The Ohio State University Consent to Participate in Research

Study Title: **The IMPACT Study: Inflammatory Responses, Mood, and Physical Fitness after Cancer Treatment**

Principal Investigator: **Janice Kiecolt-Glaser, PhD**

Sponsor: National Cancer Institute

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the 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 usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. Why is this study being done?

Cardiovascular function often declines during and following cancer treatment. This study addresses how your cardiovascular function affects your body's immune response (certain kinds of white blood cells) in ways that may be related to risks for fatigue (tiredness), negative mood, pain sensitivity, memory, and concentration, which are all particularly relevant for cancer survivors. The researchers will use a typhoid vaccine to stimulate brief changes in your immune response to see how your responses to the vaccine compare with responses to a placebo (saline or salt water). They will also measure certain hormone responses and your heart rate and blood pressure and metabolic rate to see how they respond to the vaccine compared to the placebo. The researchers also want to know if your age and/or feeling blue or depressed may affect your body's responses to the vaccine.

2. How many people will take part in this study?

240 breast cancer survivors will take part in the study.

3. What will happen if I take part in this study?

You will be scheduled for a screening appointment and two nonconsecutive full-day visits. The first screening visit and the full-day visits will take place at the Clinical Research Center (CRC), a hospital research unit located at the OSU Wexner Medical Center. All visits will occur on weekdays.

Visit	CRC Screen		Visit 1	Visit 2
Length	2 hours		9.5 hours	9.5 hours
Activity	Consenting Anemia/Diabetes blood draw Questionnaires Body measure-ments	Eligibility Determined	Blood draws Questionnaires Metabolic Measure-ments Computer tasks Heart Rate/blood pressures/temp ***Condition:*** Typhoid vaccine or Placebo/saline	Blood draws Questionnaires Metabolic Measure-ments Computer tasks Heart Rate/blood pressures/temp ***Condition:*** Typhoid vaccine or Placebo/saline

Screening visit: You will first participate in a screening appointment, which will last approximately 2 hours, to determine if you are eligible to take part in the full study. At the screening appointment, a nurse will measure your weight, height, blood pressure, and the distance around your hips and waist. A measurement will also assess the amount of fat present in your abdominal area. Ideally, the measurements are taken on bare skin or over underwear. If you are uncomfortable removing the clothing on your lower body, the measurements will be taken over your clothes.

Early in the screening session, you will have 5 ml (less than a tablespoon) of blood drawn from a vein in your arm, as well as a finger stick blood test. These blood samples will be used to determine your hemoglobin A1C (a test related to your risk for diabetes), as well as a test for anemia (a condition characterized by too few red blood cells, usually resulting in tiredness). If your blood test indicates that you may have diabetes, then you will not be able to participate further in the screening session; however, you will be compensated $5 for your time and asked to see your physician. If your blood test indicates that you may be anemic, you can complete the first screening appointment and will be compensated $25 for your time. However, you will not be able to participate in the study at that time, and you will be asked to see your physician. You have the option of being retested for anemia in 6 weeks; if you are

no longer anemic, then you may be eligible to participate in the remainder of the study. If you are still anemic, you will not be able to participate in the second screening session or the two all-day sessions. If you do not have a personal physician, you will be given contact information for OSU physicians who can treat these medical conditions.

During the screening session you will complete psychological questionnaires that include questions of a personal nature regarding your mood, feelings, health behaviors, health, and personality. In order to assess your typical food intake, you will be asked to list all the foods you ate in the last 24 hours. You will be asked about depression and anxiety symptoms that you have experienced over your lifetime and this interview will be audio-recorded so that interview responses can be formally coded; all digital recordings will be kept in our password-protected computer system. At the end of the screening appointment, as part of standard procedures, you will be provided with a list of psychological counseling services should you wish to talk with someone at that time or in the future about any problems you are having. Finally, in order to measure hand strength, you will be asked to squeeze an instrument that measures your grip strength.

If you are eligible for the rest of the study, you will be scheduled for two full-day visits to the CRC. These visits will be scheduled 14-30 days apart.

In preparation for the visits: Recent exercise and alcohol use can affect your body's immune responses. For the two days before each full-day visit, you will be asked to refrain from consuming alcohol and to avoid any strenuous physical activity. If you have been instructed by your physician to take aspirin daily, you can continue to take it; otherwise, you should refrain from taking aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) for the 7 days prior to each visit. You should not change your diet or start taking any new dietary supplements or vitamins because this could influence the immune and hormone measures that the study is examining. If you make any important changes to your diet or if you begin taking dietary supplements during the course of the study, you must inform the researchers.

