UPCC 09124 (IRB #pending)

PENN MEDICINE
RESEARCH SUBJECT
COMBINED INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Protocol Title:	**QuantifyHER** Quantitative Immunofluorescence and/or RT-qPCR for Measuring HER2 in HER2-low Metastatic Breast Cancer
Sponsor:	Penn Medicine
Partial Funding Sponsor:	Johns Hopkins University on behalf of the Translational Breast Cancer Research Consortium (TBCRC) Danaher, Inc.
Principal Investigator:	Angela DeMichele, MD, MSCE Abramson Cancer Center of the University of Pennsylvania Philadelphia, PA 19104 (215)-662-4000
Sub-investigators:	Eleanor Taranto MD
Emergency Contact:	24 Hour Emergency – Call 215-662-4000 Ask for Oncologist On-Call

Overview and Key Information

You are being invited to take part in a research study called QuantifyHER. Your choice to take part is voluntary, and you should only participate if you completely understand what you will be asked to do. You should also understand the risks of taking part in this study. You should ask the study team any questions you have about taking part in the study before agreeing to join the study. If you have any questions about joining this study or your rights as a participant, please contact the Institutional Review Board (IRB) at (215) 898-2614 for help. You can contact the IRB at any time before, during, or after joining this study.

This research study is being done in patients with metastatic HER2-low breast cancer (MBC). This study will look at whether we can better predict which patients will benefit from HER2-directed treatments.

For patients with metastatic breast cancer (MBC), our goal is to give the most effective treatment possible and preserve the best possible quality of life. Trastuzumab-deruxtecan (T-DXd) is a new drug that was initially used to treat HER2-positive breast cancer. T-

DXd is an antibody against the HER2 protein that is attached to a chemotherapy molecule. This allows chemotherapy to be delivered directly into tumor cells that have HER2 on their surface. Importantly, the chemotherapy can be delivered to tumors with even low levels of HER2 protein. This is different from previous HER2 treatments which needed higher levels of HER2 on the cell surface to work. T-DXd was therefore recently approved by the Food and Drug Administration for patients with MBC with low amounts of HER2 protein on their tumor cells. This is also known as "HER2-low" disease.

The current test for HER2 on tumor cells measures the amount of HER2 by immunohistochemistry (or IHC). This test can measure high amounts but cannot reliably measure low levels of HER2. Using this test can lead to incorrect and variable measurements of HER2 protein on tumor cells. We need a reliable test to measure low amounts of HER2. Without a reliable test, it is likely that there are patients who are not getting this effective drug. Since up to 50% (half) of all MBC patients have "HER2-low" disease, it is essential to improve the accuracy of measuring HER2. This will ensure we give T-DXd to the right patients, and also reduce the chances of giving T-DXd to patients who will not benefit from this treatment and who should not be exposed to its potential side effects.

This trial will follow approximately 200 patients with HER2-low MBC starting T-DXd. The study will test a newly developed test to measure HER2 protein on tumor cells using an antibody that 'lights up' when attached to HER2. The 'light' is called fluorescence. Cells with HER2 light up when viewed under a microscope with a special light. The fluorescence strength matches with the amount of HER2 protein on the breast cancer cell. We propose to prove this test works in patients with MBC that is HER2 low (or IHC 1+) and who are beginning treatment with T-DXd. Each patient in this study will have their tumor tested using this new fluorescence test (Quantitative Immunofluorescence, or QIF). Patients will be followed for response to T-DXd. We will compare the QIF score with IHC score as they relate to patients who benefit from T-DXd. We propose that QIF will more reliably tell the difference between patients who benefit from T-DXd treatment from those who do not. We will also test another way to measure HER2 using 'messenger' RNA (mRNA). HER2 mRNA tells cells to build the HER2 protein. This combination of tests may replace standard IHC to better select patients who will benefit from treatment with T-DXd.

