INSTITUTE: National Cancer Institutes

STUDY NUMBER: 09-C-0139 PRINCIPAL INVESTIGATOR: Jay A. Berzofsky, M.D., Ph.D.

STUDY TITLE: A Pilot Study of Vaccination with Epitope-Enhanced TARP Peptide and TARP Peptide-Pulsed Dendritic Cells in the Treatment of Stage D0 Prostate Cancer

Continuing Review Approved by the IRB on 2/14/11
Amendment Approved by the IRB on 6/8/11 (AM E) Date Posted to Web: 6/15/11
Standard

INTRODUCTION

We invite you to take part in a research study at the National Institutes of Health (NIH).

First, we want you to know that:

Taking part in NIH research is entirely voluntary.

You may choose not to take part, or you may withdraw from the study at any time. In either case, you will not lose any benefits to which you are otherwise entitled. However, to receive care at the NIH, you must be taking part in a study or be under evaluation for study participation.

You may receive no benefit from taking part. The research may give us knowledge that may help people in the future.

Second, some people have personal, religious or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). If you have such beliefs, please discuss them with your NIH doctors or research team before you agree to the study.

Now we will describe this research study. Before you decide to take part, please take as much time as you need to ask any questions and discuss this study with anyone at NIH, or with family, friends or your personal physician or other health professional.

Background Information

We invite you to participate in this research study because you still have elevated levels in your blood of a protein called PSA following your initial treatment for prostate cancer, even though there is no evidence that the prostate cancer has spread (or metastasized) to other organs in your body. PSA stands for prostate specific antigen. It is a protein found on normal and cancerous prostate cells. Levels of this protein are used to identify men who are at risk for prostate cancer and to monitor responses to treatment in men who have been diagnosed with prostate cancer.

Research has shown that men who continue to have an elevated or rising PSA level following their primary treatment for prostate cancer are at increased risk for their cancer to progress. The time it takes for the prostate cancer to

progress can be highly variable- from months to many years. One measure that has been shown in studies to be accurate in predicting how quickly someone is likely to progress is based on the change in PSA levels over time or PSA doubling time (PSADT). Individuals that have a PSADT less than 3 months are more likely to experience disease progression, have lower survival rates and are not eligible for this study. In contrast, individuals that have a slow PSADT of greater than 15 months have an extremely low risk of death from prostate cancer; they are also not eligible for this study. This study seeks to determine if vaccination with a prostate cancer vaccine can slow down PSADT in men with an intermediate PSADT of 3 to 15 months.

The experimental prostate cancer vaccine being used in this study is made up of peptides (small pieces or portions of a protein) from another protein called TARP. TARP stands for T-cell receptor alternate reading frame protein. Like PSA, TARP is also expressed by both normal and cancerous prostate cells, is known to stimulate the immune system (to be immunogenic) and hence is a good potential target to use in vaccination. TARP peptides can be made even more immunogenic by changing their genetic sequence that in turn allows them to bind more tightly to proteins involved in generating an immune response. The process of changing the genetic sequence of peptides to make them more stimulating to the immune system is called epitope-enhancement. Both unmodified (or wild type) as well as modified (epitope-enhanced) TARP peptides will be used in the experimental vaccine in this study.

Because it isn't clear what is the best way to give peptide vaccines to stimulate a maximum immune response, you will be randomly assigned to receive vaccination with the TARP peptides using a vaccine made from your own immune cells (dendritic cells) or with two substances that are known to stimulate the immune system: Montanide ISA 51 and sargramostim (also known as granulocyte-macrophage colony stimulating factor or GM-CSF). Dendritic cells are potent immune cells that typically present peptides to the immune system. Both types of vaccine injections will be given into the skin rather than the muscle.

To evaluate what type of response the vaccine has on your immune system, we will collect a large amount of white blood cells (lymphocytes) for study by a process called apheresis. Apheresis will also be used for cell collection and preparation of the TARP peptide dendritic cell vaccine in those individuals randomly assigned to receive the dendritic cell vaccine. You will undergo the apheresis procedure 4 times while on study: once before starting the study, at week 24, week 48 and week 96.