You cannot eat anything after 7:30 PM on the nights before the two full-day visits, but you can drink as much water as you want, and you should take any prescription medications as scheduled. On the day of each visit, you will be given a standardized breakfast as soon as you receive either the vaccine or saline (placebo) injection. You will also receive a standardized lunch later in the day.

You provided information about any medications and current physical problems when you were scheduled for this study. If you have started taking any new medications, have developed any significant health problems, or received a new vaccine, you must inform the researchers immediately.

Full-day visits 1 and 2: Recent illness can affect your body's immune response. If you have a temperature greater than 99.7°F when you arrive to the CRC, we will cancel the session and reschedule for a later date.

At the beginning of each of your full-day visits, a catheter (a small, hollow plastic tube) will be inserted into a vein in your arm so that small amounts of blood can be drawn at different times across the visit. The catheter will be removed at the end of each visit. You will have a total of 250 ml (1 cup + 1 tablespoon) of blood drawn during each of the 9½ hour visits. At the end of the research day a final teaspoon of blood will be drawn from your arm which does not have the catheter inserted; this is to confirm that immune changes are not just reflecting local changes at the catheter site. A total of 510 ml of blood (just under 2 1/4 cups) will be drawn across the screening visit and both study visits that are ideally scheduled over the span of 3-4 weeks. These samples will be used to examine the blood levels of hormones and immune function indicators.

The nurse will administer an injection into your upper arm that contains either saline (salt water) or a typhoid vaccine. Neither you nor the research staff will know the injection type for the day. This is because a person's expectations can sometimes influence the way that she feels throughout the day. If you are not willing to receive the injections, you will not be able to participate in the study.

At each visit, a nurse will place a Polar™ band or similar sensor that wraps around your chest to assess your heart rate and a sensor on each wrist to assess your perspiration. You will be asked to time your breathing to a pre-recorded tape for five minutes in order to help us better understand how your normal breathing affects your heart rate. Throughout your full-day visits, nurses will monitor your blood pressure, heart rate, and body temperature.

During both of the full-day visits you will complete questionnaires and interviews that include personal questions about mood, feelings, health behaviors, health, and personality; the interviews will be audio-recorded. In order to assess your typical food intake, you will be asked to list all the foods you ate in the last 24 hours. You will also be asked to perform several tasks on the computer and with the research assistant, including tests that measure aspects of concentration and memory.

At your first full-day visit, body composition (fat tissue mass and lean tissue mass) will be assessed using a DEXA (dual x-ray absorptiometry) machine. You will be asked to wear clothing with minimal metal, remove all jewelry, empty your pockets, and take off your glasses and shoes before lying down on the DEXA table. You will be instructed to remain still in position on the DEXA table while being scanned for 15-20 minutes. If you have any doubt about whether you are postmenopausal, we will ask for a urine sample to make sure you are not pregnant prior to the test.

At several times during both visits you will be asked to talk out loud into a tape recorder for a minute or two about your thoughts about your health, the study, the setting, the experimenter, or other things you may have been thinking about during the study. Researchers will not be present while you record your thoughts. These tapes will be used to assess your reactions to different parts of the study and your thoughts about your health.

You will be asked to perform a temperature sensitivity test, to study how the vaccine-related changes affect your sensitivity to heat and cold. During this task, you will be asked to place your non-dominant hand on a thermal plate (a device that changes temperature). The temperature of the plate will gradually increase and decrease. You will be asked to rate how painful the temperatures feel, and to remove your hand if the temperature becomes too painful.

In order to measure hand strength, you will be asked to squeeze an instrument that measures your grip strength.

You will provide 15 saliva samples to measure how hormones related to the immune response may have changed during each of the full-day visits. For this purpose, you will put a piece of dental cotton in your mouth for 1-2 minutes each time to saturate the cotton.

During both visits your metabolic response to the vaccine and placebo will be measured 6-8 times. For this purpose you will lay in a hospital bed with a facemask that covers your nose and mouth for about 20 minutes each time. During these times, you will be asked to lay still and breathe normally.

To provide a uniform experience during parts of the visits, you will be asked to watch DVDs of nature shows or documentaries. During the time you are in the CRC, you will only be able to use your cell phone to make or receive calls or e-mails at set times. In the case of an emergency, however, your family will be able to reach you at 614-293-8750.

You will be called the day following each of your long visits, and asked to answer questions which should take 5 to 10 minutes about your sleep, fatigue, pain, and thinking since your visit.

We will get information from your doctor's treatment records about the tests you have had for your breast cancer, as well as information on the type of breast cancer, the stage, and the treatment you received, any current medications, and other health conditions so we can see if these are related to your immune responses. If you have already participated in one of our ongoing studies, such as THRIVE or Yoga for Breast Cancer Survivors Research Program, we will also use the health information that you shared at that time, as well as collecting any new updated information on medications or health conditions.