To take part in the study, you must have a tumor sample from a metastatic site (a site outside the breast) that showed HER2-low disease. You must also be planning to start treatment with T-DXd or have started T-DXd within the last 30 days, and be willing to undergo routine imaging. Routine imaging with CT scans will be done as per your doctor to measure the extent of your breast cancer.

After joining the study, a part of your previous tumor sample will be sent to the study laboratory at Yale School of Medicine. The Yale laboratory will do the immunofluorescence (QIF) test on part of your tumor sample. A part of the tumor sample will also be used to do the mRNA test as well. If you chose to take part (consent) to future

research, the tumor sample will be kept for future use by the study team. There may be other tests developed in the future for which it makes sense to use these samples.

The immunofluorescence (QIF) test has been validated as accurate by a standardizing lab. You and your treating physician will have the opportunity to receive the results of the QIF test when you complete your part in the study. You can decline to receive this information. The mRNA test has not yet been standardized or clinically validated, so the results of the mRNA test will not be shared with you.

The main risk from this study is that your personal health information may accidentally be shared. The study team takes precautions and uses secure databases to minimize this risk.

There are other factors to consider before agreeing to take part in this study. Please read the full consent for other factors to consider. If you are interested in taking part in this study, a member of the study team will review the full information with you. You are free to decline or stop taking part at any time.

Why am I being asked to volunteer?

You are being asked to take part in this research study because you have previously been diagnosed with HER2-low metastatic breast cancer and are planning to start treatment with a drug called Trastuzumab Deruxtecan (T-DXd), or have just started this medication. This study will enroll approximately 200 patients with HER2-low MBC who are planning to start treatment with T-DXd.

Your choice to take part in this study is voluntary. This means you can choose whether or not you want to take part. If you choose not to participate, your clinical care will not be affected. If you choose to take part in the study, you can withdraw your permission to continue participation at any time. Before agreeing to take part in this research study, it is important that you read the following explanation of the study procedures and how long you will be in the study. This document describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time.

Please take time to read the following information carefully. You may wish to discuss it with your family, friends, and your personal doctor (i.e., your family doctor or primary care doctor). If you have any questions, you may ask your study doctor and/or the research team for more information. Take time to decide whether or not you wish to take part. If you decide to take part in the study, you will sign this form and you will receive a copy for your records. If you decide to take part in the study, you can change your mind at any time and withdraw from the study without giving a reason.

Who is sponsoring this study?

Angela DeMichele, MD, MSCE, the Principal Investigator, is the sponsor of this study (the entity responsible for the design, conduct and regulatory oversight of the study). Dr.

David Rimm is the co-investigator and created the quantitative immunofluorescence (QIF) assay that will be evaluated; he runs the lab at Yale University School of Medicine that will be performing bioassays on and storing the tumor samples. Danaher is the company that created the mRNA test and will be funding the study. Dr. DeMichele and Penn Medicine will receive payments to cover the research costs such as the collecting/reporting study information associated with the conduct of the study. The American Society for Clinical Oncology (ASCO) is also supporting this research with salary and trial support. Johns Hopkins University on behalf of the Translational Breast Cancer Research Consortium (TBCRC) is providing administrative support for this study. The TBCRC is a group of academic medical centers across the United States that work together to conduct breast cancer research.

How long will I be in the study?

You will be in this study until you stop receiving T-DXd as treatment for your breast cancer.

What am I being asked to do?

First, the study team will determine if you are eligible for the study. Your records will be reviewed to determine the following:

- You have been diagnosed with metastatic breast cancer (cancer that has spread outside of the breast).
- You have a tumor sample from a previous biopsy—either at the time of diagnosis with metastatic cancer or from before this—showing HER2-low breast cancer.
- You are planning to start Trastuzumab Deruxtecan (T-DXd) treatment for your cancer, or you have just started T-DXd within the last 30 days.

If you are eligible to take part in the QuantifyHER study, you will be asked to allow the researchers to request a part of the tumor tissue sample that was removed at the time of your biopsy confirming metastatic breast cancer. They may also request part of previous tumor tissue samples if they showed HER2-low disease. If a tumor sample is not available, you will not be eligible to take part in this study. You will be asked to undergo routine imaging tests at normal time points, the timing of which will be directed by your treating physician. The results of these studies will be shared with the study team.