The main purposes of this study are:

- To determine the safety and toxicity of TARP peptide vaccination.
- To determine the reactivity of the immune system in response to vaccination with TARP peptides.
- To determine the effect of TARP peptide vaccination on PSADT.

Description of Research Study Procedures

What will I need before screening for the study?

Information regarding your cancer will be requested from your local oncologist. You will need to sign a Medical release form so that your information (progress notes, pathology reports, tissue slides) can be forwarded to the NIH.
You will have the **HLA –A*201** screening blood test drawn at your local lab or at NIH. Blood samples drawn at outside institutions will be sent to NIH for HLA typing. You will need to sign a separate HLA screening consent to have this done.
The NIH department of Pathology will review your prostate cancer tissue biopsy (or slides) to confirm the diagnosis of prostate cancer.

What will I need to do before I begin the study?

You will need to have the screening examinations, tests or procedures to find out if you can be in the study. Some of these examinations, test or procedures may be repeated during the study to assure your safety and to assess your response to TARP peptide vaccination. Some of these screening tests may also be performed at your outside home institution.

During your initial visit to the clinical center you will complete the "screening process". You will be under the care of a specialist in internal medicine, oncology and/or immunology. The examinations, tests, and procedures are a part of the screening process and the results from these studies will determine your eligibility to participate in this study.

You will be asked to take part in this research study if we determine from screening that:

- You have prostate cancer and an elevated or increasing PSA level following completion of primary treatment for your cancer.
- You have no evidence that the prostate cancer has spread to other organs in your body.
- You are not currently receiving androgen deprivation hormone therapy (prior therapy is allowed).
- You have a PSA doubling time (PSADT) between 3 and 15 months.
- You screened positive for the immune system protein HLA-A*201 that binds TARP peptides. HLA is the major set of proteins that allows cells to be identified as self or non-self by the immune system.

What happens next?

After you have been found eligible for this study you will be scheduled for apheresis. During the apheresis blood will be collected to study T-cell receptors (immune cells). T-cells are important in the body's immunological defense. A large number of cells are required before treatment for comparison with later samples obtained after treatment. A description of the apheresis procedure is below.

Apheresis:
The procedure for obtaining certain types of blood cells through apheresis is a very common procedure that is done routinely here in the Clinical Center with very few risks. Apheresis requires you to have a needle placed in your arm where the blood can be removed from you and circulated through a cell separator machine (a machine that divides whole blood into red cells, plasma (the serum part) and white cells (that includes lymphocytes and monocytes). The white blood cells are removed and the plasma and red cells are returned to you through another needle in your other arm. The procedure takes approximately 1 to 3 hours to complete. One of the purposes of this procedure is to allow the investigator to collect a sufficient amount of immune cells to measure the immune response to the vaccine. This testing will provide no benefit to you and is part of the experimental portion of this research study. Patients do not need to be hospitalized for the procedure. The apheresis procedure will be done at the Department of Transfusion Medicine (Blood Bank) in the NIH Clinical Center and is carried out by trained nurses supervised by Blood Bank physicians.

FLuMist™ Vaccination:
You will also be vaccinated with an approved, licensed influenza vaccine called FluMist™ that is given as a nasal mist. FluMist™ contains very weakened but still live flu virus strains: other flu vaccines given into the muscle contain killed flu virus strains. To reduce the risk of transmitting the weakened virus to other patients, it will be administered immediately prior to your leaving the Clinical Center after your first visit. Following FluMist™ vaccination, the body develops an immune response to the weakened viruses that are in the vaccine. This vaccination will let us know how well your

immune system is working and whether it can respond to vaccines designed to stimulate responses in cells of the immune system called T lymphocytes or T cells. FluMist™ vaccination should also prevent you from getting the flu.

How many people will take part in this study?

The initial accrual for this study will be 18 patients: there will be two Arms (or groups) in this study with 9 patients in each Arm. A maximum of 40 total patients could be accrued depending on the immune responses that are observed in the first 18 patients enrolled on the study.

Arm A (Group 1) will receive TARP peptides mixed with Montanide ISA-51 and sargramostim (granulocyte macrophage colony stimulating factor or GM-CSF). These agents are known as adjuvants and help increase the reaction of your immune system to the peptides. This vaccine will be given as a deep subcutaneous injection (in the fatty part under the skin).

