Are you participating in any other research studies? _____ Yes _____No

Introduction to Research Studies

A research study is designed to answer specific questions, sometimes about a drug's safety and effectiveness. Being in a research study is different from being a patient. When you are a patient, you and your doctor have a great deal of freedom in making decisions about your health care. When you are a research participant, the Protocol Director and the research staff will follow the rules of the research study (protocol) as closely as possible, without compromising your health.

Introduction

You are invited to take part in a research study because you are receiving cancer treatment (e.g. chemotherapy or biologics such as trastuzumab [Herceptin®]) for breast cancer and have experienced the onset or worsened sleep difficulties. Before you decide to be a part of this study, you need to understand the risks and benefits.

This consent form provides information about the research study. A staff member of the research study will be available to answer your questions and provide further explanations. If you agree to take part in the study, you will be asked to sign this consent form. Your decision to take part in the study is strictly voluntary. You are free to choose whether or not you will take part in the study.

Purpose of the Study

Sleep disturbance, particularly insomnia, is a common problem for cancer patients. Insomnia can be described as difficulty falling asleep, waking up many times during the night or waking up earlier than you would like. Insomnia can increase fatigue and affect your quality of life in a negative way. The purpose of this study is to determine the efficacy of the Brief Behavioral Therapy for Insomnia (BBT-I) in comparison with Healthy Eating EducAtion Learning (HEAL) in reducing insomnia, fatigue, and cognitive difficulties in breast cancer patients. In addition, this study will examine the potential involvement of several demographic and medical variables (e.g., anxiety, hot flashes), specific behavioral mechanisms (maladaptive sleep behaviors, dysfunctional beliefs and attitudes), and physiological mechanisms (e.g., dysregulated circadian rhythms, inflammation disrupted wake-sleep cycles, and autonomic tone) as potential mediators of intervention-related changes in insomnia and the secondary outcomes of fatigue and cognitive difficulties.

There will be approximately 180 participants in this study.

The study has been divided into two parts. By signing this consent form you are agreeing to participate, if eligible, in both parts of the study. The purpose of the first part of the study, the Screening/Baseline Period is to determine if you will be eligible to participate in the second part of the study. The purpose of the second part of the study, which will last for 6 weeks, is to examine the effectiveness of BBT-I and HEAL interventions for the treatment and prevention of acute insomnia and subsequent chronic insomnia. In addition, there will be a follow-up assessment six and twelve months later.

Some of your sessions with the therapist may be audio recorded for training purposes and to ensure that we are consistently following the study protocol. The audio recordings will be destroyed at the end of the study.

Description of Procedures

Pre-Baseline

If the results of the preliminary screening indicate that you remain eligible to participate in the study, we will schedule you a baseline appointment. The week prior to your appointment, you will be asked to fill out baseline forms at home that keep track of your sleep habits (daily sleep diaries) for a period of one week. In addition during this time, we will ask you to wear a watch-like device (Actiwatch ®). The two days prior to your baseline visit, we will ask you to take saliva samples.

Baseline Appointment

During your baseline appointment, we will ask you to complete questionnaires, neuropsychological testing, heart rate variability, and a fasting blood draw. We will also ask you to bring in your sleep diaries and saliva samples. All procedures are described in "Other Assessments." After these assessments are complete, you will be randomized to the treatment group.

Treatment Groups

If you meet all the criteria to qualify for the study and agree to continue, you will be randomized into one of two intervention groups. Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor the researcher will choose what group you will be in; a computer determines which group you are put in. You will have an equal chance of being placed in either group, and will begin intervention on the same day immediately following your baseline visit.