The Quantitative Immunofluorescence (QIF) and a new mRNA expression investigational test will be done on a part of your tumor samples at Dr. Rimm's lab. The QIF test has been validated by a standardizing lab as providing consistent results. You will be asked whether you would like to receive the results of this test.

Your care team for your breast cancer will be your normal care team—and your own oncologist. You will not have to work with the study team to receive any of your direct care, as your treatment will all occur through your own oncologist as it would have otherwise. You will have no extra visits with the study team except perhaps the first visit when you initially enroll in the study.

UPCC 09124 (IRB #pending)

We also are asking for your permission to re-contact you in the future for new research studies or questions that may come up during this study. If you are re-contacted, the new research will be explained, and you can choose whether or not to take part. It is important to note that when research is done on your samples, the researchers doing this research will protect the access to any identifying information such as your name or medical record number.

What are the possible risks of the study?

This is an observational study, which means that we will observe you during your usual treatment. There are no research treatments or procedures planned. Imaging will be done at routine times. There are no additional tests, blood draws, or biopsies required to join this study.

If you choose to take part in the QuantifyHER study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or study doctor's office than usual during the screening and enrollment process for the study.
- You may be asked sensitive or private questions which you normally do not discuss, although you may choose not to answer.

The main risk from this study is that your personal health information may accidentally be shared. The study team takes precautions to minimize this risk and uses secure databases to avoid this.

Risks of Using Up Stored Tumor Tissue Samples

Stored tumor samples from a previous biopsy of your metastatic tumor or other previous biopsies may be collected as part of this study. To minimize the risk of the whole tumor sample being used up, we are requesting only 10 slides, and are explicitly requesting that the amount requested and sent not use up all of the remaining tumor sample.

Risks of Genetic Research

This research may include genetic testing. Even without your name or other identifiers, your genetic information is unique to you. The research team will be primarily responsible for safeguarding your genetic information. Only a unique code will be used to identify your specimens and data. However, because there will be a link between the code and your identity, confidentiality cannot be guaranteed. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

There can be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a research study. Even though your genes are unique, you share some of the same genes with your blood relatives. Although we are not able to know all the risks from taking part in research on inherited traits, we believe that the risks to you and your family are very low, because your samples will be coded. Research results will not be returned to you or

your doctor because they are performed in a research laboratory and have not been approved for clinical use.

Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law (Genetic Information Non-Discrimination Act, GINA) helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long-term care insurance. If you want to learn more about GINA, you can find information about it on the internet or ask the study staff.

What if new information becomes available about the study?

During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. If we discover new information about the study that could affect your decision to stay in the study, you will be notified in a timely manner. You will be able to ask questions about this new information and can discuss it with your family, friends, or doctor. It is always your decision to continue in the study or leave the study.

What are the possible benefits of the study?

Knowledge of the exact amount of HER2 protein on your tumor may be clinically important for your care in the future. Understanding who is likely to benefit from HER2-targeted treatments could apply not only to trastuzumab deruxtecan (T-DXd) but to other HER2-targeted therapies. This study may help physicians to decide about whether you—and others—may benefit from other HER2-targeted treatments. Both tests being evaluated may eventually be used clinically, as part of usual care—for you or others. So, while you may not benefit directly, right now, the knowledge learned from your participation may help inform future studies and clinical decision-making.

What other choices do I have if I do not participate?

Your participation in this trial is entirely voluntary, and you may withdraw your consent at any time. If you decide not to participate in this trial, you will not lose any benefits to which you would otherwise be entitled. Talk to your doctor about your choices before you decide if you will take part in this study.

Will I be paid for being in this study?

You will not be paid for taking part in this study.

UPCC 09124 (IRB #pending)

Will I have to pay for anything?

You and/or your insurance provider will be responsible for any deductibles or applicable co-pays associated with standard tests, exams or procedures that would be done for your routine clinical care. There will be no charge to you for providing a sample of your tumor to the study lab.