Genetic studies: The study will also investigate how differences in genetic material (DNA and RNA) may be related to an individual's vaccine responses. The researchers are trying to determine if particular genetic markers (certain characteristics of a person's DNA) among those who also have certain immune responses and/or have recent stressful experiences are associated with changes in the immune response, and stress and appetite hormones in comparison to individuals who do not have the same genetic markers. The researchers will use frozen samples of your white blood cells as one source of DNA, as well as saliva samples.

No medical report will be added to your medical records based on this testing or any other part of your research participation. Your sample will not have identifying information such as your name, initials, or address on it, only a code number. The specimens for testing will be stored with the same code number that is used on all the questionnaires and other forms you have completed; the results of the testing will be kept confidential and will not be released. Names and other identifying information will be kept separate from the samples. No identifying information will be in any publication or reports; only group results, with no personal code number or other identifiers, will be reported. Scientists working with your DNA samples will not have access to any identifying information. The researchers for this study will store your DNA samples in a secure room with limited access.

Neither you nor your doctor will receive the results of your DNA testing. If you decide that you want to pursue genetic testing in the future based on results reported for this study, it will be at your expense and you will be referred to the genetic testing and counseling services in the OSU Medical Center. It may be a long time (months or years) before results from this study are available. In the unlikely event that any profitable discoveries are made using your biological material, you will not receive any personal financial benefit. If there are any patent or commercial uses of your DNA data, any identifiable information linking the data to you will be destroyed (e.g. your name, address, phone number, and social security number).

You can decide not to participate in the genetic portion of this research study but still be able to take part in the main research study.

____ I wish to participate in the genetic portion of this research study

____ I do NOT wish to participate in the genetic portion of this research study

4. How long will I be in the study?

Your participation will be complete in about 3-5 weeks, depending on scheduling availability in the Clinical Research Center and your personal schedule. There are a total of 3 sessions at the CRC, 1 screening session and 2 all-day visits. The screening visit will last approximately 2 hours. The full-day visits will take 9½ hours each, and will be scheduled 14-30 days apart. The total anticipated participation time for all visits and the interviews is 21-23 hours.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University. In addition, your study participation can be stopped without your consent if we cannot obtain blood samples or exercise testing data, or if you refuse the vaccine or saline injections. Any results obtained prior to your withdrawal from the study will be part of the overall study results.

You can withdraw from this study at any time and withdraw your consent for the use of your white blood cells for genetic research. Upon withdrawing consent, your samples for genetic

research will be destroyed (along with any study code number) if they have not already been used. Any results obtained prior to your withdrawing from the study will be part of the overall study results.

6. What risks, side effects or discomforts can I expect from being in the study?

For the blood draws and the catheter: You may experience bruising at the blood draw site, infection, pain, fainting, and redness. These are risks that occur whenever blood is drawn. There is a minor risk of an allergic response to the tape used to hold the catheter in place that may include redness, rash, swelling, small blisters, itching, and discomfort on the arm where the skin was covered by the tape. There is also a minor risk of anemia (a condition characterized by too few red blood cells, usually resulting in tiredness or light-headedness) associated with having your blood drawn. Therefore, you are advised not to donate blood within 8 week of study participation.

For blood pressure and heart rate: You may experience mild discomfort from the blood pressure cuff that will be used approximately every hour. During the exercise test, you may feel some skin irritation at the site where the heart rate adhesive sensors are removed, much like you experience when you pull off Band-Aids from your skin.

For the typhoid vaccine: If you take part in this research, you will receive a typhoid vaccine at one of your full-day visits. The vaccine has a well-established safety profile and is well-tolerated in adults. Side effects are mild and infrequent. You may experience local pain, redness, raised skin, or swelling at the injection site. About 1 in 10 people who receive the vaccine report feeling feverish or experience a headache; the likelihood that you will experience a clinical fever (as measured by a nurse) is about 1 in 100. Other side effects, such as a rash, muscle or joint pain, or gastrointestinal discomfort are also rare, and occur in about 2 out of 100 people. There is a rare risk of severe allergic reaction that could require emergency medical treatment.

For the DEXA scan: If you take part in this research, you will have one medical imaging procedure (DEXA) which uses radiation, in order to get a lean body mass measurement. To give you an idea about how much radiation you will receive, we will make a comparison with an every-day situation: a single DEXA scan produces a very small amount of radiation, approximately $1/10^{th}$ of that experienced during a cross-country air flight or $1/120^{th}$ of what you would experience during a dental scan.

Everyone receives a small amount of unavoidable radiation each year. Some of this radiation comes from space and some from naturally-occurring radioactive forms of water and minerals. This research gives your body the equivalent of about 4 extra days' worth of this natural radiation. The radiation dose we have discussed is what you will receive from this study only and does not include any exposure you may have received or will receive from other tests.