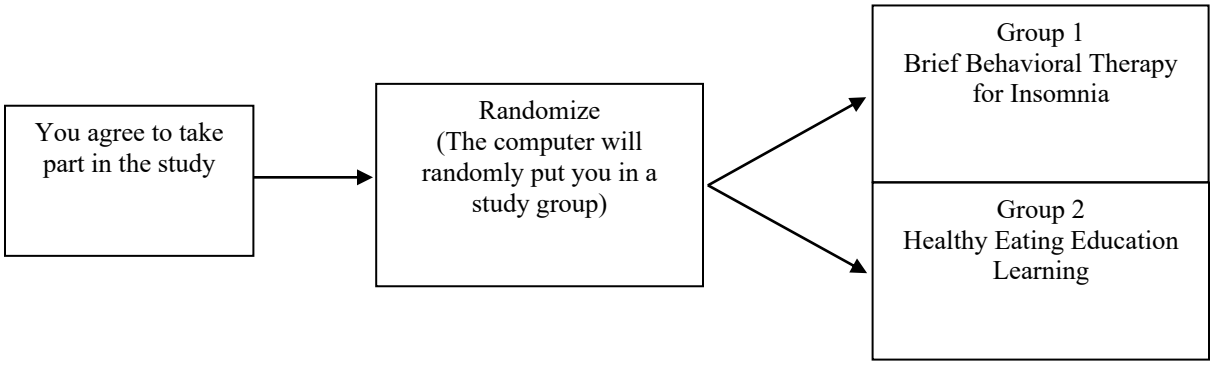
- **Group 1** will receive the Brief Behavioral Therapy for Insomnia (BBT-I). You will receive 2 individual, face-to-face sessions of BBT-I and 4 weekly phone call sessions for a total of 6 weeks. These sessions will be administered by trained and supervised clinical research staff. Face-to-face sessions run approximately 60 minutes. Your sessions may be audio recorded for training purposes and to ensure that we are consistently following the study protocol. The audio recordings will be destroyed at the end of the study. During these sessions the clinical research staff will discuss your sleep habits and provide suggestions on how to improve your sleep. Weekly phone calls will last approximately 15 minutes each time.

- **Group 2** will receive information on Healthy Eating Education Learning. People in this group will also receive 2 individual face-to-face sessions and 4 weekly phone calls, for a total of 6 weeks. These sessions will also be conducted by trained staff. Your sessions may be audio recorded for training purposes. The audio recordings will be destroyed at the end of the study. Face-to-face sessions run approximately 60 minutes, and the weekly phone calls will last approximately 15 minutes each time. The content of the intervention is provided by the National Cancer Institute: PDQ® Nutrition in Cancer Care. The topics discussed in these sessions will include nutritional implications of chemotherapy, nutrition screening and assessment, oral nourishment, and nutritional suggestions for symptom management

(anorexia, alterations of taste and smell, dry mouth, mouth sores, nausea, diarrhea, constipation, a decrease in the number of white blood cells you have, and dehydration).

A computer will randomly assign you to one of the two study groups. This is done because no one knows if one study group is more effective, the same, or less effective than the other. Once you are put in one group, you cannot switch to the other group. Neither you nor your doctor can choose which group you will be in.

Another way to understand what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in the study?

The total time in this study is approximately 14 months. In addition to the 6 weeks of the behavioral intervention, either BBT –I or Healthy Eating Education, there are four 1-week assessment periods: one week immediately before the intervention starts, one week immediately following the intervention, one week prior to your 6 months follow-up and one week prior to your 12 months follow-up.

Your participation in this study is entirely voluntary. Your decision whether or not to participate will not prejudice you or your medical care. If you decide to participate, you are free to withdraw your consent, *and* to discontinue participation at any time without prejudice to you or effect on your medical care. If you decide to terminate your participation in this study, you should notify Oxana Palesh, Ph.D., M.P.H. at [redacted]

Other Assessments

Questionnaires: You will be asked to complete online or paper-and-pencil assessments of sleep, fatigue, depression, anxiety, cognitive functioning, medical symptoms, nutrition and levels of stress before you are assigned to a group, one week following the intervention, and at 6 and 12 months follow-up. The set of questionnaires takes about 30-60 minutes to complete. However, it might take you a little bit less or more time depending on individuals' needs.

Neuropsychological Assessment: A trained clinician will give you some tests, which measure memory, attention, problem solving and processing speed as well as psychiatric symptoms (like depression and anxiety). This will take approximately 30-45 minutes. We will ask you to complete these tests at

baseline, one week following intervention and at 6 and 12 months follow-up. We might obtain your neuropsychological assessment data from another source (such as another research study) if the neuropsychological assessment portion of this study is not completed due to your participation in other research that requires a neuropsychological assessment.

Daily Sleep Diaries: Study participants will also be required to maintain a daily sleep diary for one week at the beginning of the study, one week immediately following the intervention, and for an additional one week at 6 months and 12 months follow-up. A researcher will be giving you a reminder call to start filling out the diaries. If you provide us with your email, we will send reminders and study materials to you electronically. We will use encrypted email if we are including any sensitive information. We will discuss your preferences during consent.

Actiwatch: We will ask you to wear an actiwatch on your wrist. The actiwatch is a small device that looks just like a personal watch, but it records your activity levels and sleep cycles. We will ask you to wear that watch for one week at the beginning of the study, one week immediately following the intervention, and for one week prior to each of the 6-month and 12-month follow-ups. A researcher will be giving you a reminder call to put on the watch.

