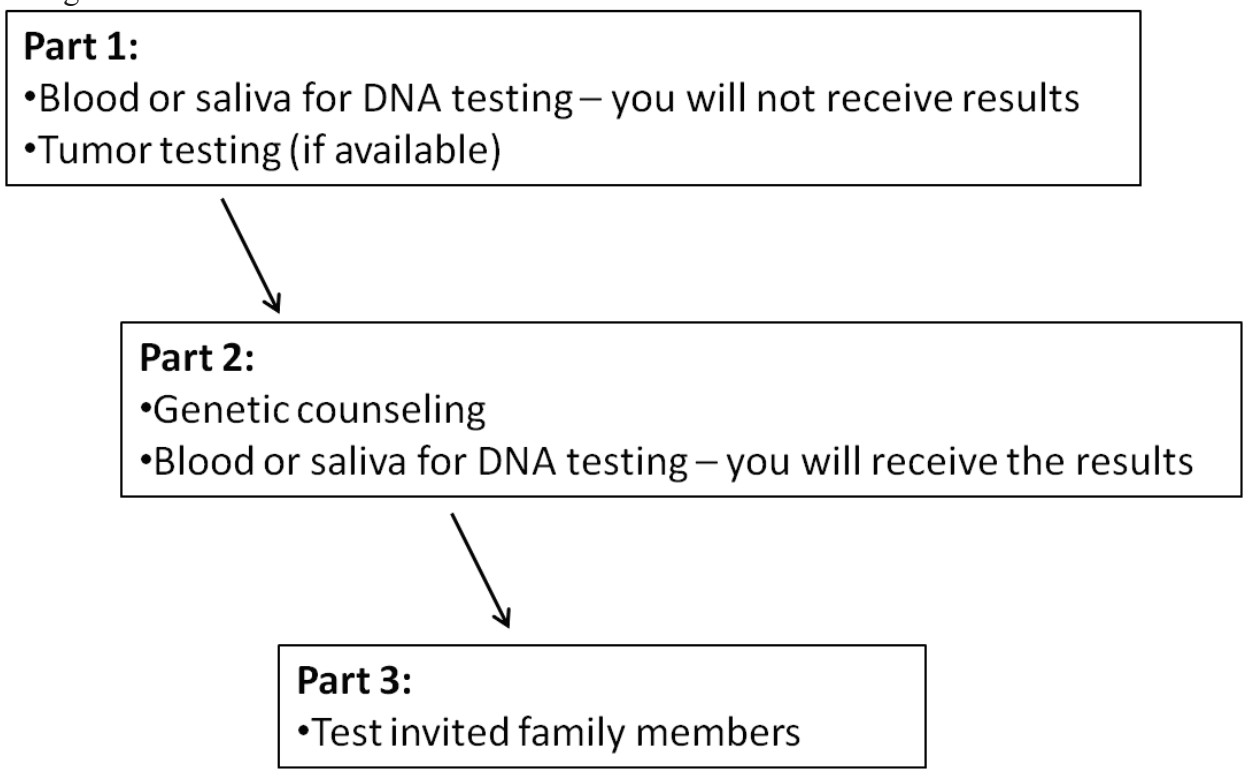
- Answer questions about your personal medical history and cancers that may run in your family.
- Give us a blood sample (2 tubes, 2 tablespoons), which we will try to get when you are having other blood drawn. If you cannot or do not wish to give blood, we will ask you to give us a sample of saliva (spit). The blood or saliva sample will be split into several parts. One part will have your name and all identifying information removed from it so that it cannot be connected to you ever again. This sample will then be tested for mutations in *BAP1* or other genes that may be involved in mesothelioma, uveal melanoma, or choroidal nevi. If a mutation is found, it will not be possible to link the result to you.

If your medical history or family history suggests a possible inherited risk for mesothelioma or uveal melanoma, a genetic counselor will contact you to talk about whether or not you would allow a blood or saliva sample with your name on it to be tested for mutations in *BAP1* or other

genes that may cause melanoma, uveal melanoma, or mesothelioma. If you agree to part 2 of this study, you will need to sign another consent form (Consent 2). If this testing finds a mutation in *BAP1* or another gene that increases the risk of cancer, we will ask you to meet with a genetic counselor to hear your result. You will then be asked to give a new blood or spit sample to confirm the result. If the result is confirmed, we will ask you to contact your relatives and offer them testing and participation in this study. Your relatives are free to decline to take part.