Please talk to your doctor and study team about putting you in touch with a financial counselor to determine exactly what the deductible and co-pay will be for you; this is highly variable depending on your type of insurance.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Website at: http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Website.

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.

When is the Study over? Can I leave the Study before it ends?

Your participation in the QuantifyHER research study will be over when you stop taking T-DXd.

You may choose to stop participating at any time. You can also choose to leave the study at any time without giving a reason. It is important to tell your doctor if you are thinking about stopping. Leaving will not affect your future medical care.

Your doctor or the research investigators may stop you from taking part in this research study at any time if he/she believes that it is in your best interest, or if the study is stopped. If you are removed, your study doctor will explain to you why you were removed. The study doctor and study team will help arrange for your continued care.

How will my personal information be protected during the study?

If you decide to participate in this study, the study doctor and staff will collect medical and personal information about you as part of completing the study screening. We will do our best to make sure that the personal information in your medical record is 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. Please refer to the information below which explains more specifically how your personal information will be protected. If you do not want to allow these uses, you should not

participate in this study. Information identifying you will be kept confidential as described below.

While collected as part of this study by your study doctor and study team, identifying information (including your name, address, telephone number, medical record number, or any number/codes that will directly identify you) will be kept as confidential as possible and will not be routinely disclosed outside of the study team. Personal health information that could be used to identify you will not be sent to the Funder and/or their designated representatives.

You will be assigned a unique subject registration number upon enrollment in the study. This number will be used to identify you throughout the course of this study so that your identity is protected. The key to this code (which links your name back to the personal health information collected during this study) will be stored in a secure area and only the lead study team and your own institution will have access to this code identifying you. However, some of the study data (e.g., date of birth) could be used in combination with other information, in order to identify you.

Your tumor biopsy slides will be identified by your unique study identifier, which will be shared across institutions as the samples will be shipped to a laboratory at Yale University School of Medicine for biomarker analysis. While your name will not be shared across institutions and will be stored in a secured database, some of the study data (e.g., date of birth) could be used in combination with other information, in order to identify you. If you have questions about the specific information that will be released, you should ask your study doctor.

If you have questions about the specific information that will be released, you should ask your study team.

Will information about this study be available to the public?

A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US 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 any time.

The results of this research study may be published. You will not be identified in publications without permission. Additionally, a summary of results will be posted on the TBCRC website www.tbcrc.org when the results of the study are published.

UPCC 09124 (IRB #pending)

What may happen to my information and samples collected on this study?

Your tumor samples may be used to make medical or scientific discoveries or to create products, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family. Most uses of biospecimens or information do not lead to commercial products or to profit for anyone.

Electronic Medical Record and Release of Study Related Information

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of your medical chart within a health system. An EMR is simply a computerized version of a paper medical record.

If you have never received care within Penn Medicine and are participating in a Penn Medicine research study that uses Penn Medicine healthcare related services, an EMR will be created for you for the purpose of maintaining any information produced from your participation in this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e., your name, the name of your primary doctor, the type of insurance you have). If you have been a patient at Penn Medicine in the past, information from your research participation will be added to your existing medical record.

What may be placed in the EMR?

Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, and clinical procedures, etc.) will be placed in your EMR maintained by Penn Medicine.

Once placed in your EMR, your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g., health insurance company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety, and efficiency of your healthcare.

To request that your health information not be shared through HIEs, please call 215-662-4484.

Will I, as a participant, have access to research related information within the EMR?

Please note the following about diagnostic test and/or imaging results:

The 21st Century Cures Act requires healthcare institutions to allow patients increased access to their electronic medical record. As part of your participation in this research, you will have access to research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

Some information specific to this clinical research study may be shared with you in a delayed manner, shared with you at the end of the study, or not shared with you. Not sharing or delaying certain research information within your EMR may be necessary to protect the integrity of the study results or for other reasons.

