INFORMED CONSENT DOCUMENT
FDA IND #9706
DOD HSRRB #A14059.1

Project Title: **Phase II study of adenovirus/PSA vaccine in men with recurrent prostate cancer after local therapy**

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This consent form describes the research study to help you decide if you want to participate. This form provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research subject.

- If you have any questions about or do not understand something in this form, you should ask the research team for more information.
- You should discuss your participation with anyone you choose such as family or friends.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We are inviting you to participate in this research study because you have recurrent cancer of the prostate. This study involves a research intervention with an Ad/PSA vaccine. This is a virus vaccine in which the gene for prostate specific antigen (PSA) has been placed into a common cold virus termed adenovirus (Ad) to produce this Ad/PSA product. Adenovirus is a common virus found in human respiratory systems. In its normal state, it can reproduce and cause a respiratory infection. Respiratory illnesses caused by adenovirus infections range from the common cold to pneumonia, croup and bronchitis. The adenovirus used in this research study will not be infectious, but may still cause flu or cold like symptoms. PSA is produced by normal and cancerous prostate cells. Since you have previously been treated for your prostate cancer by surgery or irradiation the only cells that will be secreting PSA are the remaining cancer cells.

The purpose of this study is to determine whether vaccination with the Ad/PSA prostate cancer vaccine will activate the immune system against PSA, which might have a positive effect on prostate cancer. Other scientists have also been working on cancer vaccines and, although many show promising results in pre-clinical studies and are in Phase II and Phase III clinical studies, none have been approved for therapeutic use.

The Ad/PSA vaccine is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 85 people will take part in this study at the University of Iowa and the Iowa City Veterans Affairs Medical Center.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last for approximately 2 years, perhaps longer. Much depends upon the effect of the vaccine on your cancer. You will receive a total of three vaccinations. After each of the vaccinations, you will be asked to stay in our Clinical Research Unit (CRU) for 2 hours so we can monitor how you respond to the vaccination. You will be asked to return to the clinic at regularly scheduled times after the vaccinations to undergo a physical examination and blood tests to evaluate whether the vaccine is causing any side effects. On some visits you will also have x-rays and scans to monitor the progress of your prostate cancer following the vaccinations**.** After the first vaccination you will have visits on days 30 (vaccination 2), 44, 60 (vaccination 3), 74, 90, and 6, 9, and 12 months**.** Depending upon how you respond to the vaccination you will be asked to return every six months after the 12 month visit and have the same examinations and blood tests. These visits will continue until you show progression of your prostate cancer. If you are a patient from the Mercy Cancer Center, Des Moines, IA (hereafter referred to as DMMCC) your follow up visits on days 44, 74 and 6, 9, and 12 months plus any subsequent visits will take place at the DMMCC.

WHAT WILL HAPPEN DURING THIS STUDY?

If you are interested in participating in this study, you will first be asked to sign this informed consent document before any research specific testing is initiated. Once the consent has been signed, you will be scheduled to complete tests and procedures to determine if you are eligible to participate in this study. By signing this Informed Consent document you grant permission for the study investigators to access your medical records for the purposes of evaluating your eligibility for entrance into this vaccine study. If you are eligible and would like to participate, you will be randomly placed into one of two research interventions – Arm A or Arm B. In Arm A, you would receive the vaccination once every 30 days for a total of three vaccinations. In Arm B, you would be asked to start on androgen deprivation therapy 14 days before receiving the three monthly vaccinations. The androgen deprivation therapy will continue for the first 9 months of the study. You will also be given a second medication to prevent a temporary increase in testosterone following the start of androgen deprivation therapy.