Heart Rate Monitor: We will measure your heart rate variability with a small portable non-intrusive device during these four assessments for at least 10 minutes.

Saliva Samples: You will be asked to collect a small amount of saliva in a small tube for two days 5 times a day at baseline, post-intervention, 6 and 12 months follow-ups to assess the biomarkers associated with stress and sleep. A researcher will be giving you a reminder call to start saliva samples.

Blood Draws: A fasting blood draw (about 1-2 tablespoons) will be taken in order to measure biomarkers associated with stress, inflammation and stress before your scheduled chemotherapy appointment, one week following the intervention (6 weeks later), and also at 6 and 12 months follow-ups approximately. We will ask you to come in for blood draw collection at baseline (before the study intervention), one week following the intervention (at 6 weeks) and at 6 and 12 months follow-ups. We are asking you to not eat after midnight on the day of the blood collection; however, water may be consumed. We will ask you to come in the morning to collect blood after which we will provide you with breakfast. Additionally, we will try and make blood draws more convenient. If you are already receiving a blood draw immediately prior to your treatment, we will add-on our blood draw to the regular procedure. If you are coming in for your appointment in the morning, we ask you to not eat before midnight. If your appointment is in the afternoon, we ask you to fast for a minimum of four hours.

We will also use the blood samples for analysis of genetic markers linked to symptoms such as sleep disruption and cognitive dysfunction associated with breast cancer. The genetic markers that we are testing for currently have no application for diagnosis or treatment of cancer or cancer-related side effects. In addition, we will use the blood samples to investigate new approaches for developing biomarkers that can be used in behavioral and cancer research. It is possible that with future discoveries, we will analyze the serum for other health related biomarker and other outcomes.

Any of your samples that are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of samples do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

The clinic research visits will take a total of approximately 2.5 hours for baseline and 1.5 hours for each subsequent visit. In addition, participation involves 2 hours of intervention therapy (both phone calls and in person). Your visits will be scheduled to accommodate your needs as best we can.

In addition to these visits, you will be asked to grant the Protocol Director, her research team and designated staff permission to review your medical records so that we can obtain information about the course of your cancer treatment.

Blood and Tissue Sampling for Research

Research using tissues is an important way to try to understand human disease. You have been given this information because the investigators want to include your blood and tissues in a research project and because they want to save the samples for future research. There are several things you should know before allowing your tissues to be studied.

- Your blood sample might be linked to Stanford Tissue Bank
- Your blood and tissue will be coded and the code number will be linked to your medical record, but only known in a secure manner to the Study Coordinators or Investigators involved in the study
- You have the right to refuse to allow your blood to be studied now or saved for future study. You may withdraw from this study at any time.
- The results of the study of your samples will be used for research purposes only and you will not be told the results of the tests.

_____ I consent to my samples being saved for future research

_____ I do not consent to my samples being saved for future research

Tissue Sampling for Genetic Testing

As part of the analysis on your samples, the investigators will do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

The results of the study of your samples from this project will be used for research purposes only, and you will not be told the results of the tests.

Duration of Study Involvement

This research study is expected to take approximately 63 days of active participation by each participant; and approximately 13 months of collection of medical information for each participant.

Participant Responsibilities

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant. Complete your questionnaires as instructed.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

While participating in this research study, you should not take part in any other research project without approval from the Protocol Director of this study. This is to protect you from possible injury arising from such things possible interaction(s) of research drugs.

Withdrawal from Study

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled. If you would like to withdraw from the study, you may phone Oxana Palesh, Ph.D., M.P.H. at Stanford University at [redacted].

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.

- Unanticipated circumstances.

Risks and Discomforts

BBT-I may result in temporary increases in daytime fatigue and/or sleepiness, and/or memory and concentration difficulties. Completing questionnaires and neuropsychological testing can cause mild anxiety and fatigue; however, these feelings are transient.

Blood drawing may cause pain and bruising at the site where the blood is taken, and sometimes, it causes people to feel light-headed or even to faint. Rarely you might get an infection at the site of the needle stick.

Heart rate monitor electrodes and the gel used to attach them may cause a skin reaction.

The Actiwatch device worn around the wrist may cause a skin reaction.

Potential Benefits

Knowledge gained from this study may be used to develop improved therapies for the side effects of breast cancer treatment. WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY.

Alternatives

While there is no standard treatment for insomnia for breast cancer patients, you may choose to seek medical (pharmacological) treatment for your sleep difficulties. You may choose not to be in the study.