Information about your quantitative immunofluorescence (QIF) HER2 results will be shared with you and your treating physician at the end of your participation in the trial but will not be shared in the electronic medical record. Information about the mRNA test will not be shared with you as this is an investigational test. If this or any other tests become clinically validated, these tests will be shared with you down the line.

Will I receive the results of research testing that may be relevant to my health?

Research results that have been validated clinically will be disclosed to you in the future if you choose to receive them; this will be done in the context of discussion with your study doctor and/or clinical treatment team. As discussed above in the "What am I being asked to do" section, the Quantitative Immunofluorescence (QIF) test results, which have been standardized and validated by CLIA as a measure of HER2 expression, will be reported to you and your treating physician at completion of trial participation—unless you do not consent to the return of these results below. Tell us, by checking the correct box at the bottom of this section, if you would like to receive the results of your QIF testing.

Many of the tests done in research studies are only for research and have no clear impact on your healthcare. The investigational mRNA test results have not been clinically validated yet and therefore will not be reported to you as this test is, at present, only for research and will have no clear impact on your healthcare. Any other investigational tests which may be performed on your tissue samples in the future, should you consent to future research, will not be returned to you. In addition to the results described above, this study may generate additional research results from testing on your tissue samples in the future. These results will not be returned to you because they would not be relevant to your healthcare.

As we learn more about the meaning and validation of these tests, we may consider offering you the opportunity to receive these results. After the research has been explained, you would decide whether to receive the results or to decline them. Tell us, by

checking the correct box below, if you would like to be contacted in the future about this. If you consent to this process, we will contact you if these research results are available.

1. I would like to receive the results of QIF testing when they are available:

☐ Yes ☐ No Please initial here: _____ Date: _____

2. I would like to be contacted in the future about having my research results returned to me:

☐ Yes ☐ No Please initial here: _____ Date: _____

What information about me may be collected, used, or shared with others?

The following personal health information will be collected and used for the purposes of this study.

- Name, address, telephone number, email address, gender, date of birth
- The history and diagnosis of your disease
- Specific information about the therapy you received, including previous treatment(s) you may have had.
- Information about other medical conditions that may affect your care.
- Medical data including laboratory test results, health status, pathology results, etc.
- Genetic information/results related to research samples collected from you.
- Information on side effects (adverse events) you may experience, and how these were treated.
- Long-term information about your general health status and the status of your disease. This may include information from other health care providers.
- Data that may be related to tissue samples that may be collected from you.
- Numbers or codes that will identify you, such as your medical record number.
- Information related to study visits and other tests/procedures performed while you are participating on this study.

Why is my personal health information being used?

Your personal contact information is important for the research team to be able to contact you during the study. For this study we may need to contact you via email to provide you information about scheduling, appointments notes or to send you information about your participation in the study. Email communications are often not secure and may be seen by

others as a result. By signing below, you accept this risk. If you wish for us to use a different means to communicate with you during the course of this trial, please discuss this with the research team and alternative methods can be arranged.

Your personal health information and results of tests and procedures are being collected as part of this research study and will be used to conduct and oversee this research study.

Where may my information be stored?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS) through a secure database system called REDCap. This clinical trial management system (CTMS) will be used to register your information as a participant in a study and to keep track of your visits as they occur. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS, your information may be accessible only to other authorized personnel that support research operations. There will be study-assigned numbers (subject IDs) for each individual participant so that data and samples can be identified correctly and kept track of, both within the database and when the samples are shipped to Yale University.

Who can see or use my information?

Which study personnel may use or disclose my personal health information?
The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the Investigator's study team
- Authorized members of the workforce of Penn Medicine, and Penn Medicine support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide care as part of this study or as part of your routine care, to manage accounting or billing matters, etc.). This includes members of the Institutional Review Board (IRB), an Ethics Committee at Penn Medicine who are responsible for reviewing and overseeing research studies to ensure that they are safe and being well managed.
- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB.

Who might receive my personal health information?