Listed are the tests and procedures that take place for screening and at the study visits.
SCREENING VISIT:

- Physical exam
- Chest X-ray
- Abdominal/pelvic CT
- Bone scan
- Blood tests*
- Urine tests

VISIT 1 (first vaccination):

- Physical exam
- Blood tests*

VISIT 2 (second vaccination):

- Physical exam

- Blood tests*
- Urine tests
- Chest X-ray[a]

VISITS 3 AND 5 (Days 44 and 74):

- Blood tests*

VISIT 4 (third vaccination):

- Physical exam
- Blood tests*
- Urine tests
- Chest X-ray[a]

VISIT 6 (Day 90):

- Physical exam
- Blood tests*
- Urine tests
- Chest X-ray[a]
- Bone Scan[b]

VISIT 8 (9 months)

- Blood tests*
- Chest X-ray[a]

VISITS 7 and 9 (6 and 12 months)

- Blood tests*
- Chest X-ray[a]
- Abdominal/pelvic CT[b]
- Bone scan[b]

VISITS OCCURING EVERY 6 MONTHS UNTIL COMPLETION OF STUDY

- Blood tests*
- Chest X-ray[a]

VISITS OCCURING ANNUALLY UNTIL COMPLETION OF THE STUDY

- Abdominal/pelvic CT[b]
- Bone scan[b]

*4 tablespoons of blood will be obtained at each time point for all clinical and research testing of blood counts, liver function, and kidney function.
[a] Will be performed only a fever develops.
[b] Will be performed only if there is a rise in PSA.

PSA measurements, CT and bone scans are routinely used to follow disease recurrence and/or progression in individual prostate cancer patients and are considered standard of care. Laboratory measurements such as blood counts, liver function and kidney function tests, are routinely used to follow

the health of a prostate cancer patient; however, they would not normally be performed as often as they will in this study to assess possible vaccination toxicities. Therefore, they would be considered part of the research protocol.

Immune responses are measured in this study as a measure of the effects of vaccination. However, if your cancer were to grow despite the vaccinations, the study team would still be interested in obtaining additional measurements of your immune response up to the 12 month time point, in order to better understand how the vaccine works.

Do you agree to return for additional study visits and research lab tests to document immune response, *every 3 months* up to 12 months from study entry, in case your cancer progresses prior to the 12 month time point?

(Circle one) YES NO _____ (initials)

WHAT ARE THE RISKS OF THIS STUDY?

VACCINE:

There may be some risks from being in this research study. This study uses a form of gene transfer. Since gene transfer is a new method of treating disease not all of the risks associated with this research intervention are known. In a previous study using adenoviruses, a death did occur. In 1999 a young man died from liver failure when a very high dose of an adenovirus was injected directly into the vein leading to the liver. However, results from our first study of the vaccine indicated that none of the subjects suffered any severe vaccine-related side effects when the vaccine was injected subcutaneously. However, the first study used a single vaccination whereas this study will use three vaccinations. Pre-clinical studies in laboratory animals did not produce any adverse events using the three injection schedule to be used in this clinical study. Based upon our first study, the adenovirus vaccine may cause a local redness and swelling at the site of vaccination, some flu or cold like symptoms, a decrease in white blood cell count (which could result in an increased risk of infection), temporary leakage of protein into your urine, headaches, or fever. Temporary leakage of protein into the urine, which in small amounts does not cause any adverse effects. In large amounts, it can cause swelling and kidney damage in the short or long term. However, the chances of large amounts of protein leakage are very small. If you experience discomfort as a result of the vaccinations you may take over the counter pain relief such as aspirin, Tylenol, or ibuprofen. Do not use any oral steroids such as prednisone as this will depress your ability to develop immune responses to the PSA and compromise the research study.

The vaccine will be mixed with collagen and injected into your thigh. Although there were no additional side effects when the vaccine was administered in collagen as compared to the vaccine alone in the first study, there is the possibility of infection, fluid accumulation or bruising at the injection site. If this occurs you may take the same over the counter medications listed above that will ease your discomfort and lower any fever that may occur, but do not take oral steroids.