After the study…

After you are finished with the study, we may want to keep in touch with you. We may want to keep track of your medical condition. We will do this by phone and/or mail. Checking on your condition helps us to know the long-term outcome after gene testing.



How long will I be in the study?

You will be asked to take part in the study until you withdraw consent from the study or are deceased.

It will take about 15 minutes to fill out the questionnaire and a few minutes to provide the blood or saliva sample. You will only be asked to do this once, unless you agree to the optional additional questions in the "Optional" section of this consent form.

If you are in offered testing through the 2nd part of this study, the genetic counseling for research testing can be done over the phone. We do not know how long it will take to get test results for those who agree to have testing done. It could take many months. When results are available, we

will contact you. If there is a positive result, we will invite you for in-person genetic counseling and confirmatory testing.

We may call you in the future to see how you are doing and to ask you if you or your family members have any new medical problems.

If you agree, we may also contact you in the future to offer you the chance to take part in new research studies that may be relevant to you or your family. We would like to encourage you to tell us the name of a family member who we can contact if you are not available to talk about your results or future studies. You can indicate your preference for this in the "Optional" section of this consent document.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. If you stop being in the study, we will destroy your blood or saliva DNA sample. Information from testing that has already been done cannot be erased, however.

The study doctor may stop you from taking part in this study at any time if:

- It is considered to be in your best interest
- The study procedures are found to be unsafe or ineffective
- There is any problem with following study procedures
- There are any problems with research funding
- Or for any other reason

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

There are risks to taking part in any research study.
Answering questions about your family history of cancer may be upsetting to you. There are no other risks to taking part in this part of the study. If you are asked to consider genetic testing for *BAP1* mutations or other mutations associated with melanoma, uveal melanoma, or mesothelioma, you will be told about the risks and benefits of genetic testing and be asked to sign another consent form.

During the study, you will be provided with any new information that may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this reserch study.

Are there benefits to taking part in the study?

Taking part in this research study may or may not benefit you directly. We hope the information learned from this research study will provide more information about the features associated with inherited forms of mesothelioma and uveal melanoma. This would allow clinicians to develop appropriate screening recommendations for individuals and families at-risk.

Who owns my blood or saliva sample?

Your blood or saliva sample for this research will belong to MSKCC. You will keep the right to have this blood or saliva sample thrown out if you withdraw from the study. If you die or cannot make your wishes known, the future use of your sample passes to a person other than you. That person is the executor of your estate. Control of your sample may also pass to your next-of-kin.

Will I receive the results from the study?

You will not receive the results of testing that is done in this part of the study.

How will my blood or saliva sample be used?

Your blood or saliva sample will be used to isolate DNA. This DNA will be used in research about genes causing cancer, especially mesothelioma, uveal melanoma, and choroidal nevi. Such research can take a long time. Your blood or saliva sample will be stored for several years but it will not be stored forever. If you want to store your DNA for your own future use, you need "DNA banking." We will provide you the name of a center that provides DNA banking if you wish. You will need to pay for DNA banking.

It is possible that your blood or saliva sample may run out. If this happens, we hope that you will give us the chance to get another blood or saliva sample. If you would agree to give us an extra sample, please indicate this in the "Optional" section of this consent document.

If you agree, we may use your blood or saliva sample in the future to find new cancer genes. If you agree to this, you will indicate this on in the "Optional" section of this consent document. This is optional and not mandatory to participate in this study.

We expect that extra DNA will remain after testing is done. Memorial Hospital may retain any part of the blood, saliva, or tumor sample that is left. It may also preserve or dispose this blood, saliva, or tumor sample. If you agree, we may use your blood, saliva, or tumor sample in the future to find new cancer genes. We may also use your blood, saliva, or tumor sample to study new genes whose cancer risk is not known. It is not possible to predict what kinds of tests may be done on your blood, saliva, or tumor sample in the future. We may perform "sequencing" on your blood, saliva, or tumor sample, which means that we will study all the genes in your DNA at the same time, trying to find new genes linked to mesothelioma, uveal melanoma, or other cancers. "Sequencing" may find changes in genes that are linked to risks of diseases other than cancer, or changes that are of unknown importance. We will not be able to inform you of these changes because the testing is being done in a research setting. However, we may wish to contact you to ask you to donate a second blood, saliva, or tumor sample to confirm changes found by sequencing. If you are not available, we may wish to discuss your test results with your family members. If you think your family would be interested in getting information if you are not available, we ask that you give us the contact information of a contact person for the family. That person should stay in touch with us so we can reach them in the future, if needed.