Participants Rights

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director. You will still receive care for your disease and will not lose any benefits to which you would otherwise be entitled. You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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

Confidentiality

Your identity will be kept as confidential as possible as required by law. Except as required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Your research records may be disclosed outside of Stanford, but in this case, you will be identified only by a unique code number. Information about the code will be kept in a secure location and access limited to research study personnel.

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. However, your identity will not be disclosed**.** Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

CERTIFICATE OF CONFIDENTIALITY

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Cancer Institute which is funding this project 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 from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

This study will examine the efficacy of BBT-I vs. HEAL for the treatment and prevention of acute insomnia and subsequent chronic insomnia for women undergoing treatment for breast cancer. Blood samples may be used for analysis of inflammation, telomeres, and genetic markers linked to symptoms such as sleep disruption and cognitive dysfunction

associated with breast cancer. The saliva and blood samples may be used to investigate new approaches for developing biomarkers that can be used in behavioral and cancer research.

Do I have to sign this authorization form?
You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study and receive any research-related treatment. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?
If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Oxana Palesh, Ph.D., M.P.H., Department of Psychiatry and Behavioral Science, Stanford University School of Medicine, Quarry Road, Stanford, CA 94305-5718.

What personal information will be obtained, used or disclosed?
Your health information related to this study may be used or disclosed in connection with this research study, including, but not limited to, information relating to your medical history, genetic information related to breast cancer, and treatment outcome.

Who may use or disclose the information?
The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director: Oxana Palesh, Ph.D., M.P.H.
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff

Who May Receive or Use the Information?
The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- FDA
- National Cancer Institute
- University of Rochester, NY
- Laval University, Quebec, Canada
- MD Anderson Cancer Center
- Research investigators, staff, and other collaborators as identified by the study team

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?
Your authorization for the use and/or disclosure of your health information will expire on December 31, 2060.

Will access to my medical record be limited during the study?
To maintain the integrity of this research study, you may not have access to any health information developed as part of this study until it is completed. At that point, you would have access to such health information if it was used to make a medical or billing decision about you (e.g., if included in your official medical record).

_____ _____
Signature of Adult Participant Date

_____
Print name of Adult Participant

Financial Considerations

Payment: Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. Payment for participation in the study:

No payment will be given for: eligibility screening and informed consent.

Participants will be eligible to receive up to $230 for the entire study. Participants will receive up to $50 for the baseline assessment ($40 for questionnaires + assessments and $10 for saliva collection), up to $55 for the post-follow-up assessment ($45 for questionnaires + assessments and $10 for saliva

collection), up to $60 for the 6-month follow-up assessment ($50 for questionnaires + assessments and $10 for saliva collection), and up to $65 ($55 for questionnaires + assessments and $10 for saliva collection) for the 12-month follow-up assessment.

Costs: There will be no direct cost to you to take part in the study. If you participate in this study, it will require you to use the personal time to come to all of the study visits.

The study will pay for those services, supplies, procedures, and care associated with this study that are not a part of your routine medical care. If you would like to review the list of such covered services, supplies, procedures and care, please tell us now or at any time during the study.

Participation in this study is not a substitute for health insurance. You and/or your health insurance must pay for those services, supplies, procedures, and care that you require during this study for routine medical care. You will be responsible for any co-payments and/or deductibles as required by your insurance.

Sponsor: This study is funded by the National Cancer Institute (NCI R01).

Compensation for Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

Additionally, Stanford is not responsible for research and medical care by other institutions or personnel participating in this study. You do not waive any liability rights for personal injury by signing this form.

Contact Persons

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Oxana Palesh, Ph.D. You should also contact her at any time at [redacted] if you feel you have been hurt by being a part of this study.

If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at [redacted]

[redacted] or toll free at 1-[redacted]. You can also write to the Stanford IRB, Stanford University, El Camino Real, Palo Alto, CA 94306.

Experimental Subjects Bill of Rights

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized
- be given a description of any attendant discomforts and risks reasonably to be expected
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits
- be informed of the avenues of medical treatment, if any available to the subject after the experiment, if complications should arise
- be given an opportunity to ask questions concerning the experiment or the procedures involved
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice
- be given a copy of the signed and dated consent form
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision

May we contact you about future studies that may be of interest to you? _____ Yes ____ No

I give consent to be audio recorded during this study: Please initial: _____ Yes _____ No

Signing your name means you agree to be in this study and that you were given a copy of this consent form.

_____ _____
Signature of Adult Participant Date

_____
Print name of Adult Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Print name of Person Obtaining Consent