There may be some local tenderness, reddening, or swelling at the vaccination site, but this will normally disappear within a few days. The PSA vaccine may induce antibodies against PSA protein. This could interfere with the ability of your health care provider to monitor your PSA blood levels. The antibodies to PSA may lower the amount of the PSA protein in your blood that would not necessarily reflect a clinical change in your cancer. For example, the anti-PSA antibodies may attach to the PSA in your blood and that would not permit the PSA to be measured by the current tests. We are working with other scientists

to study this possibility. We are not certain how long the potential for lowering your serum PSA levels will last during the study. However, other methods of follow-up include physical examination, imaging studies (for example, CT, MRI, bone scan), and selected laboratory studies such as alkaline phosphatase will still be useful to follow your disease. Results of these tests will be included in a letter to your local referring physician.

The Ad/PSA vaccine will be injected in a collagen Gelfoam matrix, a mixture that has been shown in our pre-clinical research to enhance the production of immune responses to the PSA protein. Gelfoam is a product derived from pigs. If you object to the use of, or are allergic to, a pork product you have the right to decline participation in this study.

Your physician will be checking you closely to see if any side effects are occurring. Routine blood and urine tests will be done to monitor the effects of the investigational vaccine. Many side effects disappear after the drug is stopped. In the meantime, your health care provider may prescribe medications to keep these side effects under control.

There is no need for the use of contraceptive devices following injection of the adenovirus/PSA vaccine since the virus will not be present in the semen and cannot be transmitted to your partner.

The following summarizes the known risks of the Ad/PSA vaccine. There is still very limited experience with the vaccine and there could be other side effects we do not yet know about. As with any investigational product, there is always some chance of unexpected serious or even life-threatening side effects.

Likely/Common Risks (more than 35%)
Life Threatening – none
Serious – none
Mild – local tenderness, reddening, swelling at vaccination site

Rare (less than 10%)
Life Threatening – none
Serious – decrease in white blood cell count
Mild – flu or cold-like symptoms
protein leakage into urine
headache
fever

ANDROGEN DEPRIVATION (HORMONE) THERAPY:

If you are in the group of subjects that will also receive androgen deprivation therapy, there are some side effects associated with this intervention. Common side effects include fluid retention, hair loss, hot flashes, nausea, vomiting, bone pain, memory changes, and depression. These side effects are not expected from the vaccine and should not interfere with the identification of vaccine-associated side effects. However, you will be closely monitored by the research team for the development of hormone-related side effects. If side effects occur, investigators will take necessary steps to treat them, including discontinuation of the medication and/or terminating your participation in the study.

Likely/Common (more than 35%)
Like Threatening - none
Serious – bone calcium loss

Mild – hot flashes

Less Likely/Less Common (10% - 35%)
Life Threatening - none
Serious - none
Mild – hair loss, fluid retention

Rare (less than 10%)
Like Threatening - none
Serious – nausea, vomiting, bone pain, memory changes
Mild - depression

ANTI-ANDROGEN (CASODEX) TREATMENT

To prevent what is known as a "testosterone flare" which can occur after initiation of androgen deprivation therapy you will also be prescribed Casodex (bicalutamide), which is a pill and will start at the same time as the hormone injection and continue for 30 days. Side effects may include allergic reactions (hives; difficulty breathing; swelling of your face, lips, tongue, or throat), hot flashes, breast pain or swelling, weakness, back pain, pelvic pain, joint or muscle pain, increased nighttime urination, stomach pain, nausea, vomiting, loss of appetite, diarrhea or constipation, weight changes, impotence, loss of interest in sex, or trouble having an orgasm, dizziness, headache; or sore throat, runny nose or other cold symptoms.

Likely/Common (more than 35%)
Like Threatening - none
Serious – pain
Mild – hot flashes

Less Likely/Less Common (10% - 35%)
Life Threatening - none
Serious – peripheral edema, pelvic pain, anemia, back pain, muscle weakness, shortness of breath, infection
Mild – constipation, nausea, diarrhea, abdominal pain, increased nighttime urination, blood in urine

Rare (less than 10%)
Like Threatening – none
Serious – chest pain or heart attack
Mild - dizziness, headache, sleep problems, anxiety, depression

BLOOD DRAW

During the screening for eligibility and all follow up visits you will have blood drawn for testing. This may cause bruising or infection at the needle site and/or fainting. We will attempt to minimize these possible side effects by using a trained professional for all blood draws.