Do I have to take part in this study?

The choice to take part in this study or not is yours. Make your choice based on what we have explained to you and what you have read about the study.

Taking part in this research study is voluntary. Instead of being in this research study, you have the following options:

- Decide not to participate in this research study
- Participate in another research study
- Obtain genetic counseling and/or genetic testing through available clinical programs

Whether or not you decide to participate in this study, you may still be able to obtain genetic counseling and/or genetic testing through clinical programs at this center or at other centers. If you have clinical testing, you may still enroll in this study if you are willing to share your information. If you decide not to participate in this study, your care at this institution will not be affected.

Will my medical information be kept private?

Every effort will be made to keep your study records private. It is the responsibility of the research staff at Memorial Hospital to make sure that your records are managed to protect your privacy. If information from this study is used in any reports or publications, your name and anything else that could identify you will not be used. Trained staff at Memorial Hospital may review your records if necessary. Access to your medical information will be limited to those listed in the Research Authorization Form, which is a part of the informed consent process.

A description of this clinical trial may be available on http://www.ClinicalTrials.gov. 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.

To help protect your confidentiality, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identity you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The results of tests done on your blood, saliva, or tumor sample may be shared with other researchers. The information shared will not contain your name or other Protected Health

Information. Results of tests performed on your blood, saliva, or tumor sample may also be included in databases that are only available to researchers who apply to the National Institutes of Health. Although your name and Protected Health Information will not be included in these databases, it is theoretically possible that someone could find out that your blood or saliva sample was included in the database, especially if they had access to another sample of your DNA.

What are the costs of taking part in this study?

If you choose to participate in this study, you will not be charged for the following:

- Anonymous genetic analysis (you will not receive these genetic results) of the *BAP1* gene
- Research genetic analysis of the *BAP1* gene

Additional tests (such as more frequent eye exams or CT scans) may be recommended if your doctor is concerned that you are at risk for carrying an altered gene. These will not be covered by the study. You or your insurance company will be charged for other portions of your care that are considered standard care. You may be responsible for co-payments and deductibles that are standard for your insurance coverage. For example, if you have been diagnosed with mesothelioma or uveal melanoma, you would continue to have treatment as has been recommended by your doctor.

What happens if I am injured because I took part in this study?

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 the medical treatment.

What are my rights if I take part in this 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 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.

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

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 Marjorie Zauderer, MD at 646-888-4656.

Any hospital that does research on people has an institutional review board (IRB). This board reviews all new studies to make sure that the patient's rights and welfare are protected. The IRB at MSKCC has reviewed this study.

For a non-physician whom you may call for more information about the consent process, research patients' rights, or research related injury is Jorge Capote, RN, Patient Representative, telephone number: (212) 639-8254.

Optional: Please review the sentences below and check "Yes" or "No." You do not have to agree to this in order to take part in the study.

1. I agree that my sample (blood, saliva, or tumor) may be used in the future to identify other genes that are associated with cancer.

   Please check one:
   ___YES ___NO

2. I agree that researchers may contact me in the future for an additional blood or saliva sample.

   Please check one:
   ___YES ___NO

3. I agree that researchers may contact me in the future for other studies which might be appropriate for my family or me.

   Please check one:
   ___YES ___NO

The following family member should be contacted in the event that I am not available to discuss new findings or studies related to my participation in this study:

Name: _____

Address:_____

_____

City: _____ State:_____ Zip _____

Telephone:_____ E-mail: _____

RESEARCH AUTHORIZATION

Clinical and Histopathologic Characteristics of *BAP1* Mutations

Research Participant Name: _____

Research Participant MRN :_____

Information about you and your health is personal. It is "Protected Health Information." We cannot use any of your health information for research unless you tell us that we can. If you take part in this research, the people or organizations that can look at your information are listed below. You will have to sign this form to tell us we have your permission to share your protected health information.