Arm B (Group 2) will receive TARP peptides loaded onto dendritic cells. The dendritic cells will be made from monocytes (a type of white blood cell) that are collected during apheresis. Monocytes can be grown in the presence of growth factors and turned into dendritic cells. The monocytes are grown in presence of three blood cell growth factors known as interleukin-4 (IL-4), GM-CSF, and lipopolysaccharide (LPS). All three of these factors are made in the laboratory without using human cells or blood products and will be washed from the dendritic cells prior to your receiving them. The matured dendritic cells will then be pulsed with KLH, a protein known to provide "help" to the immune system and the TARP peptides.
The TARP peptide-pulsed vaccine will be given intradermally (just under the top layer of the skin).

How long will the research study last?

This study is 144 weeks years in duration. There will not be a long term follow up or post study evaluations.

Schedule of Study Procedures and Visits

Schedule study Events Weeks 0-48												
	Screen D-14 to D-1	**Wk 0 D1**	**Wk 0 D3 or D5**	**Wk 3**	**Wk 6**	**Wk 9**	**Wk 12**	**Wk 15**	**Wk 18**	**Wk 24**	**Wk 36**	**Wk48**
HLA-A*0201 Testing *Prior to* Screening												
Informed Consent	X											
Medical History & ROS	X			X	X	X	X	X	X	X	X	X
Physical Examination	X			X	X	X	X	X	X	X	X	X
Performance Status	X			X	X	X	X	X	X	X	X	X
Height	X			X	X	X	X	X	X	X	X	X
Weight	X			X	X	X	X	X	X	X	X	X
Vital Signs	X			X	X	X	X	X	X	X	X	X
Apheresis			X							X		X
FluMist™ Flu Vaccine			X									
TARP Peptide Vaccine				X	X	X	X	X			X*	X
Vaccine Report Card				X	X	X	X	X			X*	X
CBC/differential, plts	X			X	X	X	X	X	X	X	X	X
PT / PTT	X											
Acute Panel	X			X	X	X	X	X	X	X	X	X
Hepatic Panel	X			X	X	X	X	X	X	X	X	X
Mineral Panel	X			X	X	X	X	X	X	X	X	X
Lipid Panel	X											X
Amylase / Lipase	X											X
Vitamin D, 25 hydroxy	X											
PSA	X			X	X	X	X	X	X	X	X	X
PSADT Calculation	X						X			X	X	X
Serum Testosterone	X			X	X	X	X	X	X	X	X	X
Urinalysis	X						X			X		X
HIV Serology	X											
Hepatitis B Serology	X											
Hepatitis C Serology	X											
HTLV-1 Serology	X											
VDRL	X											
EKG	X											
CT Scan Chest/Abd/Pelvis	X											X
Bone Scan	X											X
Lymphocyte Subsets	X						X			X		X
Anti-TARP Antibody		X					X		X	X	X	X
NKT Cell Assessment		X					X		X	X		
Tetramer Staining		X					X		X	X	X	X
IFN-γ ELISPOT		X					X		X	X	X	X
^{51}Cr CTL Assay#		X					X		X	X	X	X
PBMCs for Storage		X		X			X		X	X	X	X
Serum for Storage		X					X		X	X	X	X