As part of the study, the Principal Investigator, the study team, and others listed above, may disclose your study-related records, including the results of the research study tests and procedures, to those listed below. This study data would be processed and transmitted using secure computer systems. In all disclosures outside of your own medical center and the secure database above, you will not be identified by name,

medical record number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. In records and information disclosed outside of the home institution, you will be assigned a unique study ID number.

Your original medical records also may be reviewed by the sponsor of this study or its designated representatives, the IRB overseeing this study, and any of the regulatory or safety oversight organizations outlined below. They may review these records for the purpose of checking data collected for the study, to make sure the study is being done properly, and to analyze the results of the study.

Individuals or organizations responsible for administering the study:

- Angela DeMichele, MD, MSCE (the sponsor of this study) and their designated representatives, including Eleanor Taranto MD, co-investigator at Penn Medicine.
- David Rimm, MD PhD (co-investigator, who will be performing the bioassay) at Yale University School of Medicine, and his designated representatives.
- Cepheid, Leica and their designated representatives (the manufacturer of the mRNA test).
- Authorized representatives of Penn Medicine.
- Authorized representatives of TBCRC sites who are enrolling patients on the study.
- Johns Hopkins University on behalf of the Translational Breast Cancer Research Consortium (TBCRC)

Regulatory and safety oversight organizations

- The U.S. Food and Drug Administration (FDA)
- Other regulatory agencies and/or their designated representatives, including international agencies.
- Public Health agencies and other government agencies (including non-U.S.) as authorized or required by law.

Once your personal health information is disclosed to others outside of Penn Medicine, it may no longer be covered by United States federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

How long may Penn Medicine be able to use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. If you sign this form, we will collect your health information until the end of the research study. We may collect some information from your medical records even after you finish taking part in this study or after your death. We will keep all of the

information forever in case we need to look at it again. We will protect this information and keep it confidential.

Your information will be held in a research database through REDCap. However, Penn Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization to do so.
- Penn Medicine's IRB grants permission after ensuring that appropriate privacy safeguards are in place.
- As permitted by law

The data from this study may be published or used for teaching purposes, however you will not be personally identified in any publication. Your identity will remain confidential unless disclosure is required by law.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to participate in this research study.

Can I change my mind?

You have the right to withdraw your permission for the use of your personal health information, but if you do so, you must stop taking part in this study. You must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, your personal health information that was collected before we received your written request may still be used and disclosed, as necessary for the study. If you withdraw your permission to use your personal health information, you will also be withdrawn from the research study and no new information will be collected.

Will I be able to access my research records?

You have the right to see and get a copy of your medical records kept by Penn Medicine, and at other sites accordingly. However, you will not be able to review or receive some of your records related to the study until after the entire study has been completed. When the study is over, you may write to the study doctor to ask to see or copy all of your medical information that was collected during the study. You also have the right to say how your medical information may be used, and to have any incorrect data about yourself updated or corrected.

By signing this document, you are permitting the study team to use and disclose personal health information collected about you for research purposes as described above.

UPCC 09124 (IRB #pending)

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns, or complaints regarding your participation in this study, or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs at Penn Medicine with any questions, concerns, or complaints by calling (215) 898-2614.

Where can I get more information?

You may visit the National Cancer Institute (NCI) Website at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

Optional Future Research

WHAT ABOUT USE OF MY TISSUE AND BLOOD FOR FUTURE RESEARCH?

If part of the tissue from the required biopsies as described above is leftover after the proposed tests are done, we ask you to donate those left over samples for future research. If you do not want to take part in this optional portion of this study, you may still take part in the main study as described above.

If you agree, your samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples.

What research will be done on my leftover samples and what information will be collected?
The future research may also include looking at genes (DNA) and how they affect health and disease. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

In addition to your samples, we will store some basic information about you. This will include things like age, sex, and race or ethnic group. We will store information about your family's health history. If you agree, we will collect this information from your medical record.

We will also collect information from your medical record that is related to your health and/or disease history. Some examples include results of tests, medical procedures, images (such as X-rays), and medicines you take. Researchers will use this information to better understand how genes affect health and response to treatment. We will look at your medical record from time to time to update this information. This will take place for as long as your sample is stored, which may be many years, unless you tell us to stop.