Likely/Common Risks (more than 35%)
Life Threatening – none
Serious – none

Mild – local tenderness, reddening, swelling at blood draw site

ARE THERE ANY UNFORESEEN RISKS?

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if you will benefit from being in this study. However, we hope that, in the future, other people might benefit from this study as data obtained from this study may indicate the level of benefit obtained from the vaccination.

WHAT OTHER TREATMENT OPTIONS ARE THERE?

Before you decide whether or not to be in this study, the study physician will discuss the other options that are available to you. Instead of being in this study, alternatives which could be considered in your case include watchful waiting or hormonal therapy, if you are not already on this treatment. Your study health care provider can provide detailed information about your disease and the benefits of hormonal therapy. You should feel free to discuss your disease and prognosis with your health care provider.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

There may be additional costs for being on this study. These include time lost at work and travel expenses. The vaccine Ad/PSA, the costs of administration, and your stay in the CRU will be provided to you without cost. You and/or your insurance company will not be billed for any procedures related specifically to this study. You and/or your insurance company will be responsible for the cost of Casodex.

You and/or your medical/hospital insurance carrier will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

Other than medical care that may be provided and any other payment specifically stated in the consent form, there is no other compensation available for your participation in this research.

WHO IS FUNDING THIS STUDY?

The U.S. Department of Defense (DOD) is funding this research study. This means that the University of Iowa is receiving payments from the DOD to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the DOD for conducting this study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

- If you are injured or become ill from taking part in this study, medical treatment is available at the University of Iowa Hospitals and Clinics.
- No compensation for treatment of research-related illness or injury is available from the University of Iowa unless it is proven to be the direct result of negligence by a University employee.
- If you experience a research-related illness or injury, you and/or your medical or hospital insurance carrier will be responsible for the cost of treatment.
- If you are hurt or get sick because of this research study, you can also receive medical care at an Army hospital or clinic free of charge. You will only be treated for injuries that are directly caused by the research study. The Army will not pay for your transportation to and from the hospital or clinic. If you have questions about this medical care, talk to the principal investigator for this study, (David M. Lubaroff, PhD, 319-335-8423). If you pay out-of-pocket for medical care elsewhere for injuries caused by this research study, contact Dr Lubaroff. If the issue cannot be resolved, contact the U.S. Army Medical Research and Materiel Command (USAMRMC) Office of the Staff Judge Advocate (legal office) at (301) 619-7663/2221.
- In the event of an emergency you should seek immediate care by calling 911, your local physician, the University of Iowa (319-356-1616) or Iowa City VA Medical Center urology staff on call (319-338-0581).

WHAT ABOUT CONFIDENTIALITY?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people may become aware of your participation in this study. For example, federal government regulatory agencies, the National Institutes of Health/Office of Biologic Activities (NIH/OBA), the Department of Defense, the U.S. Food and Drug Administration, auditing departments from the University of Iowa, and the University of Iowa Institutional Review Board (a committee that reviews and approves research studies) may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

In the future, the granting agency may continue to use your health information that is collected as part of this study. For example, they may combine information from this study with the results of other studies to re-analyze the safety and effectiveness of the study medication, to evaluate other products or therapies, to develop a better understanding of a disease, or to improve the design of future research studies. The funding agency may also share information from this study with regulatory agencies in foreign countries.

To help protect your confidentiality, we will assign a specific coded number to your file that will appear on the data forms and files, all written files will be kept in a locked office and information on computers will be protected by secure passwords. Only your University of Iowa Hospitals and Clinics or VA Medical Center records will contain information that associates your name with the research study. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

The University of Iowa Hospitals and Clinics generally requires that we document in your medical record chart that you are participating in this study. The information included in the chart will provide contact information for the research team as well as information about the risks associated with this study. We will keep this Informed Consent Document in our research files; it will not be placed in your

medical record chart.

WILL MY HEALTH INFORMATION BE USED DURING THIS STUDY?