Schedule study Events Weeks 60-144								
	Wk 60	**Wk 72**	**Wk 84**	**Wk 96**	**Wk 108**	**Wk 120**	**Wk 132**	**Wk 144**
HLA-A*0201 Testing *Prior to* Screening								
Informed Consent								
Medical History & ROS	X	X	X	X	X	X	X	X
Physical Examination	X	X	X	X	X	X	X	X
Performance Status	X	X	X	X	X	X	X	X
Height	X	X	X	X	X	X	X	X
Weight	X	X	X	X	X	X	X	X
Vital Signs	X	X	X	X	X	X	X	X
Apheresis				X				
FluMist™ Flu Vaccine								
TARP Peptide Vaccine				X				
Vaccine Report Card				X				
CBC/differential, plts	X	X	X	X	X	X	X	X
PT / PTT								
Acute Panel	X	X	X	X	X	X	X	X
Hepatic Panel	X	X	X	X	X	X	X	X
Mineral Panel	X	X	X	X	X	X	X	X
Lipid Panel				X				X
Amylase / Lipase				X				X
Vitamin D, 25 hydroxy								
PSA	X	X	X	X	X	X	X	X
PSADT Calculation	X	X	X	X	X	X	X	X
Serum Testosterone	X	X	X	X	X	X	X	X
Urinalysis				X				X
HIV Serology								
Hepatitis B Serology								
Hepatitis C Serology								
HTLV-1 Serology								
VDRL								
EKG								
CT Scan Chest/Abd/Pelvis				X				X
Bone Scan				X				X
Lymphocyte Subsets	X			X				X
Anti-TARP Antibody	X			X				X
NKT Cell Assessment								
Tetramer Staining	X	X	X	X	X	X		X
IFN-γ ELISPOT	X	X	X	X	X	X		X
^{51}Cr CTL Assay#	X	X	X	X	X	X		X
PBMCs for Storage	X	X	X	X	X	X		X
Serum for Storage	X	X	X	X	X	X		X

X*: Patients who are PSA doubling time or immunologic responders at Week 24 will be eligible to receive a 6th dose of TARP peptide vaccine at Week 36. All patients will receive a booster dose of TARP peptide vaccine at Week 48 and 96.

Optional Studies

We would like to keep some of the blood that is collected during this study for future research. These blood specimens will be identified by a number and not your name. The use of your specimens will be for research purposes only and will not benefit you. It is also possible that the stored specimens may never be used. Results of research done on your specimens will not be available to you or your local doctor. It might help people who have cancer and other diseases in the future.

If you decide now that your blood can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your blood. Then any blood that remains will be destroyed.

Please read each sentence below and think about your choice. After reading each sentence, circle and initial the answer that is right for you. No matter what you decide to do, it will not affect your care.

1. My blood may be kept for use in research to learn about, prevent, or treat cancer.
Yes No Initials_____

2. My blood may be kept for use in research to learn about, prevent or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease).

Yes No Initials_____

3. Someone may contact me in the future to ask permission to use my specimen(s) in new research not included in this consent.

Yes No Initials_____

Alternative Approaches or Treatment

Treatment options for patients with elevated PSA levels but no evidence of disease spread to other organs following primary treatment for their prostate cancer includes watchful waiting or androgen deprivation hormone therapy. However it is unclear for patients with this stage of disease (Stage D0) what is the best approach. Because many patients prefer to avoid the side effects of hormonal treatment (impotence, hot flashes, loss of libido, breast tenderness, osteoporosis and bone fractures) watchful waiting is often chosen.

If you develop evidence of disease progression, involving spread of your prostate cancer to the bone, brain or other organs, alternative treatments/therapy for your cancer may include:

- Treatment with hormone therapy, radiotherapy, chemotherapy or a combination of these approaches.
- Supportive care (treatment designed only to help with symptoms from your cancer such as pain medication)
- Experimental treatments such as other types of immune therapy or investigational chemotherapy
- No further therapy at all

Each of these alternative therapies has a unique set of benefits and risks. Your physician will discuss these options with you. Furthermore, other centers are performing clinical trials with investigational agents including immune-based therapies and vaccines as well as standard chemotherapy that you may want to consider as an alternative to this proposed trial.

The decision not to participate in this study will not compromise your eligibility for other studies in the future. If you choose not to participate in the study, you will be referred back to your regular physician for medical care.

Risks or Discomforts of Participation

The vaccines described in this study are experimental and whether the vaccines will induce an immune response and the side effects of the vaccine are not known. Everyone taking part in the study will be monitored very carefully for any side effects and we will ask you to fill out a Vaccine Report Card to monitor any symptoms you may have following your vaccine injection. Since we don't know all the side effects that may be associated with these vaccines, it is very important that you report any changes that you may notice, even if your study team does not specifically ask about them. Many side effects go away shortly after the study vaccine is stopped, but in some cases, side effects may be serious, long lasting, and may even cause death. You should talk to your study team about all side effects that you have while taking part in the study. It is important that you discuss any drugs (over-the-counter, prescription, illegal, or herbal) with your study team while you are participating in this study.