This procedure will not add to the risk of the research. However, if you have concerns about your total radiation exposure, you should discuss them with your physician.

For questionnaires, interviews, and cognitive tests: Personal questions may make you uncomfortable or be stressful. Should you reveal suicidal intent, the researchers are required to evaluate risk and may contact appropriate authorities if you appear to be at imminent risk for harm to yourself or others.

For the temperature sensitivity test: You may experience short-term pain or discomfort associated with exposing your hand to hot or cold temperatures. You may remove your hand from the plate when the pain or discomfort becomes too great. The test will be stopped before reaching extreme temperatures (55° C or -4°C), therefore the temperatures used are not hot or cold enough for any lasting temperature effects to occur.

For grip strength assessments: You may experience some slight hand and/or arm soreness.

Incidental findings from routine hospital blood analyses: Any potentially abnormal results from the hospital lab data (blood cell count and triglycerides) will be first discussed with Dr. Malarkey to confirm the nature and seriousness of the problem; if there appears to be reason for concern, you will be informed of the abnormal value and advised to seek treatment from your personal physician. Neither you nor your doctor will receive the results of the immune or hormone tests unless the results appear potentially abnormal.

For genetic testing: Because you will not be receiving your personal results from this study, most of the usual psychological risks associated with genetic testing do not apply to you. If you decide, at your expense, to undergo clinical genetic testing in the future based on discoveries made as part of this study, the risks of receiving genetic test results will be discussed with you at that time.

The results of the testing will be kept confidential to the fullest extent possible. Although the specimens will be stored with a code number, if this confidentiality were broken, a researcher could learn something about you that you do not want them to know (i.e., name, address, or other personal information you do not want them to have).

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions about your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this federal law. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under Ohio law, health insurance companies cannot ask about the results of a genetic test or use any information obtained from genetic testing to make decisions about providing coverage or benefits for health care services.

7. What benefits can I expect from being in the study?

You will receive a report based on your answers to the diet questionnaires and interviews. The report will tell you about your eating patterns, such as how closely your number of servings in each food group consumed daily matches USDA recommendations. In addition, this report will show your average daily intake of different nutrients and recommendations for improving your diet.

You will receive the results of your DEXA scan. The results obtained from the DEXA scan will provide you with information about your muscle and fat composition, bone mineral density, and the amount of calories your body uses at rest in a 24 hour period.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State

University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

The NIH has issued a Certificate of Confidentiality for this study. This Certificate provides extra protection for you and your study information, documents, or samples (blood, tissue, etc.). The Certificates are issued so that we cannot be required to disclose any identifiable, sensitive information collected about you as a part of this study in a lawsuit or legal proceeding. We are also prevented from releasing your study information without your consent. This is a layer of protection over and above the already existing protections in place for you and your information, documents, or samples.

However, these protections do not apply in some situations. For example, we may have to release your information if a law requires us to do so, the Agency that is funding this study requests the information, or if the FDA tells us to release this information. We may also use your information to conduct other scientific research as allowed by federal regulations.

Study information that has health implications may be placed in your medical record where authorized employees may see the information. Further, authorized requests for your records (medical record release for continuity of care) may result in research-related information being released.

Please talk to your study team, or contact the Office of Responsible Research Practices at 614-688-8641, if you have questions.

You may also visit the NIH website at https://humansubjects.nih.gov/coc/faqs to learn more.

10. What are the costs of taking part in this study?

There are no costs if you take part in this study. All procedures are paid by the study, and participants do not pay for any procedures.

11. Will I be paid for taking part in this study?

You will be compensated for your time. At all visits, you will receive free parking. You will receive $25 for completing the first screening session. You will receive $250 for completing each full day visit. Therefore, you will have an opportunity to receive a total of $525. If you are not able to complete the full day visit, your payment will be pro-rated based on the percentage of the visit that you actually completed. Payment will be sent after completing all visits that will ideally be scheduled within about a month; if your visits are more than a month apart, a check in the appropriate amount will be mailed to you within 2-4 weeks of each phase of study completion. If you do not receive your check within 4 weeks of study completion, please notify the researchers. By law, payments to subjects are considered taxable income.

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

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

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

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact the study coordinator at 614-293-4736.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Janice Kiecolt-Glaser, PhD at 614-293-3499 or William Malarkey, MD at 614-293-8775.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form.

Printed name of subject	**Signature of subject**
	AM/PM
	Date and time
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)**
	AM/PM
Relationship to the subject	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent**
	AM/PM
	Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness**
	AM/PM
	Date and time
Printed name of witness	**Signature of witness**
	AM/PM
	Date and time