Who will have access to my leftover samples and information?
We will store your samples and information in a tissue bank. Your samples will be coded similarly as described previously.

Researchers can ask to study the materials stored in the tissue bank. This includes researchers from within the TBCRC Institutions, as well as from other universities, the government, and drug or health companies. Some researchers will be from the U.S.; some may be from other countries around the world. An oversight committee will review each request. This kind of review is to make sure that any risks are minimized and that your rights and welfare are protected. If a study is approved, we might give a part of your sample and information to the researchers. We would give them your materials along with samples and information from many other people. We may also

share your materials with other tissue bank and research projects. We will not share information that could directly identify you (like your name, social security number, and address) without your permission.

There is no limit on the length of time we will store your samples and information. We may keep using them for research indefinitely unless you decide to withdraw from the project.

Who else will have access to my genetic information?

Researchers can do more powerful studies when they share with each other the information they get from studying human samples. They share this information with each other by putting it into scientific databases. These databases store information from many studies conducted in many different places. Researchers can then study the combined information to learn even more about health and many different diseases.

There are different kinds of databases; some are publicly accessible, and some are restricted. Anyone on the Internet can access publicly accessible databases. Only researchers who apply and are approved can access restricted databases. There are many restricted databases; the researchers in this study maintain some, the federal government maintains some, and private companies maintain some. Some of your health information could be placed into one or more of these publicly accessible or restricted databases.

Your name and other information that could directly identify you (such as address or social security number) will not be placed into any scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

Will I find out the results of the research?

You should not expect to get personal results from research done through the tissue bank. Researchers will study samples and information from many people, and it may take many years before they know the results or if they have any meaning. However, it is possible that researchers will learn something that might be important to your health, such as results of genetic or similar testing done on your samples. We expect these situations to be very rare. If this happens, we will seek appropriate approvals from the IRB and/or ethics committee and may contact you directly or through your doctor to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted. The findings may lead to additional testing or changes to your care and could be a stressful situation to you and your family. If this happens, care will be taken to make sure the findings are carefully explained, and that support is available for you.

Will this future research cost me anything or will I be paid?
You will not be asked to pay any costs related to this research. You will not be paid for agreeing to allow your samples to be used for future research.

The research done with your tissue and blood may lead to the development of new products in the future. You will not own any product or idea created by the researchers working on blood or tissue obtained from you during this study. You will not receive any financial benefit from the creation, use or sale of such a product or idea from blood or tissue obtained from you during this study.

Your tissue will be used only for research and will not be sold.

What are the risks?
One risk of giving samples for this research may be the accidental release of your name that could link you to the stored samples and/or the release of results of the tests run on your samples, including genetic testing, if this is performed. There are safeguards in place such as coding your samples and information, secure buildings and equipment, and the Genetic Information Nondiscrimination Act (GINA) as described previously.

What are the benefits?
You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Will I be contacted in the future about this or other research?
We, the local site Study Team, may want to contact you in the future. You can decide now whether or not you want to be contacted. You can also change your mind later.

If you agree, we may contact you for several reasons. For example, over time, stored samples may be used up or decrease in quality, so we may contact you to ask for more samples. We may also contact you to update basic information or request information about your health.

Additionally, we may want to contact you to see if you want to participate in other research. We will not notify you every time your samples and information are used. However, some researchers might apply to do a study for which they would need to contact you. For example, they might want to ask you to give another sample or to fill out a survey, or they might ask you to do a phone interview or come in to be seen by a researcher or doctor. If a study like this is approved, someone from this project will contact you. They will tell you about the study so you can decide if you want to receive more information. There will be a new consent process just for that study. You can decide then to take part or not take part. If at any time you decide you no longer want to be contacted about future studies, please tell us.

Can I change my mind after I agree to let my samples be used?