Your time commitment to this study would involve visits to the NIH Clinical Center every three weeks for the vaccine administration, blood collection, and clinic visits that generally involve a two day stay. A total of five vaccines will be given. Individuals who have evidence that they have developed an immune response or PSA doubling time response to TARP peptide vaccination at 24 weeks will be eligible to receive a sixth dose of vaccine at Week 36. *All* patients will receive a booster dose of TARP vaccine at Weeks 48 and 96 and undergo repeat staging scans: CT scan (chest, abdomen, pelvis) and bone scan.

Potential side affects associated with specific components of this research study are as follows:

- **Apheresis:** You may have some tingling in your face and lips due to the medicine used to keep your blood from clotting during the procedure. The nurses may give you calcium-containing tablets, such as TUMS, to chew that takes away this tingling. Some patients may feel faint or light-headed during or after this procedure. We ask that you make sure you have a good meal prior to coming to the apheresis lab to prevent this. Trained nurses will carry out all apheresis procedures.

- **FluMist Vaccine™(given intranasally):** This vaccine cannot be given to you if you are allergic to eggs or egg products. It is unlikely, but you could experience an allergic reaction to the vaccine including shortness of breath, wheezing, or difficulty breathing; swelling of the face, lips, tongue, or other parts of the body; skin rash, itching, or hives. Some people also experience symptoms consistent with a very mild cold such as runny nose or nasal congestion.

- **TARP Peptide Vaccine (given subcutaneously or intradermally)** – The vaccine may produce some discomfort, such as redness, swelling and tenderness at the injection site. These are known as local injection site reactions. Fever, chills, rash and flu-like symptoms may also occur. All of these are temporary. You will be monitored closely during vaccine administration for any complications. It is possible that you could develop an immune response to the TARP peptide that will cause inflammation in your prostate gland. This may produce discomfort. We do not anticipate significant systemic or organ toxicities, but because this is an investigational agent it is possible that other risks not mentioned could occur. In generally, peptide vaccines given to cancer patients have been found to be safe and very well tolerated.

- **Risks of blood draws**: There is a risk of discomfort or pain, bleeding, as well as mild arm bruising and swelling in the area where the blood is drawn. Rarely, a clot or infection may occur at the site of the blood draw. Some people also become faint, dizzy, or light-headed during or immediately after the blood draw.

- **Risks from X-rays and/or Scans**: As part of this study, you will have imaging scans. These tests are necessary to monitor your disease. As a result of participating in this study, you will be exposed to a moderate amount of radiation (approximately 6.5 cGy). This amount is more than you would receive from a year of natural exposure, which is approximately 0.16 cGy. This exposure may slightly increase your chances of developing cancer in the future. If you are especially concerned with radiation exposure or you have had a lot of x-rays already, you should discuss this with your study team.

Potential Benefits of Participation

Taking part in this study may or may not provide a direct benefit to you. It is unknown whether vaccination with TARP peptides will stimulate an immune response by your body. If an immune response is stimulated, it is also unknown what kind of effect this immune response will have on the PSA doubling time (PSADT): it could increase your PSADT (desirable effect), decrease your PSADT (undesirable effect) or have no effect. If TARP peptide vaccination stimulates an immune response that increases your PSADT, it may help your body to fight your prostate cancer more effectively. Since this is an experimental therapy, no benefit can be promised. However, the information we obtain from both the laboratory studies and your response to vaccination may also allow us advance the understanding and treatment of cancer for future patients.

Research Subject's Rights

Participation in this research study is voluntary. You will get a copy of this Informed Consent and you may withdraw your consent to participate at any time. There are no penalties for leaving the study. Patients may ask our staff to answer any and all questions and we invite you to do so.

Unexpected or unforeseeable side affects may also occur. Your participation in this protocol may be stopped without your consent if we find unacceptable side effects or feel that it would not be safe for you to continue. Any significant findings that relate to your treatment will be discussed with you.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission. Organizations that may look at and /or copy your medical records for research, quality assurance, and data analysis include qualified representatives of the National Cancer Institute (NCI) and other government agencies such as the Food and Drug Administration (FDA).