The following persons and/or organizations may use or disclose your information for purposes related to this research:

- The people in charge of the study and their assistants and support staff.

The following persons and/or organizations may look at your information for purposes related to this research:

- Members and staff of the hospital's Office of Clinical Research, Computing Resource Group that manages research databases, Data Safety Monitoring Board, and the Quality Assurance Committee.
- Members and staff of the hospital's Institutional Review Board and Privacy Board.
- The National Cancer Institute, National Institutes of Health, U.S. Food and Drug Administration, and other agencies responsible for oversight.
- The following sponsor(s) of this research: Memorial Sloan-Kettering Cancer Center
- Others: The study is funded by the United States Department of Defense (DOD).

The following information will be used and/or disclosed for this research:

- Your entire research record.
- HIV-related information. This includes any information showing that you had an HIV-related test, have HIV infection, HIV-related illnesses or AIDS, or any information that could mean you might have been exposed to HIV. New York State requires us to obtain this consent.
- HIV-related information collected during this study if you choose to disclose it when talking to any of the staff.
- Your medical records from the hospital
- The following information:
    - Blood, Saliva and Tissue Samples
    - Questionnaires

If you sign this form, it means you are giving us permission to share your protected health information. We can only share it with the people or organizations describe above. The purpose for the use and sharing of this information is to conduct this study. This signed form allows us to make sure that everyone who needs information related to this study can get it.

Your protected health information may also be used for your research treatment, to collect payment for care you receive while on the study (when applicable), and to run the business operations of the hospital.

Some of the people or organizations listed above may not be subject to privacy laws. This means they could share your information again.

You do not have to sign this form. If you do not sign it, you will not be able to take part in the study. Your health care outside the study will not be affected. The payment for your health care or your health benefits will not be affected.

You have the right to withdraw from the study at any time. If you sign this authorization form, you also the right to withdraw it at any time. If you withdraw it, we cannot use or share anymore of your research data. If the hospital has already used or shared your information, it cannot be taken back. This authorization allows us to use your information until you say we cannot use it anymore. If you want to withdraw your authorization, write to: Marjorie Zauderer, MD at the Department of Medicine, Memorial Sloan-Kettering Cancer Center.

Notice About HIV-Related Information

Once we have shared your HIV-related information, it can only be shared again if federal or state laws allow it. You have the right to ask for a list of any people who get your HIV-related information that are not listed above. There are two agencies to help protect your rights. Call them if you think you have been singled out or harmed because of HIV-related information.

- New York State Division of Human Rights (888) 392-3644
- New York City Commission of Human Rights (212) 306-7500

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Statement of professional obtaining consent

I have fully explained this clinical research study to the participant or his/her Legally Authorized Representative (**LAR**). In my judgment and the participant's or that of his/her Legally Authorized Representative, there was sufficient access to information, including risks and benefits to make an informed decision.

Consenting Professional Must Personally Sign & Date		
Assent (Minor between the ages of 7 and less than 18): If the participant is a minor, I have obtained his/her assent to participate in the study to the best of their ability to understand. ☐ **YES** ☐ **NO** ☐ **N/A (Adult or Child <7)**		
Consenting Professional's Signature		**Date:**
Consenting Professional's Name (Print)		

Participant's (or Legally Authorized Representative's (LAR)) statement

I have read this form with the description of the clinical research study. I have also talked it over with the consenting professional to my satisfaction. By signing below, I am agreeing to the following: (1) to voluntarily be a participant in this clinical research study (2) authorizing for the use and disclosure of my/their protected health information (data about myself) and (3) that I received a signed copy of this consent form.

Participant/LAR Must Personally Sign & Date		
Participant/LAR Signature		**Date:**
Participant/LAR Name (Print)		
LAR Relationship to Participant		

Witness Signature (If Required)

☐ **Non-English Speaking Participant Witness and/or Interpreter:** I declare that I am fluent in both English and participant's (or LAR) language and confirm that the consent discussion was appropriately translated for the participant (or LAR).

☐ **Other:** I confirm that the consent discussion was appropriate for the participant's (or LAR's) understanding of the study.

Name of Witness: _____

Signature of Witness: _____ Date: _____

The Participant/Legally Authorized Representative Must Be Provided With A Signed Copy Of This Form.