The Federal Health Insurance Portability and Accountability Act (HIPAA) requires the University of Iowa Health Care or the Iowa City VA Medical Center to obtain your permission for the research team to access or create "protected health information" about you for purposes of this research study. Protected health information is information that personally identifies you and relates to your past, present, or future physical or mental health condition or care. We will access or create health information about you, as described in this document, for purposes of this research study and for your treatment. Once the University of Iowa Health Care or Iowa City VA Medical Center has disclosed your protected health information to us, it may no longer be protected by the Federal HIPAA privacy regulations, but we will continue to protect your confidentiality as described under "Confidentiality."

We may share your health information related to this study with other parties including federal government regulatory agencies, the NIH/OBA, the DOD, the University of Iowa Institutional Review Boards and support staff.

You cannot participate in this study unless you permit us to use your protected health information. If you choose *not* to allow us to use your protected health information, we will discuss any non-research alternatives available to you. Your decision will not affect your right to medical care that is not research-related. Your signature on this Consent Document authorizes the University of Iowa Health Care to give us permission to use or create health information about you.

Although you may not be allowed to see study information until after this study is over, you may be given access to your health care records by contacting your health care provider. Your permission for us to access or create protected health information about you for purposes of this study has no expiration date. You may withdraw your permission for us to use your health information for this research study by sending a written notice to David M. Lubaroff, PhD, Department of Urology, 200 Hawkins Drive, Iowa City, IA 52242. However, we may still use your health information that was collected before withdrawing your permission. Also, if we have sent your health information to a third party, such as the study sponsor, or we have removed your identifying information, it may not be possible to prevent its future use. You will receive a copy of this signed document.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

WHAT IF I DECIDE TO DROP OUT OF THE STUDY?

If you decide to stop participating in the study, we would like to continue to obtain follow-up information about your health through contact with your other physicians and/or periodic phone calls to you from our research staff, unless you notify us otherwise. An important follow-up visit will be 30 days after your last injection. Even if you decide not to continue participating in the study we would like you to keep this appointment.

WILL I RECEIVE NEW INFORMATION ABOUT THE STUDY WHILE PARTICIPATING?

If we obtain any new information during this study that might affect your willingness to continue participating in the study or directly affect your continued health, we will promptly provide you with that information.

CAN SOMEONE ELSE END MY PARTICIPATION IN THIS STUDY?

Under certain circumstances, the researchers or the study sponsor might decide to end your participation in this research study earlier than planned. This might happen for any one or more of the following reasons: (a) in our judgment it would not be safe for you to continue, (b) because your condition has become worse, or (c) because funding for the research study has ended.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: David Lubaroff at (319) 335-8425, Dr. Daniel Vaena (319) 356-2757 of the Department of Internal Medicine Hematology/Oncology or Dr. James Brown (319) 356-2273 of the Department of Urology. If you are calling after hours please call 319-356-1616, ask for the Urology Resident or Oncology Fellow on call and tell the operator you are a research subject.

If you have questions, concerns, complaints about your rights as a research subject or about research related injury, please contact the Human Subjects Office, 105 Hardin Library for the Health Sciences, 600 Newton Road, Iowa City, Iowa, 52242-1098, (319) 335-6564, or e-mail irb@uiowa.edu. General information about being a research subject can be found by clicking “Info for Public” on the Human Subjects Office web site, http://research.uiowa.edu/hso.

FOR IRB USE ONLY
APPROVED BY: IRB-03
IRB ID #: 200605706
APPROVAL DATE: 12/10/13
EXPIRATION DATE: 08/19/14

This Informed Consent Document is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by signing this Informed Consent Document. Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a copy of this form.

Subject's Name (printed): _____

Do not sign this form if today's date is on or after EXPIRATION DATE: 08/19/14.

_____ _____
(Signature of Subject) (Date)

Permanent Address (printed): _____

_____

Statement of Person Who Obtained Consent

I have discussed the above points with the subject or, where appropriate, with the subject's legally authorized representative. It is my opinion that the subject understands the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)