It is possible that the information obtained from your participation on this study may become valuable for commercial research and development purposes (included patentable inventions) that may be of significant benefit to society, the sponsor of this study, individual researchers, or third parties. The sponsor of this study is Dr. Jay A. Berzofsky. You will not receive direct financial benefit from such research and development. If information from this study is published in a medical journal, you will not be identified by name.

The National Institutes of Health reviews NIH staff researchers at least yearly for conflicts of interest. The following link contains details of this process: http://ethics.od.nih.gov/forms/Protocol-Review-Guide.pdf. You may ask your research team for additional information or a copy of the Protocol Review Guide.

If you refuse to participate, withdraw from the protocol or at the completion of the protocol, we will attempt to offer you participation in other NIH protocols if these are available. If there is no suitable research study you will be referred back to your home physician for further management. It is important that you understand and agree that participation in this protocol does not constitute a promise of long-term medical care here at the NIH Clinical Center.

What are the costs of taking part in this study?

While you are taking part in the study at the National Cancer Institute, your medical care and the costs of the laboratory and radiographic studies, medications and treatments associated with the study carried out at the Clinical Center, NIH, will be provided at no charge to you. NIH cannot, however, assume the cost of your overall medical care; laboratory or diagnostic radiographic studies performed outside of the NIH.

Any studies done outside of the NCI may require you or your insurance company to cover the costs of the service. You will not be paid for taking part in this study. For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site. Another way to get information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

Where can I get more information?

- NCI Web site at http://cancer.gov/
- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/

For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

OTHER PERTINENT INFORMATION

1. Confidentiality. When results of an NIH research study are reported in medical journals or at scientific meetings, the people who take part are not named and identified. In most cases, the NIH will not release any information about your research involvement without your written permission. However, if you sign a release of information form, for example, for an insurance company, the NIH will give the insurance company information from your medical record. This information might affect (either favorably or unfavorably) the willingness of the insurance company to sell you insurance.

The Federal Privacy Act protects the confidentiality of your NIH medical records. However, you should know that the Act allows release of some information from your medical record without your permission, for example, if it is required by the Food and Drug Administration (FDA), members of Congress, law enforcement officials, or authorized hospital accreditation organizations.

2. Policy Regarding Research-Related Injuries. The Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the National Institutes of Health, the Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

3. Payments. The amount of payment to research volunteers is guided by the National Institutes of Health policies. In general, patients are not paid for taking part in research studies at the National Institutes of Health. Reimbursement of travel and subsistence will be offered consistent with NIH guidelines.

4. Problems or Questions. If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Jay A. Berzofsky, M.D., Ph.D.; Building 10, Room 6B04, Telephone: (301) 496-6874. Other researchers you may call are the Lead Associate Investigator, Lauren V. Wood, M.D. at (301) 402-0199 or the Research Study Coordinator, Brenda Roberson R.N. at (301-435-4733. If you have any questions about the use of your tissue for future research studies, please contact the Office of the Clinical Director, Telephone: 301-496-4251.

You may also call the Clinical Center Patient Representative at (301) 496-2626.

5. Consent Document. Please keep a copy of this document in case you want to read it again.

COMPLETE APPROPRIATE ITEM(S) BELOW:

A. Adult Patient's Consent

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby consent to take part in this study.

Signature of Adult Patient/Legal Representative _____ Date _____

Print Name _____

B. Parent's Permission for Minor Patient.

I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I hereby give permission for my child to take part in this study.
(Attach NIH 2514-2, Minor's Assent, if applicable.)

Signature of Parent(s)/Guardian _____ Date _____

Print Name _____

C. Child's Verbal Assent (If Applicable)

The information in the above consent was described to my child and my child agrees to participate in the study.

Signature of Parent(s)/Guardian _____ Date _____ Print Name _____

THIS CONSENT DOCUMENT HAS BEEN APPROVED FOR USE FROM FEBRUARY 14, 2011 THROUGH FEBRUARY 13, 2012.

Signature of Investigator _____ Date _____

Print Name _____

Signature of Witness _____ Date _____

Print Name _____