You have the right change your mind about the future use of your leftover biospecimens and information at any time. If you want to leave the project, let us know. You will be given some options and can choose what you want us to do with your unused samples. You can also tell us to stop using your medical records. However, you cannot withdraw your samples and information from studies that have already begun. We cannot get samples and information back once they are shared with other researchers. In addition, it may not be possible to remove your genetic information from scientific databases once it has been de-identified.

MAKING YOUR DECISION

You have a say in how your leftover biospecimens and information are used in future research. Donating samples for future research is your choice and you may be in the study even if you do not want your samples used or stored for future research.

Please review each question below and choose the answer that is best for you:

1. I permit leftover samples to be stored and used for future research to learn about, prevent, or treat cancer.

☐ Yes ☐ No Please initial here: _____ Date: _____

2. I permit my samples to be stored and used for future research about other health problems (for example: causes of diabetes, heart disease, and Alzheimer's, or genetic links to alcoholism).

☐ Yes ☐ No Please initial here: _____ Date: _____

3. I agree that someone may contact me in the future to ask me to take part in more research.

☐ Yes ☐ No Please initial here: _____ Date: _____

4. I agree to have my coded genetic information and coded medical information placed in password-protected secured databases for research analyses.

☐ Yes ☐ No Please initial here: _____ Date: _____

Q: What is a Genome-Wide Association Study?

Genome-wide association studies (GWAS) look at the genetic differences that exist in the entire human genome (the complete set of human genes) and the association between these differences and health conditions.

As part of this study, we will be collecting information about your health and your individual genes. This information will be sent to the National Institutes of Health (NIH) GWAS database called dbGaP (Database of Genotypes and Phenotypes).

The aim of collecting this information is to look for genetic connections that:

- may make people more likely to get a certain disease (such as asthma, cancer, diabetes, heart disease or mental illness) or a condition (such as high blood pressure or obesity)
- may affect the progress of a certain disease or condition
- may affect treatments (medicines, etc.) that work for certain diseases in some people, but not in others

We will remove direct identifiers and code your information before sending it to the NIH. NIH will never get this code or the identifiers we have removed.

Penn will not know what types of research will be done with the data that are sent to the database.

GWAS data will be shared with other researchers world-wide through the dbGaP Database. This database is kept at the National Center for Biotechnology Information (NCBI) at the NIH.

Researchers must apply to NIH to use the dbGaP database. Special review committees will look at these applications to decide whether to share the data. Researchers must agree to keep data safe and use the data only for the purpose approved by the NIH.

What are the risks of data being stored for GWAS?
There may be risks to your privacy and the privacy of your relatives from storing your information in a GWAS database.

Although we believe that the NIH privacy measures make this unlikely, there is a risk that your identity could become re-connected with your genetic and health information.

If this happened -
- Information could be revealed that could lead to denial of employment or insurance for you or a relative, or
- Law enforcement agencies might be able to demand information about you in connection with an investigation.

Are there benefits to being in a GWAS study?
There is no direct benefit to you from GWAS research. The information from your data may lead to a better understanding of how genes affect health.

Please review the question below and choose the answer that is best for you:

5. I agree that my data may be stored in a GWAS registry.
☐ Yes ☐ No Please initial here: _____ Date: _____

UPCC 09124 (IRB #pending)

When you sign this form, you are agreeing to take part in this research process. This means that you have read the consent form, the study has been explained to you, your questions have been answered, you have had time to make your decision, and you have decided to volunteer to participate. You have been given the names of study staff that you can contact if you need assistance or if you have any additional questions or concerns. You agree to follow all of the instructions of your study doctor to the best of your ability and report any changes in your health that may occur during the study.

Your signature also means that you are permitting Penn Medicine to use your personal health information collected about you for research purposes within our institution. You are also allowing Penn Medicine to disclose that personal health information to outside organizations or people involved with the operations of this study.

You agree that your primary care physician can be informed about your participation in this research study.

A copy of this signed and dated consent form will be given to you.

Name of Participant (Print)	Signature of Participant	Date

Name of Person Obtaining Authorization (Print)	Signature of Person Obtaining Authorization	Date

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